Communication from the ASGE Standards of Practice Committee

GUIDELINE

Endoscopic eradication therapy for patients with Barrett's esophagus–associated dysplasia and intramucosal cancer

Prepared by: STANDARDS OF PRACTICE COMMITTEE

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Barrett's esophagus (BE) is defined by the replacement of the normal squamous epithelium of the distal esophagus with metaplastic intestinal-type columnar epithelium.[1-3] BE is an adverse event of chronic GERD and the only identifiable premalignant condition for esophageal adenocarcinoma (EAC), a cancer that continues to increase in incidence. In 2014 there were approximately 18,170 incident cases of esophageal cancer in the United States, nearly 60% of which were EAC.[4-6] Although uncommon, EAC is a highly lethal cancer associated with a poor 5-year survival rate of 15% to 20% and an overall median survival of <1 year in cases with advanced disease.[5-7] It is estimated that BE is present in 1% to 2% of the general adult population.[8,9] The stepwise and hypothesized progression of BE to invasive EAC is believed to occur through the histopathologic stages of intestinal metaplasia to low-grade dysplasia (LGD) to high-grade dysplasia (HGD) to intramucosal EAC and finally to invasive EAC.[3,10-13]

Endoscopic eradication therapy (EET) has significantly changed the management of patients with BE-related neoplasia and allows a minimally invasive treatment approach that avoids the morbidity and mortality associated with esophagectomy. Contemporary EET, supported by published literature, entails endoscopic mucosal resection (EMR) of visible lesions within the Barrett's segment and ablative techniques that include radiofrequency ablation (RFA) and cryotherapy. Several studies, including randomized controlled trials (RCTs), large observational studies, and population-based studies, have demonstrated the efficacy, effectiveness, and safety of EET to achieve complete eradication of intestinal metaplasia (CE-IM) and neoplasia while maintaining disease remission.[14-22] In addition, population-based studies report comparable outcomes between esophagectomy and EET in the management of BE-related HGD and mucosal EAC.[23] Available data suggest that EET is being performed not only at academic and tertiary care centers but also among community practices.[14,18]

AIMS/SCOPE

The aim of this document is to offer evidence-based recommendations and clinical guidelines addressing key issues related to EET in the management of BE-related neoplasia. This document addresses the following clinical questions:

1. What is the role of confirmation of diagnosis by an expert GI pathologist or by a panel of pathologists in BE patients with dysplasia or intramucosal EAC referred for EET?
2. Comparing EET with surveillance, what is the optimal management strategy in BE patients with dysplasia (HGD and LGD) and intramucosal EAC?
3. Comparing EET with esophagectomy, what is the optimal management strategy in BE patients with HGD and intramucosal EAC?
4. What is the role of EMR in BE patients with a visible lesion detected during screening or surveillance?
5. What is the role of ablation of the remaining BE segment after EMR of all visible lesions in BE patients referred for EET?
6. Comparing EMR of visible lesions followed by ablation of remaining BE segment with EMR of entire BE segment, what is the optimal EET approach in BE patients with dysplasia or intramucosal EAC referred for EET?
7. After achieving CE-IM, what is the role of surveillance endoscopy?

This document was approved by the American Society for Gastrointestinal Endoscopy (ASGE) Governing Board and represents the official recommendations of the ASGE.

METHODS

Overview

This document was prepared by a working group of the Standards of Practice Committee of the ASGE in

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0016-5107/$36.00
https://doi.org/10.1016/j.gie.2017.10.011

conjunction with a Grading of Recommendations Assessment, Development and Evaluation (GRADE) methodologist. It includes a systematic review of available literature along with guidelines for EET in the management of BE-related dysplasia and intramucosal EAC patients, developed using the GRADE framework.[24] After evidence synthesis, recommendations were drafted by the full panel during a face-to-face meeting on March 23, 2017 and approved by the Standards of Practice committee members and the ASGE Governing Board.

