Barrett's Esophagus

Diagnosis, follow-up and treatment

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SUMMARY

Barrett's Esophagus (BE) is a premalignant condition in the esophagus. Esophageal adenocarcinomas have the fastest increase of incidence of all solid tumors in the western world. BE is defined as areas with macroscopic visible columnar epithelium and intestinal metaplasia oral of the anatomical gastro-esophageal junction.

The extent of the endoscopic findings is described by the Prague classification.

The metaplasia is histologically confirmed by the presence of intestinal metaplasia.

The diagnosis of BE can only be made by a combined macroscopic and microscopic examination.

The histological description should include evaluation of dysplasia, and if present it should be classified as low or high grade dysplasia.

All patients are offered relevant antireflux treatment with PPI or surgery.

Ablation or mucosal resection of metaplastic epithelia with or without low grade dysplasia is experimental and it is not recommended outside controlled studies.

Treatment of high grade dysplasia and carcinoma in situ is handled in departments treating esophageal cancer.

Follow-up with endoscopy and biopsy can be offered. Follow up endoscopy with biopsy can only be recommended after thorough information to the patients, as evidence for the value is scarce.

QUICK GUIDE

Diagnosis

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The extent of the endoscopic findings is described by the Prague classification.

The metaplasia is confirmed histologically by the presence of intestinal metaplasia.

The histological description should include evaluation of dysplasia, classified as low or high grade dysplasia.

Macroscopic and microscopic evaluation is best performed after treatment of concomitant reflux esophagitis, and findings of suspected dysplasia can only be evaluated after proton pump inhibitor (PPI) treatment.

Follow-up

Endoscopy with biopsy can be offered to patients, who after counselling want to be followed with regular control, and given that the patient is a potential candidate for endoscopic or surgical treatment of high grade dysplasia or carcinoma.

Intervals:

Intestinal metaplasia: every 3 years.

Low grade dysplasia: every 6 months. After two consecutive examinations without dysplasia, the flow chart for intestinal metaplasia is followed.

High grade dysplasia or carcinoma in situ: referral to a centre treating esophageal cancer.

Treatment

All patients are offered relevant antireflux treatment with PPI or surgery.

Ablation or mucosal resection of metaplastic epithelium with or without low grade dysplasia are experimental procedures and only recommended for evaluation in controlled Studies.

Treatment of high grade dysplasia and carcinoma in situ is handled in departments treating esophageal cancer.

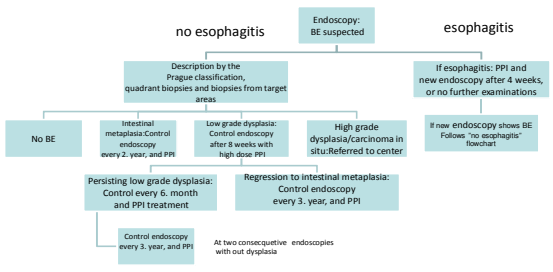

Figure 1. Flowchart for the diagnosis and treatment of BE

INTRODUCTION

Background

BE is a premalignant condition in the esophagus. Esophageal adenocarcinomas have the fastest increasing incidence of all solid tumours in the western world. The incidence has increased 5 times over the last 30 years. Early diagnosis and treatment significantly increase survival. The incidence of adenocarcinoma and/or high grade dysplasia in the esophagus is reported from 0.12-0.5/100 person-years(1-3). Risk factors besides reflux disease are smoking, alcohol, BMI>30, male sex, Caucasian race, and age over 45 years. A few studies indicate a possible genetic component with increased representation in first degree relatives, but no genes have been identified(4).

BE is defined as areas with macroscopic visible columnar epithelium and intestinal metaplasia oral to the anatomical gastro-esophageal junction replacing the normal squamous epithelium.

TOPICS

Diagnosis

A diagnosis of BE can only be made by a combined macroscopic and microscopic examination.

Endoscopic examination: The diagnosis is suspected by findings of changed epithelium oral to the gastro-esophageal junction. The gastro-esophageal junction is localized by endoscopy where the longitudinal gastric folds ends and the tube shaped esophagus is recognized(5).

The Prague classification is recommended to describe the extent of the suspected BE segment. The Prague classification indicates with a C and M value the circumferential extend and the maximum length of"tongues" in the BE segment. It is important to exclude the length of a hiatal hernia if present (5) (see figure 2).

Biopsies are taken from the suspect area as follows: Quadrant biopsies from the oral and distal limitation of the BE segment. If the BE segments is longer than 5 cm, quadrant biopsies are also taken from the middle. Besides this, targeted biopsies are taken from suspicious areas (changed vascular pattern, ulcerations/erosions and changed surface level or/and structure). This recommendation deviates from some international recommendations, where quadrant biopsies from every 2 cm of BE segment are recommended. This is, however, by the present authors, not thought to be practically possible and therefore the recommendations have been changed to the above.

