STATEMENT 6

Biopsy samples should be taken from all visible mucosal abnormalities. In addition, random 4-quadrant biopsies should be collected every 2 cm within the Barrett's segment, starting from the upper end of the gastric folds. Biopsies from each level should be collected in and presented to the pathologist in a separate container.

- Agreement between merged guidelines
- No new evidence available on this statement
- Consensus on current statement between Working Group members

STATEMENT 7

Surveillance intervals for nondysplastic BE should be stratified according to the length of the Barrett's segment.
i. Irregular Z-line/columnar-lined esophagus < 1 cm: no endoscopic surveillance
ii. Maximum extent of BE ≥ 1 cm, *and* < 3 cm: 5 years
iii. Maximum extent of BE ≥ 3 cm *and* < 10 cm: 3 years
Patients with BE with a maximum extent ≥ 10 cm should be referred for surveillance endoscopies to a BE expert center.
If a patient has reached 75 years of age at the time of his/her last surveillance endoscopy and has no previous evidence of dysplasia, no subsequent surveillance endoscopies should be performed.

- Disagreement between merged guidelines
- New evidence available on this statement
- Consensus on current statement between Working Group members

Comments

The extent of BE is an accepted risk factor for malignant progression [8]. The suggested cutoff levels are arbitrary.

The cutoff of 10 cm for referral to a BE expert center is based on the finding that the risk for progression in these patients might reach a level comparable to that of patients with a confirmed diagnosis of low grade dysplasia (LGD) (see Statement 12 below) for which referral to an expert center is also advised (see Statement 17 below).

The age cutoff is also arbitrary, and is based on average life expectancy; hence, surveillance extension up to 80 years can be considered in individual cases.

Contrary to earlier guidelines, the Working Group does not recommend a standard follow-up endoscopy at 1 year after the first diagnosis of BE, provided that the initial (diagnostic) endoscopy is performed according to the standards as described in this Position Statement (e. g. high definition endoscopy, adequate setting, sufficient number of random biopsies).

STATEMENT 8

Prophylactic endoscopic therapy (such as ablation therapy) for non-neoplastic BE should not be performed.

- Disagreement between merged guidelines
- No new evidence available on this statement
- Consensus on current statement between Working Group members

Comments

The average risk of cancer progression in patients with nondysplastic BE is low, estimated at about 0.3 % per year [1]. This leads to a high number-needed-to-treat for the prevention of a single case of cancer, and consequently to unfavorable cost – effectiveness. In addition, uncertainty exists on the need for long-term follow-up in patients with nondysplastic BE post ablation.

STATEMENT 9

The diagnosis of any degree of dysplasia (including "indefinite for dysplasia") in BE requires confirmation by an expert GI pathologist.

- Agreement between merged guidelines
- New evidence available on this statement
- Consensus on current statement between Working Group members

Comments

An accepted definition of the term "expert GI pathologist" is lacking. The Working Group suggests the following description: "an expert GI pathologist is a pathologist with special interest in GI pathology recognized as such by his/her peers." When considering endoscopic treatment, confirmation by an independent pathologist from an independent institution is preferable in order to increase robustness of the diagnosis.

The addition of p53 immunostaining to the histopathological assessment may improve the diagnostic reproducibility of a diagnosis of dysplasia in BE and should be considered as an adjunct to routine clinical diagnosis.

The importance of expert histopathology review is underscored by studies showing that the majority of patients with a community diagnosis of LGD are downstaged to nondysplastic BE by expert GI pathologists. In patients with confirmed LGD, however, progression rates to high grade dysplasia (HGD) and cancer are considerable [9, 10].

STATEMENT 10

Patients with a diagnosis of "indefinite for dysplasia" confirmed by a second expert GI pathologist should be managed with optimization of antireflux medication and repeat endoscopy at 6 months. If no definite dysplasia is found in subsequent biopsy samples (including if the biopsies are again classified as "indefinite for dysplasia"), then the surveillance strategy should follow the recommendation for nondysplastic BE.

- Recommendation only present in one guideline
- No new evidence available on this statement
- Consensus on current statement between Working Group members

STATEMENT 11

Patients with visible lesions in BE diagnosed as dysplasia or early cancer should be referred to a BE expert center. All visible abnormalities, regardless of the degree of dysplasia, should be removed by means of endoscopic resection techniques in order to obtain optimal histopathological staging.

- Agreement between merged guidelines
- New evidence available on this statement
- Consensus on current statement between Working Group members

Comments

For Barrett's lesions containing dysplasia or early cancer, endoscopic submucosal dissection (ESD) and endoscopic mucosal resection (EMR) are both highly effective. ESD was not shown to provide improved overall patient outcome compared with EMR, yet it is considered to be technically more difficult and is associated with a higher rate of complications [11, 12]. Therefore, EMR is the preferred resection technique for early Barrett's neoplasia. ESD may be indicated for removal of lesions with a significant luminal component ("bulky lesions") that cannot be removed by cap-based techniques, and for lesions where submucosal invasion is suspected.

STATEMENT 12

Patients with LGD on random biopsies confirmed by a second expert GI pathologist should be referred to a BE expert center. A surveillance interval of 6 months after confirmed LGD diagnosis is recommended.

i. If no dysplasia is found at the 6-month endoscopy, the interval can be broadened to 1 year. After two subsequent endoscopies negative for dysplasia, standard surveillance for patients with nondysplastic BE can be initiated.

ii. If a confirmed diagnosis of LGD is found in the subsequent endoscopies, endoscopic ablation should be offered.

