

ESGE STUDY EUROBA

EVOLUTIVITY OF SHORT SEGMENT BARRETT ESOPHAGUS (TONGUE)

Introduction

Barrett's esophagus (BE) is an acquired condition in which the normal squamous epithelium of the esophagus is replaced by a metaplastic columnar lining. This change is strongly related to chronic gastroesophageal reflux. BE predisposes to malignancy and is associated with a risk of esophageal adenocarcinoma. Recent data indicate that the median incidence of adenocarcinoma in patients with BE is about 1 cancer per 200 patient-years of follow-up.

Two different endoscopic patterns of BE have been described: long-segment BE, in which the salmon-colored glandular epithelium extends 3cm or more proximally from the esogastric junction, short-segment BE in which the metaplastic epithelium projects less than 3cm from the esophagogastric junction. The length of the columnar-lined epithelium is statistically significantly increased in patients with adenocarcinoma compared to patients without: the risk of progression to adenocarcinoma is thus considered to be lower in short segment BE than in long segment BE.

However the incidence of adenocarcinoma located at the cardia is increasing in occidental countries and the studies focused on the carcinomatous risk of short segment BE are scarce and include small cohort of patients: Sharma et al. followed up 32 patients with short segment BE on a mean period of 37 months. 3 patients developed a low grade dysplasia and 2 a high grade dysplasia (6%). Rudolph et al. conducted the same study on a series of 83 patients (mean follow-up: 36 months): incidence of high grade dysplasia or cancer was 2.5%. Finally, in both studies, the risk of cancer is not different from the risk reported in series with long segment BE. At least, it appeared that the risk with short segment BE and especially with tongue of BE has not been specifically studied in a large multicenter cohort study.

2- Study description

a) Study design

Phase II study

b) Study duration

Estimate duration of recruitment of 12 months

Follow-up: 8 years

3-Purpose

To determine the optimal surveillance program for patients presenting with Barrett esophagus without and with low grade dysplasia

4-Endpoints

a) Primary endpoint

Incidence rate of high grade dysplasia or carcinoma in patients with BE of 3 cm or less (short-segment (SS) BE) and with a tongue pattern.

b) Secondary endpoints

Incidence rate of low grade dysplasia in patients with SS BE (tongue) without dysplasia

Incidence rate of high grade dysplasia or carcinoma in patients with SS BE (tongue) and low grade dysplasia

c) Covariate factors

Role of the following items on incidence rate of high grade dysplasia or carcinoma in patients with SS BE (tongue):

- age
- gender

- weight
- BMI
- Medication, i.e., protonpump inhibitors, aspirin/NSAID
- tobacco and alcohol abuse
- history of cholecystectomy
- Pattern of ultrashort BE: tongues, circular
- number of BE tongues
- length of SS BE
- family history of BE

5-Enrolment criteria

a) Inclusion criteria

Barrett :

Endoscopic and histological diagnosis of BE : presence of intestinal metaplasia at the lower part of the esophagus

Minimal length of BE (ultrashort BE): 5mm

Maximal length of BE: 3cm

Absence of high grade dysplasia or carcinoma on histology

Absence of ulcer, nodule or stenosis on the BE

Absence of previous endoscopic or surgical treatment of the BE

Absence of previous endoscopic or surgical treatment of hiatal hernia or gastroesophageal reflux

Patient :

Age : 18-75 years

Expected life survival > 5 years

Absence of life threatening disease

Absence of participation to another study

b) Exclusion criteria

Barrett :

Minimal length of BE (ultrashort BE) < 5mm

Circumferential BE

High grade dysplasia or carcinoma on histology

Ulcer, nodule or stenosis on the BE

History of gastric or esophageal carcinoma

History of duodenal ulcer

History of portal hypertension

Previous endoscopic or surgical treatment of the BE

Previous endoscopic or surgical treatment of hiatal hernia or gastroesophageal reflux

Coagulation abnormalities (coagulopathies, drug-related...)

Patient :

Age < 18 or > 75 years

Expected life survival < 5 years

Life threatening disease

Participation to another study

6- Calculation of number of patients to be included and followed-up

The statistical analysis is based on the publication of Sharma et al. who observed an incidence rate of 2% of high grade dysplasia and carcinoma in patients with SSBE.

For a similar study, but with a follow-up of 8 years, the cumulated rate of the event is 0.12.

The probability to observe the event prior 8 years is 0.11 ($1 - \exp(-0.12)$) For an accuracy of 15%, the number of patients to be followed up on 8 years is 410. Taken into account 10% of patients lost during the follow-up, 456 patients have to be recruited.

7- Study plan

a) Selection of participating centers

b) Preinclusion endoscopic assessment

Patients without dysplasia will have a first assessment by the investigators prior inclusion. Patients with low grade dysplasia will have two examinations at 3-6 months interval. During this period, the patients will be treated using standard doses of PPI.

c) Patient inclusion

d) Frequency of endoscopic assessment

Patients with no dysplasia : endoscopy at 2 years, 5 years and 8 years

Patients with low grade dysplasia : endoscopy every one year

The patients initially without dysplasia and with low grade dysplasia on control will enter the follow-up schedule of patients with low grade dysplasia

The patients with high grade dysplasia and/or carcinoma will be administered PPI and will have a second examination two months later.

The patients who develop during the surveillance a circumferential BE will continue to have a follow-up within the protocol

e) Modalities of endoscopic assessment

Concerning sedation or general anaesthesia, endoscopy will be performed according to the usual local modalities. The patient will receive also information on endoscopy and sedation or general anaesthesia, according to the local regulations.

f) Modalities of biopsy samplings

Seattle protocol (with standard biopsy channel):

- Biopsies on any mucosal abnormalities (nodule, erosion,)

- 1 or 2 Biopsies every cm on tongues:

1 biopsy if the width of the tongue < 25% of the esophageal circumference

2 biopsies if the width of the tongue > 25% of the esophageal circumference

- Biopsies on normal Z-line between the tongues: 1-4 biopsies

1 bottle per tongue, 1 bottle per mucosal abnormality

g) pictures:

Electronic (one general view)

h) Modalities of histological analysis

Biopsies analyzed by two histopathologists or by local pathologist plus a centralized lecture conservation of histological plates

Data to be collected

Medications (PPI) taken in the past

pt history

weight, BMI

endoscopic reports

pictures or videotapes

histological reports

histological plates

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