Early detection of Barrett's esophagus and esophageal cancer: accuracy and acceptability of a novel screening strategy in primary care.

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To determine the accuracy and acceptability of a minimal-invasive screening strategy (breath testing (eNose) followed by unsedated transnasal endoscopy (uTNE)) for Barrett*s esophagus (BE) and esophageal adenocarcinoma (EAC).

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

Summary

ID

NL-OMON49567

Source
ToetsingOnline

Brief title
Early detection Barrett's esophagus and esophageal cancer in primary care.

Condition

- Malignant and unspecified neoplasms gastrointestinal NEC

Synonym
Barrett's esophagus, esophageal adenocarcinoma, Esophageal cancer

Research involving
Human

Sponsors and support

Primary sponsor: Radboud Universitair Medisch Centrum

Source(s) of monetary or material Support: MLDS

Intervention

Keyword: Barrett, esophageal cancer, primary care, screening

Outcome measures

Primary outcome

Main study parameter / endpoint: accuracy (PPV, NPV, sensitivity, and specificity) of the eNose for detecting confirmed BE with the diagnosis made by transnasal endoscopy and upper endoscopy as the reference standard in primary care.

Gold standard: transnasal endoscopy and upper endoscopy.

Secondary outcome

Secondary study parameters / endpoints:

- Patient acceptability of the eNose, the uTNE and if applicable the upper endoscopy (i.e. test experience) (directly after procedure)
- Willingness to undergo repeat procedure (directly after procedure)
- CWS-8 (at baseline, 7 days and 30 days after procedure and 90 days after the last study procedure (i.e. uTNE or if applicable the upper endoscopy))
- STAI-6 (at baseline, 7 days and 30 days after procedure and 90 days after the last study procedure (i.e. uTNE or if applicable the upper endoscopy))
- IES-15 (7 days and 30 days after procedure and 90 days after the last study procedure (i.e. uTNE or if applicable the upper endoscopy))
- Endoscopic findings, procedure yield, defined as the proportion of patients found to have Barrett*s esophagus or (early stage) esophageal cancer, or

another finding

- Rate of successful intubation and complete evaluation by uTNE

- Safety of the eNose breath test and uTNE (Adverse Events)

- Reproducibility of a positive breath test

- Number of confirmed diagnoses of Barrett*s esophagus (defined as >1cm of columnar metaplasia combined with the presence of intestinal metaplasia on biopsies)

- Rate and quality of successful biopsies taken by uTNE (number, size, and quality of biopsies sufficient for histologic diagnosis)

Other study parameters:

Demographics: gender, age, civil status, employment status, social status, BMI, waist circumference.

General medical history: hypertension, cardiovascular, pulmonary, hepatic, diabetes, GERD symptoms, malignancies, infectious diseases and medication use (including heartburn medication).

Alarm symptoms: hematemesis, melena, weight loss, fever.

Lifestyle factors: tobacco use, alcohol use, physical activity, diet.

Endoscopic and histologic diagnosis: Prague classification (length of BE),

presence of esophagitis, hiatal hernia or dysplasia, other conditions.

Family history: number of first-grade relatives with BE or EAC.

Test characteristics: testing room, time of the day.

Study description

Background summary

The ongoing increasing incidence of esophageal adenocarcinoma (EAC) in the Netherlands during the last few decades and the still dismal prognosis has stimulated interest in screening for Barrett*s esophagus (BE). Although BE is a known precursor of EAC, a minority of patients with EAC (<10%) are known with a previous diagnosis of BE, and hence, most cases of BE are undiagnosed. Screening programs to detect BE followed by endoscopic surveillance and treatment of dysplasia or early neoplasia seem able to reduce the incidence of EAC and improve survival. A non-invasive screening tool, such as breath testing, could select patients at risk for BE, after which unsedated transnasal endoscopy (uTNE) can confirm or exclude the diagnosis. uTNE offers the possibility of a more acceptable and accurate endoscopic assessment of the esophagus with almost neglectable risks and lower costs compared to conventional endoscopy.

Study objective

To determine the accuracy and acceptability of a minimal-invasive screening strategy (breath testing (eNose) followed by unsedated transnasal endoscopy (uTNE)) for Barrett*s esophagus (BE) and esophageal adenocarcinoma (EAC).