- Partial agreement between merged guidelines
- New evidence available on this statement
- Consensus on current statement between Working Group members

Comments

In 30 % of patients with a single endoscopy diagnosis of confirmed LGD, the diagnosis will not be reproduced on subsequent endoscopies [9]. A single diagnosis of confirmed LGD therefore does not justify endoscopic ablation therapy.

Confirmed LGD, especially if it is repeated over time, and/or if it is documented at multiple esophageal levels, is a strong risk factor for progression to HGD and EAC [10].

Based on the currently available literature, radiofrequency ablation (RFA) has the best efficacy and safety profile, hence it is recommended as the technique of choice for ablation of BE [13].

STATEMENT 13

Patients with HGD confirmed by a second expert GI pathologist should be referred to a BE expert center. In the expert center, a high-definition endoscopy should be repeated according to the following guidelines.

i. All visible abnormalities should be removed by endoscopic resection techniques for adequate histopathological staging.

ii. If no lesions suspicious for dysplasia are seen, random 4-quadrant biopsies should be taken; if these biopsies are negative for dysplasia, endoscopy should be repeated at 3 months. If these biopsies confirm the presence of HGD, endoscopic ablation is recommended, preferably with RFA.

- Partial agreement between merged guidelines
- No new evidence available on this statement
- Consensus on current statement between Working Group members

Comments

True flat HGD without endoscopically visible lesions is rare and accounts for less than 20 % of patients with HGD. The absence of visible abnormalities in a patient with HGD is most often the result of an overlooked lesion, or over-staging of the histopathology. Flat HGD (as for flat LGD) therefore requires a confirmed diagnosis on two separate time points before treatment is initiated.

STATEMENT 14
Endoscopic resection is the first-choice therapy for T1a EAC.

- Agreement between merged guidelines
- No new evidence available on this statement
- Consensus on current statement between Working Group members

Comment

A diagnosis of esophageal adenocarcinoma is virtually always associated with an endoscopically visible abnormality, which requires endoscopic resection for staging and treatment.

In the absence of a visible lesion, a diagnosis of esophageal adenocarcinoma should be followed by a second imaging endoscopy to find the area of interest instead of performing ablation therapy for flat "invisible" cancer.

STATEMENT 15
In patients with T1b EAC, the optimal treatment strategy depends on histopathological characteristics of the endoscopic resection specimen. Endoscopic resection may be a valid alternative to surgery and is recommended in patients who are borderline fit for surgery, if the endoscopic resection specimen meets all of the following criteria:
i. submucosal invasion limited to < 500 µm;
ii. tumor differentiation grade: *well* or *moderate*;
iii. absence of tumor invasion in lymphatic vessels or blood vessels;
iv. absence of tumor infiltration in the deep resection margin.

- Partial agreement between merged guidelines
- New evidence available on this statement
- Consensus on current statement between Working Group members

Comments

The choice between endoscopic therapy and surgical resection should be based on a careful assessment of the risk of lymph node metastasis, surgical mortality and morbidity, and patient preferences. Tumors fulfilling all of the abovementioned criteria are considered as low-risk T1b cancers; the risk of lymph node metastasis appears to be low (< 2 %) [14].

STATEMENT 16
After endoscopic resection of visible abnormalities containing any degree of dysplasia or neoplasia, complete eradication of all remaining Barrett's epithelium should be strived for, preferably with RFA.

- Partial agreement between merged guidelines
- No new evidence available on this statement
- Consensus on current statement between Working Group members

Comment

After endoscopic resection of visible abnormalities, recurrence rates between 15 % in 5 years and 30 % in 3 years have been reported for patients in whom the remaining BE is left untreated.

STATEMENT 17
All patients with a BE ≥ 10 cm, a confirmed diagnosis of LGD, HGD, or early cancer should be referred to a BE expert center for surveillance and/or treatment.
A BE expert center should meet the following requirements.
i. Annual case load of ≥ 10 NEW patients with endoscopic treatment for HGD or early carcinoma per BE expert endoscopist.
ii. Endoscopic and histological care is provided by endoscopists and pathologists who have followed additional training in this field (either by courses or guest visits). A minimum of 30 supervised cases of endoscopic resection and 30 cases of endoscopic ablation should be performed to acquire competence in technical skills, management pathways, and complications.
iii. Patients with Barrett's neoplasia are discussed in multidisciplinary meetings with gastroenterologists, surgeons, oncologists, and pathologists.
iv. Access to experienced esophageal surgery.
v. All patients with BE are registered prospectively in a database.

- Partial agreement between merged guidelines
- No new evidence available on this statement
- Consensus on current statement between Working Group members

Thieme

ESGE position statements represent a consensus of best practice based on the available evidence at the time of preparation. They may not apply in all situations and should be interpreted in the light of specific clinical situations and resource availability. Further controlled clinical studies may be needed to clarify aspects of these statements, and revision may be necessary as new data appear. Clinical consideration may justify a course of action at variance to these statements. ESGE position statements are intended to be an educational device to provide information that may assist endoscopists in providing care to patients. They are not rules and should not be construed as establishing a legal standard of care or as encouraging, advocating, requiring, or discouraging any particular treatment.

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Competing interests

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