Increasing the accuracy for endoscopic detection of early Barrett neoplasia, by adding probe-based confocal laser endomicroscopy to endoscopic tri-modal imaging: A feasibility study on Endoscopic Quad-Modal Imaging (EQMI)

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

Summary

ID

NL-OMON33330

Source
ToetsingOnline

Brief title
EQMI-study

Condition

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

Synonym
(1) Barrett esophagus; (2) early esophageal neoplasia

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Barrett esophagus, Barrett neoplasia, Confocal laser endomicroscopy., Endoscopy

Outcome measures

Primary outcome

Study Phase 1:

(1) Correlation of the real-time NBI evaluation with histological outcome;

(2) Correlation of the real-time pCLE evaluation with histological outcome;

(3) Reduction of the false positive rate of WLE and AFI with NBI;

(4) Reduction of the false positive rate of WLE and AFI with pCLE.

Study Phase 2:

(1) Number of endoscopic resection specimens containing early neoplasia (i.e.

HGIN/EC) upon histological evaluation;

(2) Number of endoscopic resection specimens without early neoplasia upon

histological evaluation;

(3) Number of biopsies from areas graded as negative or indefinite upon

endoscopy, containing early neoplasia upon histological evaluation.

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 endoscopic quad-modal imaging (EQMI) a fourth imaging technique is added to ETMI: probe-based confocal laser endomicroscopy (pCLE), a new endoscopic imaging technique that allows for real-time histological evaluation of the mucosa. pCLE evaluation of AFI+ areas may be a better approach to reduce the high AFI false positive rate compared to NBI inspection. Furthermore, since it provides images equivalent with histology, pCLE may allow real-time decision making, e.g. by immediately removing lesions suspicious for early neoplasia by endoscopic resection instead of obtaining biopsies and waiting for the outcome of the histological evaluation before making a decision.

Study objective

In patients with BO undergoing surveillance or work-up endoscopy for early neoplasia, we aim to evaluate if EQMI, consisting of ETMI combined with pCLE, increases the accurary of detecting early neoplasia (study phase 1).
In addition, we aim to determine if real-time pCLE inspection followed by immediate endoscopic resection of lesions suspicious for early neoplasia, may be a valid and safe alternative to the current standard of obtaining biopsies and awaiting histological evaluation before scheduling an endoscopic resection (study phase 2).

Study design

For this prospective international multicenter study (Amsterdam, Nottingham, München, Jacksonville), a total of 60 patients 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. AFI-positive lesions are marked with argon plasma coagulation and further inspected with NBI and, after intravenous administration of 2.5ml fluorescein (10%), with pCLE. During NBI and pCLE areas are classified as 'suspicious for neoplasia', 'normal', or 'indefinite'.
During phase 1 of this study, all marked areas are sampled by two biopsies for histological correlation.
During phase 2 of this study, all areas that are graded as neoplastic with pCLE will be immediately removed by endoscopic resection whereas areas graded as normal or indefinite will be sampled by 2 biopsies, for histological correlation.

All biopsy and endoscopic resection specimens 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 pCLE for optical histopathology 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.

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 2 cm;
- BO without dysplasia or with LGIN (i.e. surveillance patients) or patients with BO referred for endoscopic work-up of HGIN/early cancer;
- Signed informed consent.

Exclusion criteria

- Prior history of surgical or endoscopic treatment of esophageal neoplasia;
- Presence of erosive oesophagitis (Los Angeles classification *B);
- Inability to obtain biopsies or to perform an endoscopic resection (e.g. due to anticoagulation, coagulation disorders, varices);
- Contraindication for fluorescein administration (e.g. allergy, pregnancy, beta-blocker use);
- 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):	01-01-2010
Enrollment:	15
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

No registrations found.

In other registers

Register	ID
CCMO	NL27455.018.09