Complete Summary

GUIDELINE TITLE

American Gastroenterological Association medical position statement: role of the gastroenterologist in the management of esophageal carcinoma.

BIBLIOGRAPHIC SOURCE(S)

Wang KK, Wongkeesong LM, Buttar NS. American Gastroenterological Association medical position statement: role of the gastroenterologist in the management of esophageal carcinoma. Gastroenterology 2005 May;128(5):1468-70. PubMed

GUIDELINE STATUS

This is the current release of the guideline.

According to the guideline developer, the Clinical Practice Committee meets three times a year to review all American Gastroenterological Association Institute (AGAI) guidelines. This review includes new literature searches of electronic databases followed by expert committee review of new evidence that has emerged since the original publication date.

COMPLETE SUMMARY CONTENT

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SCOPE

DISEASE/CONDITION(S)

Esophageal carcinoma, including squamous cell cancer and adenocarcinoma

GUIDELINE CATEGORY

Diagnosis
Evaluation

Management
Prevention
Screening
Treatment

CLINICAL SPECIALTY

Family Practice
Gastroenterology
Internal Medicine
Oncology
Radiation Oncology
Radiology
Surgery
Thoracic Surgery

INTENDED USERS

Advanced Practice Nurses
Physician Assistants
Physicians

GUIDELINE OBJECTIVE(S)

To examine the clinical practice of the gastroenterologist in the management of the patient with esophageal carcinoma

TARGET POPULATION

Adult patients at risk of or with esophageal carcinoma

INTERVENTIONS AND PRACTICES CONSIDERED

Screening and Surveillance

1. Risk assessment
2. Surveillance endoscopy
3. Biopsy
4. Endoscopic mucosal resection
5. Endoscopic ultrasonography
6. Brush cytology

Prevention

1. Acid inhibition
2. Chemoprevention
3. Lifestyle modifications including
    - Weight loss
    - Stopping tobacco use
    - Eating fresh fruits and vegetables

Diagnosis and Staging

1. Flexible endoscopy
2. Brush cytology
3. Biopsy
4. Fine needle aspiration of lymph nodes
5. Computed tomography
6. Endoscopic ultrasonography
7. Endoscopic mucosal resection
8. Positron emission tomography

Treatment

Early Esophageal Cancer T1 N0 M0

1. Surgery
2. Endoscopic mucosal resection
3. Photodynamic therapy

Advanced Esophageal Cancer

1. Surgery
    - Esophagectomy
    - Lymph node dissection
2. Chemotherapy (palliative or neoadjuvant)
    - Cis-platinum
    - 5-fluorouracil
3. Radiation therapy
4. Palliation
    - Esophageal stenting
    - Endoscopic tumor ablation with photodynamic therapy, alcohol injection, or laser therapy
5. Supportive measures
    - Nutritional support
    - Emotional and social support

MAJOR OUTCOMES CONSIDERED

- Incidence of esophageal cancer
- Morbidity and mortality
- Adverse effects of treatment
- Cost-effectiveness of surveillance
- False positive and false negative diagnostic test results
- Survival time
- Quality of life

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

A search and review of the literature available on MEDLINE and PREMEDLINE was performed on the topics of esophageal neoplasm, esophageal cancer, and Barrett's esophagus from 1968 to 2004. Bibliographies of significant reports were also reviewed to ensure that the pertinent literature was reviewed.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Levels of Evidence

Level I evidence is the presence of at least one prospective, randomized, controlled trial.

Level II evidence is based on well-designed cohort or case-controlled studies.

Level III evidence is based on case series or flawed clinical trials.

Level IV evidence is based on opinions of respected authorities or expert committees.

Level V evidence is insufficient evidence to form any opinions.

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

Not stated

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

Guideline developer reviewed published cost analyses.

METHOD OF GUIDELINE VALIDATION

Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Not stated

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Screening and Surveillance for Esophageal Cancer

Early detection is the key to the treatment of any gastrointestinal malignancy, and this is particularly true of esophageal adenocarcinoma. Intramucosal carcinomas have virtually no risk of metastasis, while cancers that penetrate into the deep mucosa or submucosa can have significant risks of dissemination. At the current time, screening and surveillance for esophageal cancer is still controversial. Screening asymptomatic populations for adenocarcinoma cannot be recommended because current studies suggest that cancers and predisposing conditions such as long-segment Barrett's esophagus are uncommon without symptoms. Screening patients with symptoms of heartburn who are older than 50 years of age may be of value because this is a higher-risk group, but this has not been proven in a prospective study. Squamous cell cancers of the esophagus are less common in the United States, and screening is not recommended except for very select subgroups such as patients with tylosis, Fanconi's anemia, and lye-induced strictures. The presence of risk factors such as long-term tobacco or alcohol use, achalasia, or squamous head and neck cancers may identify selected groups for screening.