Study design

The current study will be a mono-site cohort study in the Netherlands to assess the accuracy of exhaled VOCs analysis using an electronic nose device for the detection of BE the and acceptability of an invitation for the eNose breath test followed by uTNE with biopsy sampling. Eligible patients will be invited to undergo a breath test followed by unsedated transnasal endoscopy.

Baseline visit and breath test in general practice:
After completing these questionnaires, patients will be asked to deliver a

breath sample by in- and exhaling through the eNose (a handheld device of 650 gram) for 5 minutes. A nose clip will be used to prevent the entry of non-filtered air and patients will be instructed to enclose the mouthpiece with their mouth at all times.

Within 30 minutes after the breath test, patients will fill out a Numeric Pain Rating Scale (NPRS) to measure the degree of pain, anxiety and discomfort (0 being *none* and 10 being *severe*). A Numeric Pain Rating Scale (NPRS) is also used to measure the acceptability of the breath test (0 being *the worst experience*, 5 being *neither pleasant nor unpleasant* and 10 being *the best experience*). Additionally, the willingness to undergo a future repeat breath test will be asked.

uTNE in hospital (follow-up visit):
Subsequently 3 weeks after the breath test, patients will be invited to undergo an uTNE performed by an experienced endoscopist in the hospital. It is a safe and well tolerated procedure that can be performed under local anesthesia. Prior to the uTNE, possible adverse events will be assessed by direct observation and patient interviews. Also, concomitant therapies will be reviewed. Within 30 minutes after the uTNE, patients will fill out a Numeric Pain Rating Scale (NPRS) to measure the degree of pain, anxiety and discomfort (0 being *none* and 10 being *severe*). A Numeric Pain Rating Scale (NPRS) is also used to measure the acceptability of the uTNE (0 being *the worst experience*, 5 being *neither pleasant nor unpleasant* and 10 being *the best experience*). Additionally, the willingness to undergo a future repeat uTNE will be asked.

Follow-up questionnaires after breath test and uTNE:
7 days after the breath test and 7 and 30 days after the uTNE, patients will be sent an email with a link to additional questionnaires. These questionnaires are the Spielberger State-Trait Anxiety Inventory (STAI-6), the Cancer Worry Scale (CWS-8) and the Impact of Event Scale (IES-15).26-31 Also, 7 days after the uTNE, possible (severe) adverse events will be assessed and concomitant therapies will be reviewed via a telephone call. A patient is considered lost to follow-up if at least two attempts to contact the patient have been done.

Study burden and risks

Participants who provide informed consent will undergo a 5-minute breath measurement followed by unsedated transnasal endoscopy. No health care risks are associated with performing the breath test. Transnasal endoscopy is a safe and well tolerated procedure that can be performed under local anesthesia. Complications (epistaxis (1-2%) and vasovagal reaction (0.3%)) are infrequent and mostly self-limiting. Upper endoscopy is commonly performed and carries a low risk of adverse events. Several studies have shown that the risk of complications during endoscopy is indeed extremely low. In addition to the health-related burden, participating in this study could have a psychological

impact in terms of overdiagnosis and overtreatment. All data will be anonymized, refusal to participate in the study or desire to withdraw from this research will not lead to any difference for the participant in question. The expected benefits of this study are possibly high as this novel non-invasive screening device proves to be applicable in daily clinical practice. Furthermore, screening could identify a significant number of abnormalities that might have otherwise gone undetected until further progression of disease.

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

- Patient aged 50 to 75 years;
- Recorded diagnosis of reflux symptoms >90 days OR
- Recorded prescriptions for acid suppressant therapy for this indication for

at least 1 year in the past 5 years;
- Written informed consent.

Exclusion criteria

- Upper endoscopy in the previous 5 years;
- A current or previous diagnosis of any type of malignancy (not including basal-cell skin cancer (BCC) and squamous-cell skin cancer (SCC));
- Already known with a diagnosis of Barrett*s esophagus;
- Any argument provided by a patient*s own general practitioner not to include the patient;
- Comorbidities precluding transnasal endoscopy (e.g. inability to discontinue oral anticoagulants, history of recurrent epistaxis, allergy to lidocaine derivatives).

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	20-04-2021
Enrollment:	450
Type:	Actual

Medical products/devices used

Generic name:	Aeonose
Registration:	Yes - CE intended use

Ethics review

Approved WMO Date:	23-11-2020
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	04-01-2021
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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	NL74859.091.20