The rate of developing a biopsy-bases diagnosis of High-Grade Dysplasia or Esophageal Adenocarcinoma in patients with Barrett*s esophagus, after an extensive baseline evaluation with random biopsies and Wide Area Transepithelial Sample Esophageal brush combined with Computer Assisted 3-Dimensional Tissue Analysis (WATS3D): The WATS-EURO2 Pilot study;The WATS-EURO2 Pilot study

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To assess the feasibility of our study logistics and infrastructure, sample processing and online study database.

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

Summary

ID

NL-OMON54901

Source
ToetsingOnline

Brief title
The WATS-EURO2 pilot study

Condition

- Malignant and unspecified neoplasms gastrointestinal NEC

Synonym
Barrett's esophagus, dysplasia

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: Onderzoeksgroep

Intervention

Keyword: Barrett's esophagus, Progression, Random biopsies, WATS3D brush

Outcome measures

Primary outcome

-The rate of patients with successful inclusion per center and per inclusion day

-The rate of patients with successful data and sample collection per center and

per inclusion day

-The rate of patients with successful data and sample storage per center and

per inclusion day

Secondary outcome

-The rate of WATS brushes with sufficient material for an adequate diagnosis

-The proportion of patients developing HGD/EAC in BE patients after endoscopic

removal of visible lesions/or after a confirmed diagnosis of LGD

-The concordance/discordance for the diagnosis HGD/EAC between random biopsies and WATS brushing collected at the baseline endoscopy and follow-up endoscopies.

-The rate of progression to HGD/EAC as diagnosed on endoscopic biopsies (targeted or random) or endoscopic resection specimens during a maximum follow-up of 3 years, after a baseline WATS-positive-biopsy negative diagnosis for HGD/EAC.

-Reproducibility of a positive diagnosis for HGD or cancer in WATS samples on subsequent follow up endoscopies.

Study description

Background summary

Patients with BE are kept under endoscopic surveillance, since early detection of esophageal adenocarcinoma (EAC) significantly improves the prognosis compared to late detection. Current endoscopic surveillance strategies rely on random sampling, which is time-consuming and has an inevitable risk for significant sampling error. The WATS-3D brush samples a much wider area of the esophageal epithelium, and prior studies have suggested that it detects more dysplasia. However, the clinical value of these WATS-positive-biopsy-negative cases is unknown. Ultimately, we aim to study the rate of developing a biopsy-based diagnosis of HGD/EAC in Barrett*s patients at high risk of progression (i.e. after endoscopic removal of visible lesions containing HGD/EAC and/or a diagnosis of LGD) as well as in patients in a standard Barrett*s surveillance program, in a large European multicenter, prospective study. In these patients we will combine biopsy sampling with WATS brushing at baseline and all follow-up endoscopies. This will allow us to study the natural history of WATS-positive-biopsy-negative case and of WATS-specific outcomes such as Basal-crypt dysplasia.
Prior to starting this large study, we first want to perform a pilot study to assess the feasibility of our study infrastructure, sample processing and online study database to optimize the final study.

Study objective

To assess the feasibility of our study logistics and infrastructure, sample processing and online study database.

Study design

This is an investigator initiated, multicenter, prospective, pilot study in 5 centers with a tertiary referral function for detection and treatment of early Barrett*s neoplasia.

Study burden and risks

Our study population consists of patients with either a flat Barrett's esophagus (BE) with low grade dysplasia (LGD) or high grade dysplasia (HGD) or a flat BE after removal of visible lesions with LGD, HGD or early carcinoma. At baseline, an imaging endoscopy will be performed and after confirmation of absence of visible lesions, WATS brushing of the Barrett*s segment will be performed followed by random 4 quadrant mucosal biopsies every 2 cm. If the biopsies subsequently show HGD or esophagus adenocarcinoma (EAC), the patient has reached the study endpoint and will be managed according to the institution*s standard of care. If the baseline biopsies show LGD, indefinite (IND) or non dysplastic BE, patient will not undergo ablation therapy and will be scheduled for endoscopic follow-up. In case of prior endoscopic resection for a visible lesion containing HGD/EAC the follow-up schedule consists of endoscopies at 3, 6, 9, 12, 18, 24 and 36 months. For patients with a referral diagnosis of LGD, the follow-up consists of endoscopies at 6 and 12 months and annually thereafter