Panel composition and conflict of interest management

The panel consisted of 2 content experts with expertise in systematic reviews and meta-analysis (S.W., B.Q.), a GRADE methodologist (S.S.), oncologic surgeon, committee chair (J.D.), patient representative, and other committee members. All panel members were required to disclose potential financial and intellectual conflicts of interest, which were addressed according to ASGE policies (https://www.asge.org/forms/conflict-of-interest-disclosure and https://www.asge.org/docs/default-source/about-asge/mission-and-governance/asge-conflict-of-interest-and-disclosure-policy.pdf).

Formulation of clinical questions

A total of 7 clinical questions were developed and then approved by the ASGE Governing Board (Table 1). For each PICO question we identified the population (P), intervention (I), comparator (C), and outcomes of interest (O). For all clinical questions potentially relevant patient-important outcomes were identified a priori and rated from not important to critical through a consensus process. Relevant clinical outcomes included progression to cancer, cancer-specific and all-cause mortality, adverse events, and recurrence rates. EET in this document refers to EMR and RFA (based on the vast body of literature) unless explicitly stated otherwise.

Literature search and study selection criteria

For each of the PICO questions a literature search for existing systematic reviews and meta-analyses was performed. If none was identified, a full systematic review and meta-analysis (when possible) was conducted using the recommendations of the Preferred Reporting Items for Systematic Reviews and Meta-analyses criteria.[25] Details of the search strategy are reported in Supplementary Text 1 (available online at www.giejournal.org). A medical librarian (B.H.) performed a comprehensive literature search of Ovid Medline (Ovid MEDLINE in-process and other non-indexed citations, Ovid MEDLINE) Daily and Ovid MEDLINE 1946 to present), Embase (via Embase.com), and the Cochrane Database of Systematic Reviews/Cochrane Register of controlled trials (via Wiley Online Library). All searches ended on March 11, 2016. Inclusion and exclusion criteria were developed for each PICO question (Supplementary Text 2, available online at www.giejournal.org).

Citations were imported into EndNote (Thompson Reuters, Philadelphia, Pa), and duplicates were removed. The EndNote library was then uploaded into Covidence (www.covidence.org). Two reviewers were assigned to each search for each PICO question. Studies were first screened by title and abstract and then by full text, and all conflicts were resolved by consensus. If existing systematic reviews and meta-analyses were available, inclusion and exclusion criteria were reviewed, and methodological quality of the study was assessed using the Measurement Tool to Assess Systematic Reviews (AMSTAR) tool (https://amstar.ca/Amstar_Checklist.php).[26] Only systematic reviews and meta-analysis meeting the quality thresholds were used for data synthesis. For this guideline an arbitrary threshold (meeting 8 or more of the 11 criteria) was used. When applicable, available systematic reviews and meta-analyses were updated based on literature review as described above.

Data extraction and statistical analysis

If data extraction was needed for a meta-analysis, data were extracted by 2 independent reviewers using Microsoft Excel (Microsoft Corporation, Redmond, Wash). The primary estimate of effect was based on the outcomes of interest in the PICO question and included relative risk (RR), odds ratio (OR), or proportions (change in diagnosis, cumulative rate of disease progression, among others). For outcomes with limited or no available direct comparisons, indirect comparisons were used to estimate the magnitude and direction of effect. Heterogeneity was assessed using the I^2 and Q statistic. Significant heterogeneity was defined at $I^2 > 50\%$ and significant P value (<.05) on the Q statistic. Random-effects models were used if significant heterogeneity was detected. Otherwise, fixed-effects models were used. Studies were weighted based on their size. A priori sources of heterogeneity for each outcome were hypothesized and addressed in sensitivity analyses when applicable. Publication bias was assessed using funnel plots and the classic-fail-safe. Statistical analyses were performed using Comprehensive Meta Analysis V_3 (Biostat Inc, Englewood, NJ).

Certainty in evidence (quality of evidence)

The certainty in the body of evidence (also known as quality of the evidence or confidence in the estimated effects) was assessed for each effect estimate of the outcomes of interest, following the GRADE approach based on the following domains: risk of bias, precision, consistency and magnitude of the estimates of effects, directness of the evidence, risk of publication bias, presence of dose–effect relationship, and an assessment of the effect of residual, opposing confounding. The certainty was categorized into 4 levels ranging from very low to high (Table 2). With this approach direct evidence from RCTs starts at