Surveillance endoscopy has been used the most in the setting of Barrett's esophagus. Surveillance endoscopy is complicated by 2 major problems: sampling error (missing significant neoplastic lesions) and interpretation errors (histologic uncertainty regarding the presence of dysplasia). Sampling errors will be hopefully reduced in the future by the development of novel technologies that allow the endoscopist to visualize neoplastic lesions at the time of endoscopy, such as optical biopsy techniques or magnification techniques. Most have not been proven to be effective in trials, and some techniques such as methylene blue–assisted chromoendoscopy have been suggested to be potentially deleterious to the

mucosa. The use of molecular markers to predict the occurrence of cancer has promise to improve the yield of surveillance biopsies and potentially augment histology.

At this time, surveillance endoscopy should be performed with random biopsies with 4 biopsy specimens taken at least every 1-2 cm of esophageal mucosa with additional biopsy specimens taken of any mucosal abnormality. Patients without dysplasia or mucosal abnormalities on their initial evaluation should be examined again in 1 year with surveillance biopsies to decrease the chances of sampling error. If no dysplasia is found again, surveillance can reasonably be deferred for another 5 years until the patient reaches a point at which cancer therapy is not possible or life expectancy is limited. Surveillance should be practiced only if the patient is anticipated to have a reasonable life expectancy and can tolerate treatment for esophageal cancer. In patients in whom low-grade dysplasia is found without mucosal abnormalities, it is recommended that endoscopy be repeated again in 1 year to be certain that there is no evidence of high-grade dysplasia or cancer. If low-grade dysplasia is confirmed by 2 pathologists, then the patient should be reexamined on a yearly basis because this group tends to have an increased risk of cancer. If there is disagreement about the presence of any dysplasia, surveillance can be deferred for 2 years. If high-grade dysplasia is detected and confirmed by 2 experienced pathologists, treatment with either surgical resection or endoscopic therapy can be recommended depending on the presence and nature of any mucosal abnormalities. The presence of multifocal high-grade dysplasia appears to be associated with an increased risk of development of cancer, and these patients might be more suitable for more aggressive treatment. Surveillance can be offered if both the patient and the physician are willing to follow a careful regimen of endoscopy every 3 months with at least 8 random biopsy specimens taken every 2 cm of involved esophagus. All mucosal abnormalities should be investigated with endoscopic ultrasonography and mucosal resection if these techniques are available to be certain that there is no underlying cancer. If ablative therapy has been performed, surveillance is still needed in the same area of involvement at least as frequently as if ablation had not been performed. Efforts should be made to examine the new squamous mucosa to determine if submucosal lesions might be present.

Chemoprevention for Esophageal Cancer

Chemoprevention would seem to be ideally suited to the problem of esophageal cancer, but studies have not proven that there is a specific treatment that would decrease cancer risk. There is strong epidemiologic and preclinical data that cyclooxygenase-2 inhibition might be of value as a chemoprevention agent, but no prospective clinical studies have been performed to prove that there is a reduction in risk for cancer. Control of acid or gastroesophageal refluxate should decrease inflammation and therefore decrease cancer formation; however, epidemiologic studies do not support the use of fundoplication for prevention of cancer. Similarly, there is no clear rationale for the use of high-dose proton pump inhibitors solely as a chemoprevention agent. Lifestyle modifications such as weight loss, stopping tobacco use, and eating fresh fruits and vegetables can be recommended based on epidemiologic evidence to decrease cancer risk.

Diagnosis and Staging of Esophageal Cancer

The diagnosis of esophageal cancer is established by flexible endoscopy with biopsy to confirm histologic evidence of disease. Computed tomography is recommended as the first staging study because detection of metastasis would clearly alter therapy. Endoscopic ultrasonography can also be recommended if available to evaluate esophageal cancer if computed tomography does not find any evidence of distant metastasis or unresectable cancer. Fine needle aspirates should be performed on regional lymph nodes if present and suspicious on endoscopic ultrasonography. If the cancer was diagnosed as mucosal based on ultrasonography, endoscopic mucosal resection could then be performed to stage and potentially treat early-stage cancer if it is available. In localities where endoscopic ultrasonography and endoscopic mucosal resection are unavailable, surgical resection should be performed for early-stage cancers. Positron emission tomography scans can be performed if all of the previous studies do not show evidence of metastatic disease because it may be more sensitive for distant metastasis, which would alter the therapeutic approach.

