Proteomics in Early Neoplasia in Barrett*s Esophagus: Biomarkers for Early Detection.

Published: 16-06-2011
Last updated: 27-04-2024

To compare the protein profile of Barrett*s mucosa with and without early neoplasia in ER specimens in epithelial and stroma aiming to identify a biomarker indicating presence of early neoplasia in BE.

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

Summary

ID

NL-OMON36814

Source
ToetsingOnline

Brief title
Proteomic ER specimen

Condition

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

Synonym
Barrett's esophagus, cancer

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's esophagus, Biomarker, Dysplasia, Proteomics

Outcome measures

Primary outcome

- Identification of peptides and proteins that may indicate the presence of

early neoplasia in Barrett*s.

Secondary outcome

- Number of proteins found per cell surface area;

- Differences and similarities in protein profiles of 10 dysplastic versus 10

non-dysplastic specimens in 1) epithelial and 2) stromal cells;

Study description

Background summary

The incidence of esophageal adenocarcinoma (EAC) has increased almost fourfold in the last three decades. At a symptomatic stage, EAC carries a poor prognosis. At this stage the tumor can only be cured by extensive surgical treatment, which has a mortality rate of 3-5% and a morbidity rate of 30-50%. Furthermore, at the time of diagnosis 50% of patients are found to have local irresectable disease, distant metastases or poor general condition, making them not eligible for curative treatment. Presence of Barrett*s esophagus (BE) is the most important risk factor for developing EAC. In BE, the epithelium of the distal esophagus has been replaced by columnar epithelium containing specialized intestinal metaplasia, due to chronic gastro-esophageal reflux. Malignant transformation of BE into EAC is a gradual progress, which may take up to several decades. Progression into cancer is through the histopathological stages classified as no dysplasia, low-grade dysplasia and high-grade dysplasia. In order to detect malignant progression of BE at an early and curable stage, regular endoscopic surveillance is indicated in patients with BE. Studies have shown that patients with a BE in whom the cancer is diagnosed while under surveillance have an excellent prognosis.

In the USA the costs of Barrett*s surveillance are estimated at 290 million dollars annually, the annual Dutch costs are estimated at approximately

¤4,000,000 with approximately 8,000 gastroscopies per year. Beside the high annual costs of endoscopic surveillance, endoscopy is uncomfortable for the patient. A less invasive, less costly diagnostic test would be of great value. Analysis of protein profiles for example in serum or tissue of patients using mass spectrometry, potentially has the ability to detect specific profiles that can be used as a high-throughput diagnostic test, which could be an alternative for endoscopic surveillance and potentially even for Barrett's screening.

To obtain more information on which proteins should be looked for in the serum, the tissue protein profile of Barrett*s mucosa with and without early neoplasia (HGD and carcinoma tissue with or without early neoplasia. Mass spectrometry (MS) coupled with
Liquid Chromatography (LC) of epithelial has proven a valuable tool in proteome exploration of tissue. A drawback of the technique is that lower abundant proteins often remain undetected in complex protein samples. One approach to look more specific and deeper into tissue proteomes is by selective sampling of distinct cell types by Laser Captured Microdissection (LCM). A pilot study was performed on non-dysplastic biopsies, to assess the feasibility of the current study. This approach resulted in high numbers of protein and peptide identifications in biopsies, with good reproducibility of the detected differences between epithelial and stromal cells.

Study objective

To compare the protein profile of Barrett*s mucosa with and without early neoplasia in ER specimens in epithelial and stroma aiming to identify a biomarker indicating presence of early neoplasia in BE.

Study design

To be able to investigate a larger amount of neoplastic cells in the current study, we will use endoscopic resection (ER) specimens instead of biopsy specimens, for the following reasons: 1) an ER specimen will contain more early neoplastic cells for research than biopsies, 2) ER specimens are larger than biopsies, therefore orientation of the frozen sample before cutting is possible; orientation enables better histopathological assessment. This is important for frozen samples in particular because histopathological assessment of frozen tissue is complicated by freeze artifacts.

This non-randomized study includes two patient groups, each with 10 consecutive patients. Protein profiles of Barrett*s mucosa of patients with early neoplasia and without any dysplasia are compared on the epithelial and stromal level using mass spectrometry. Patient recruitment and sample collection will be performed at the AMC in Amsterdam. Samples will be processed and analyzed in the EMC Rotterdam at the Netherlands Proteomics Center.

Study burden and risks

In the non-dysplastic group, a regular follow-up endoscopy will be performed, with standard biopsy sampling. General risks associated with a gastroscopy are: mild irritation of the throat due to introduction of the endoscope, difficulties swallowing and retrosternal pain. 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.

Participation of patients in the dysplastic group does not contain any additional risks, given the fact that these patients undergo an endoscopic resection as a regular therapy for carcinoma or high-grade dysplasia.

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 *dysplastic* group:
- Scheduled ER for Barrett*s esophagus containing HGD or early cancer;
- Review of biopsies and histopathology specimens by an expert local pathologist;
- Written informed consent;Inclusion criteria *non-dysplastic* group:
- Scheduled surveillance endoscopy for Barrett*s esophagus without dysplasia;
- No dysplasia in biopsies, or biopsies *indefinite for dysplasia* during at least the last two years;
- No visible abnormalities in Barrett*s esophagus in the two most recent surveillance endoscopies;
- Review of biopsies and histopathology specimens by an expert local pathologist;
- Written informed consent

Exclusion criteria

Exclusion criteria *dysplastic* group:
- In case histopathological assessment of the frozen half of the ER specimen is necessary for clinical decision making, the specimen will be retrieved from the Barrett*s research tissue bank and further processed for clinical care.;Exclusion criteria *non-dysplastic* group:
- Patients that are not suitable candidates for ER because of co-morbidity;

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Other

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	10-06-2011

Enrollment:	20
Type:	Actual

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	NL35326.018.11