It is undisputed that patients referred with LGD, HGD or early cancer should have all visible lesions removed by ER techniques. In general, the endoscopic resection specimen will then show a diagnosis of HGD or early cancer. Follow-up studies have shown that the chance of the development of metachronous HGD/EAC in the remaining BE segment is about 10% per year. Therefore ablation therapy is advised for the remaining BE segment. The same 10% annual progression rate to HGD/EAC applies for patients with a confirmed diagnosis of LGD. For this category guidelines suggest that ablation therapy may be indicated for cases in which this diagnosis, apart from being confirmed by an expert pathologist, is also reproduced in subsequent endoscopies. The actual decision to ablate the remaining segment after endoscopic resection of HGD/EAC or to prophylactically ablate for LGD, is made on a per patient basis in which age and comorbidity are important factors to regard. Follow-up studies after ER of visible lesions containing HGD/EAC have found that metachronous lesions are found to be endoscopically treatable with the majority of patients not developing recurrent disease. The same holds for prophylactic ablation in cases with LGD: a

significant proportion of patients will not progress or not even manifest their baseline diagnosis of LGD upon follow-up. In the SURF-study, 30% of the LGD-patients randomized to endoscopic surveillance did not have their LGD diagnosis reproduced during 4 subsequent endoscopies in 3-years follow-up and all cases that progressed to HGD/EAC were diagnosed at an endoscopically curable stage.
Furthermore, RFA still is accompanied by complications such as esophageal stenosis and requires multiple hospital visits. Even upon complete endoscopic eradication of all Barrett*s mucosa, guidelines still dictate endoscopic surveillance after ablation virtually at the same frequency as for Barrett*s cases that are not prophylactically treated.
Therefore, keeping Barrett*s patients under strict endoscopic surveillance after ER of visible lesions or for flat LGD is a very acceptable treatment strategy that does not divert from current guidelines.

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

Inclusion criteria:
- Patients age: >= 18 years
- Willingness to undergo both WATS and random forceps biopsies while undergoing conven-tional EGD with sedation
- Ability to provide written, informed consent (approved by IRB and (biobank committee)) and understand the responsibilities of trial participation
- BE with a circumferential extent of >=2cm, or a maximum extent of >=4cm, and a total maxi-mum extent of <=18cm (in case of prior ER: BE length after ER)
- Cohort 1: Patients referred for work-up of LGD, HGD or low-risk cancer (m1 to sm1, with-out lympho-vascular invasion and poor differentiation), either diagnosed in random biopsies or in prior endoscopic resection specimen
- Cohort 2: Patients with known, non-dysplastic BE enrolled in endoscopic surveillance programs

Exclusion criteria

Exclusion criteria
- Patients with visible lesions according to the Paris classification at the time of the WATS and random biopsy testing (prior endoscopic resection is allowed)
- Patients with high-risk cancer after endoscopic resection: either sm2/3 invasion, poor dif-ferentiation, lympho-vascular invasion, or R1 vertical resection margin
- Patients within six weeks of receiving targeted forceps biopsies and/or ER
- History of esophageal or gastric surgery other than Nissen fundoplication
- History of esophageal ablation therapy
- Coagulopathy with INR >2.0, thrombocytopenia with platelet counts < 50,000
- Subject has a known history of unresolved drug or alcohol dependency that would limit ability to comprehend or follow instructions related to informed consent, post-treatment in-structions, or follow-up guidelines

Study design

Design

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

Control:	Uncontrolled
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	22-07-2020
Enrollment:	180
Type:	Actual

Ethics review

Approved WMO Date:	19-03-2020
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	12-11-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	18-06-2021
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

ID: 24680
Source: NTR

Title:

In other registers

Register	ID
CCMO	NL71034.018.19
Other	Volgt