Treatment of Esophageal Cancer

Treatment of cancer is dependent on the stage of the cancer. Early cancers T1, N0, M0 by the American Joint Commission on Cancer are the most likely to be potentially curable. If the cancer is confined to the mucosa, these cancers are usually treated with esophagectomy, although endoscopic therapy has been shown to be effective in early squamous cell cancers of the esophagus treated in Japan using endoscopic mucosal resection. There is also some evidence that this approach may be successful in early adenocarcinoma. The risk of metastasis is very low if the cancer is confined to the mucosal layers. If there is penetration into the submucosa, the risk of metastasis becomes significant and esophagectomy would be recommended if there were no signs of distant metastasis or invasion of adjacent structures. If there is definite evidence of metastasis to regional lymph nodes, neoadjuvant chemotherapy in combination with radiation therapy administered before surgical resection may improve survival. Esophagectomy can be practiced by transhiatal or transthoracic routes. Minimally invasive esophagectomy has been advocated but is still associated with substantial morbidity and mortality. More advanced disease with metastasis to other organs or distant lymph node groups should be considered for palliative therapy with chemotherapy. Most commonly, combined therapy consists of chemotherapy with multiple courses of cis-platinum and 5-fluorouracil concomitantly given with ionizing radiation.

Palliation of advanced cancer can be achieved endoscopically with dilation, although relief is short-lived. Esophageal stenting is recommended for long-term palliation of cancers that are long and located at least 2 cm from the cricopharyngeal muscle. Expandable metal stents are preferred to plastic semirigid stents and are available in a coated form to decrease tumor ingrowth. Expandable plastic stents are reasonable for intermediate-term use when removal of stents is planned. Endoscopic tumor ablation for palliation of dysphagia can be performed with photodynamic therapy, alcohol injection, or laser therapy with similar efficacy in appropriate patients, although stents are clearly the preferred method of palliation. Nutritional support should be considered before chemotherapy or radiation therapy with enteral nutrition being the preferred method. Physicians must also keep in mind the emotional support required of

these patients because esophageal cancer tends to be socially isolating as well as physically disabling.

CLINICAL ALGORITHM(S)

Clinical algorithms are provided in the Technical Review that accompanies the guideline for:

- Staging of Advanced Cancers
- Staging of Early Cancers

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The strength of the evidence upon which the statements are based is noted in the technical review paper accompanying the original guideline document, with prospective, randomized, controlled trials being the strongest. When adequate data are absent, expert consensus is used and is identified as such.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Esophageal cancer is increasing in incidence and is associated with a high mortality rate. The ability of gastroenterologists to increase survival in this disease will depend on earlier detection through screening and surveillance strategies.

POTENTIAL HARMS

- Adverse effects from surgical intervention, chemotherapy, and radiation therapy
- Surveillance endoscopy is complicated by sampling error (missing significant neoplastic lesions) and interpretation errors (histologic uncertainty).
- Biopsy is associated with risk of complications.
- Stent related morbidity
- Intratumoral injection of absolute alcohol may result in chest pain. Serious complications, including mediastinitis and tracheoesophageal fistulas, occur in up to 5% of cases.
- Endoscopic mucosal resection is associated with risk of complications.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

The guideline has been developed under the aegis of the American Gastroenterological Association (AGA) and its Clinical Practice and Economics Committee (CPEC) and was approved by the AGA Governing Board. The data used

to formulate these recommendations are derived from the data available at the time of their creation and may be supplemented and updated as new information is assimilated. These recommendations are intended for adult patients, with the intent of suggesting preferred approaches to specific medical issues or problems. They are based upon the interpretation and assimilation of scientifically valid research, derived from a comprehensive review of published literature. Ideally, the intent is to provide evidence based on prospective, randomized placebo-controlled trials; however, when this is not possible the use of experts' consensus may occur. The recommendations are intended to apply to healthcare providers of all specialties. It is important to stress that these recommendations should not be construed as a standard of care. The AGA stresses that the final decision regarding the care of the patient should be made by the physician with a focus on all aspects of the patient's current medical situation.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

IMPLEMENTATION TOOLS

Clinical Algorithm

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

End of Life Care
Getting Better
Living with Illness
Staying Healthy

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

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ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2005 May

GUIDELINE DEVELOPER(S)

American Gastroenterological Association Institute - Medical Specialty Society

SOURCE(S) OF FUNDING

American Gastroenterological Association Institute

GUIDELINE COMMITTEE

American Gastroenterological Association Clinical Practice Committee

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Authors: Kenneth K. Wang; Loius Michel Wongkeesong; Navtej S. Buttar

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

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GUIDELINE AVAILABILITY

Electronic copies: Available from the American Gastroenterological Association Institute (AGAI) Gastroenterology journal Web site.

Print copies: Available from the American Gastroenterological Association Institute, 4930 Del Ray Avenue, Bethesda, MD 20814.

AVAILABILITY OF COMPANION DOCUMENTS

The following is available:

- American Gastroenterological Association technical review on the role of the gastroenterologist in the management of esophageal carcinoma. Gastroenterology 2005 May;128(5);1471-1505.

Electronic copies: Available from the American Gastroenterological Association Institute (AGAI) Gastroenterology journal Web site.

Print copies: Available from American Gastroenterological Association Institute, 4930 Del Ray Avenue, Bethesda, MD 20814.

PATIENT RESOURCES

None available

NGC STATUS

This summary was completed by ECRI on June 14, 2005. The information was verified by the guideline developer on June 30 2005.

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Date Modified: 9/25/2006