Severe esophagitis (grade C or D after the Los Angeles classification) can make macroscopic evaluation of areas of possible BE difficult. In these cases treatment with PPI in twice the standard dose for four weeks is recommended, and after that renewed endoscopy with biopsies.

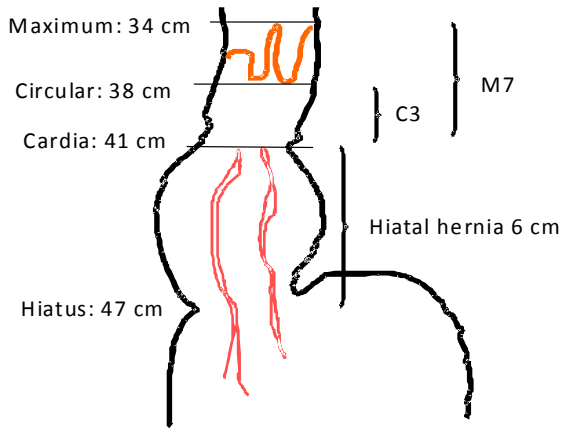

Figure 2. The Prague Classification

Histology: Biopsies from a suspected BE segment shall contain intestinal metaplasia of the columnar lined epithelium replacing the normal squamous esophageal epithelium.

Microscopic foci with intestinal metaplasia from a macroscopic normal Z-line are not included in the definition of BE.

Decisive for the definition of intestinal metaplasia is the presence of goblet cells. Columnar epithelium without goblet cells (gastric metaplasia) from a suspected segment of BE is not associated with increased cancer risk, and this is not defined as BE. Findings of gastric metaplasia, where endoscopy have shown macroscopic changes consistent with BE, should be followed by a newendoscopy with biopsies, as mosaics of gastric and intestinal metaplasia can occur. If the new biopsies still do not show intestinal metaplasia, the diagnosis of BE is not sustained.

Screening

There are no studies showing that patients with reflux symptoms benefit from screening endoscopy, in order to diagnose possible BE. A cost utility analysis has shown that there is a potential benefit in screening 50 year old males with reflux disease once(6). Screening of subjects without reflux symptoms will probably yield a smaller effect and general screening is not recommended(6).

Follow-up

There are no randomized studies that compare mortality from esophageal adenocarcinoma in endoscopically surveyed versus non-surveyed populations. In patients without dysplasia control endoscopy is very controversial, but if a surveillance program after counselling is chosen, control endoscopy every third year is recommended. Findings of low grade dysplasia are controlled every 6 months. High grade dysplasia is referred to departments treating esophageal cancer. Control and referral are done under consideration of the expected life length of the individual patient.

Adenocarcinoma development in BE

The presence of adenocarcinoma in the esophagus is clearly associated with the presence of BE. The number of adenocarcinomas in the esophagus is steeply increasing; both isolated and compared to other cancers. The incidence of adenocarcinoma is approximately 0.5/100 person-years with BE.

Risk groups

Risk factors for developing adenocarcinoma related to BE are(7):

- Male
- >45 years
- Length of BE segment
- Frequent reflux symptoms (>3 times/week)
- Chronic condition (>10 years)
- Caucasian race
- BMI >30
- Genetic disposition to gastric cancer
- Smoking
- Ulceration or stricture related to BE

Endoscopy at diagnosis and follow-up

There is at present no evidence that routine use of chromoendoscopy or narrow band imaging (NBI), neither for diagnosis nor biopsy guidance, increases the number of or the precision of diagnostic findings. However, improved endoscopic image modalities (High Definition Endoscopy, Zoom-technique and NBI) is likely to improve the identification of dysplasia, and may possibly be used in targeting biopsies in follow-up endoscopies of BE (8-10).

Treatment

Intestinal metaplasia without dysplasia: Patients should be treated with PPI or another effective antireflux treatment. PPI dosis is increased in case of acid related symptoms, until symptom relief. Without symptoms standard dose is used. In lack of symptom relief on PPI, laparoscopic fundoplication may be considered. Endoscopic mucosectomi and radiofrequency ablation are experimental treatments, and should only be used in controlled studies.

Low grade dysplasia: Twice standard dose PPI is recommended in order to discriminate reactive changes from verified dysplasia.

High grade dysplasia: Patients are referred to a centre treating esophageal cancer (Endoscopic mucosectomi, radiofrequency ablation or resection).

Table 1. Strength of evidence and recommendations in this guideline(11)

Prague classification for macroscopic description	**II B**
Microscopic diagnosis based on presence of intestinal metaplasia	**II B**
Division in intestinal metaplasia, low grade dysplasia, high grade dysplasia and carcinoma	**II B**
Biopsies from suspect areas and quadrant biopsies according to guidelines	**II B**
Screening of population or risk groups is not recommended	**III B**
Lifelong treatment with PPI	**IV C**
Endoscopic follow-up after individual assessment and discussion with the patient	**III B**

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