Adipokines gene expression in visceral adipose tissue in patients with esophageal adenocarcinoma

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The purpose of this study is to investigate the role of adipokines-secretion in visceral adipose tissue and its influence on the risk for esophageal adenocarcinoma. Examination of adipose tissue may provide important insight into mechanistic links...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Metabolism disorders NEC
Study type	Observational invasive

Summary

ID

NL-OMON36786

Source
ToetsingOnline

Brief title
Adipokines gene expression in esophageal adenocarcinoma

Condition

- Metabolism disorders NEC
- Gastrointestinal neoplasms malignant and unspecified

Synonym
esophageal adenocarcinoma (cancer of the esophagus) and obesity

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: esophageal adenocarcinoma, gene expression, obesity, risk factors

Outcome measures

Primary outcome

Collected samples will be immediately frozen in liquid nitrogen and stored at -80°C until total RNA preparation.

Total RNA will be extracted from adipose tissue and expression levels of the genes of interest are quantified with real-time-quantitative-PCR (RTq-PCR). We will use at least 2 housekeeping genes as an endogenous reference to compensate for variations in input RNA amounts.

Secondary outcome

Dependent on the results of our study on gene expression we will possibly measure the size of adipocytes in those 2 groups later in this study.
Previously validated methods include: direct microscopy and manual/automated measurement of diameters from digital images.

Influence of other patient characteristics on adipokines production/development of cancer:
Patient information on prior weight loss, tumor stage and chronic diseases will be collected from the hospital information system and preoperative status.

Other study parameters:
Patient information on smoking, alcohol use, use of PPI and LES-relaxing and other drugs, history of reflux, DM, preoperative plasma-glucose-values as well

as levels of HbA1c, cholesterol, triglycerides, CRP etc. will be collected from

the patients* charts/ Elpado hospital information system if available.

Study description

Background summary

In the last 3 decades the incidence of esophageal adenocarcinoma has been increasing rapidly in the United States and western Europe. Recent reviews showed that being overweight or obese (BMI of > 25 kg/m2 or > 30kg/m2 resp.) is associated with an approximately 2-fold increase of risk for esophageal adenocarcinoma compared to individuals with normal weight.
It is known that high BMI and abdominal fat are related to gastro-esophageal reflux disease (GERD) and Barrett*s disease. Especially visceral adipose tissue seems to play an important role as a risk factor in this context. It has been found to be larger in individuals that develop Barrett's disease than in a control population.
The exact mechanism of the effect of visceral obesity on the development of Barrett's and as a consequence adenocarcinoma still remains unclear. Increased intragastric pressure and GE-pressure gradient probably play a role in this context but don*t explain all the risk.
Another possible explanation could lie in adipose tissue itself. Adipose tissue functions as both an energy store and an active endocrine organ. It secretes a range of hormones, growth factors, enzymes, cytokines, matrix proteins and complement factors (collectively termed adipokines), among them leptin, adiponectin, Interleukin-1, -6, -8, -10 and TNF-α. Visceral fat is known to be more metabolically active than subcutaneous fat and alterations in serum level of adipokines have been linked with several cancers. Adipokines also seem to have a local effect on Barrett*s carcinogenesis.

Study objective

The purpose of this study is to investigate the role of adipokines-secretion in visceral adipose tissue and its influence on the risk for esophageal adenocarcinoma. Examination of adipose tissue may provide important insight into mechanistic links for the observed association between higher body fat and risk of esophageal cancer. Esophageal adenocarcinoma still has a 5-year survival rate of only about 15% because patients usually present late when already in advanced stages. It is therefore important to identify the risk factors for this cancer and detect subjects with a higher risk earlier.

Primary Objective:
Is there a difference in gene expression of adipokines in omental fat tissue in

subjects with esophageal adenocarcinoma compared to subjects without Barrett*s disease or cancer, independent of BMI?

Possible secondary Objectives:
Does the size of omental adipocytes differ between the 2 groups? Does the size have an influence on gene expression of adipokines and is there a difference between the two groups?
Which patient characteristics (i.e. smoking, prior weight loss, tumor stage etc) have an effect on the relation between adipokines production in fat tissue and the development of esophageal adenocarcinoma?

Study design

This will be a pilot study with the design of a case-control study.
Cases and controls will be matched for sex and BMI.

Study burden and risks

The additional risk arising from this study is negligible for the patient.
By removing a small amount of fat tissue during surgery minor bleeding can occur but those bleedings can be treated easily and directly.
The operation will not be prolonged through this procedure and neither will the hospital stay of the patients. No control visits will be necessary besides the ones related to the patients' 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

Patients with newly diagnosed esophageal adenocarcinoma who are referred to surgery at the Erasmus Medical Center will be included in our study. Sex- and BMI-matched patients who are referred for surgery at the Erasmus Medical Center for other reasons than esophageal cancer/ Barrett*s disease/GERD will be included as controls.

Exclusion criteria

- Patients with severe weight loss (>10% during the last 3 months before surgery)
- Patients without information on height and weight at the time of surgery
- Patients with a BMI < 20
- Patients with severe co-morbidities or diseases with a possible effect on body weight and/or fat distribution
- Patients in the control group with a history of Barrett*s esophagus/GERD

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	05-10-2010
Enrollment:	60
Type:	Actual

Ethics review

Approved WMO

Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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	NL32476.078.10