ASGE Technology Committee systematic review and meta-analysis assessing the ASGE Preservation and Incorporation of Valuable Endoscopic Innovations thresholds for adopting real-time imaging–assisted endoscopic targeted biopsy during endoscopic surveillance of Barrett's esophagus

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This document was reviewed and approved by the Governing Board of the American Society for Gastrointestinal Endoscopy.

Background and Aims: Endoscopic real-time imaging of Barrett's esophagus (BE) with advanced imaging technologies enables targeted biopsies and may eliminate the need for random biopsies to detect dysplasia during endoscopic surveillance of BE. This systematic review and meta-analysis was performed by the American Society for Gastrointestinal Endoscopy (ASGE) Technology Committee to specifically assess whether acceptable performance thresholds outlined by the ASGE Preservation and Incorporation of Valuable Endoscopic Innovations (PIVI) document for clinical adoption of these technologies have been met.

Methods: We conducted meta-analyses calculating the pooled sensitivity, negative predictive value (NPV), and specificity for chromoendoscopy by using acetic acid and methylene blue, electronic chromoendoscopy by using narrow-band imaging, and confocal laser endomicroscopy (CLE) for the detection of dysplasia. Random effects meta-analysis models were used. Statistical heterogeneity was evaluated by means of I^2 statistics.

Results: The pooled sensitivity, NPV, and specificity for acetic acid chromoendoscopy were 96.6% (95% confidence interval [CI], 95-98), 98.3% (95% CI, 94.8-99.4), and 84.6% (95% CI, 68.5-93.2), respectively. The pooled sensitivity, NPV, and specificity for electronic chromoendoscopy by using narrow-band imaging were 94.2% (95% CI, 82.6-98.2), 97.5% (95% CI, 95.1-98.7), and 94.4% (95% CI, 80.5-98.6), respectively. The pooled sensitivity, NPV, and specificity for endoscope-based CLE were 90.4% (95% CI, 71.9-97.2), 98.3% (95% CI, 94.2-99.5), and 92.7% (95% CI, 87-96), respectively.

Conclusions: Our meta-analysis indicates that targeted biopsies with acetic acid chromoendoscopy, electronic chromoendoscopy by using narrow-band imaging, and endoscope-based CLE meet the thresholds set by the ASGE PIVI, at least when performed by endoscopists with expertise in advanced imaging techniques. The ASGE Technology Committee therefore endorses using these advanced imaging modalities to guide targeted biopsies for the detection of dysplasia during surveillance of patients with previously nondysplastic BE, thereby replacing the currently used random biopsy protocols. (Gastrointest Endosc 2016;83:684-98.)

The American Society for Gastrointestinal Endoscopy (ASGE) Technology Committee periodically performs systematic reviews and meta-analyses to evaluate endoscopic technologies to determine whether these have met previously established Preservation and Incorporation of Valuable endoscopic Innovations (PIVI) thresholds. A subcommittee of the ASGE Technology Committee, comprising committee members chosen for their individual expertise, invited outside expert in the subject area, and the Technology Committee Chair performed the

0016-5107/$36.00
http://dx.doi.org/10.1016/j.gie.2016.01.007

systematic review and meta-analysis. The results are then reviewed and approved by the entire Technology Committee. The systematic review and meta-analysis are ultimately submitted to the ASGE Governing Board for approval. The systematic review and meta-analysis undergo peer review by outside experts in statistics and meta-analysis before receiving final ASGE Governing Board approval.

The PIVI initiative is an ASGE program, the objectives of which are to identify important clinical questions related to endoscopy and to establish a priori diagnostic and/or therapeutic thresholds for endoscopic technologies designed to resolve these clinical questions. Once endoscopic technologies meet an established PIVI threshold, those technologies are appropriate to incorporate into clinical practice, presuming the appropriate training in that endoscopic technology has been achieved. ASGE encourages and supports the appropriate use of technologies that meet its established PIVI thresholds.

INTRODUCTION

Barrett's esophagus (BE) is defined as histologic identification of characteristic specialized intestinal metaplasia within the normal stratified squamous mucosa of the esophagus.[1] BE is a known risk factor for the development of esophageal adenocarcinoma (EAC).[2,3] BE evolves into EAC via a sequence of low-grade dysplasia, high-grade dysplasia (HGD), and eventually EAC.[4] Under traditional white-light endoscopy, dysplasia and EAC may be indistinguishable from nondysplastic BE.[5,6] Moreover, the distribution of dysplasia and EAC is highly variable within the length of BE.[5,6] Therefore, current guidelines recommend endoscopic surveillance in patients with BE with random 4-quadrant biopsy specimens obtained at every 1 to 2 cm to detect dysplasia, in addition to targeted biopsies of suspicious lesions under white-light endoscopy.[7]

Current approaches for endoscopic surveillance of BE are problematic on several fronts.[8-11] Obtaining multiple biopsy specimens, especially for long-segment BE, is labor-intensive and time-intensive. Pathologic interpretation of the multiple biopsy specimens obtained is expensive. Dysplasia and EAC may not be readily distinguishable endoscopically from background BE.[5,6,12] Given the variable distribution of dysplasia and EAC, current biopsy surveillance programs also have the potential for sampling error.[5,6,12] Studies indicate that current practice guidelines are not widely followed, with marked variability noted in both technique and intervals of surveillance.[9-11]

Over the last decade, various advanced imaging techniques have been evaluated in an attempt to improve the detection of dysplasia and EAC within BE.[13] The most studied techniques include chromoendoscopy by using acetic acid or methylene blue, confocal laser endomicroscopy (CLE), and electronic chromoendoscopy with use of narrow-band imaging with or without autofluorescence imaging. In addition, other modalities of electronic chromoendoscopy including i-SCAN (Pentax Medical, Montvale, NJ) and Fujinon Intelligent Chromoendoscopy (FICE; Fujinon Inc, Wayne, NJ), endocytoscopy, volumetric laser endomicroscopy, and spectroscopy are also being evaluated for the ability to improve detection of dysplasia and EAC within BE.

The American Society for Gastrointestinal Endoscopy (ASGE) created a new initiative in 2011 entitled Preservation and Incorporation of Valuable Endoscopic Innovations (PIVI). The key objectives of the PIVI initiative are to identify important clinical questions related to endoscopy and to establish a priori, diagnostic, and/or therapeutic thresholds for endoscopic technologies designed to resolve these clinical questions. The ASGE has identified endoscopic real-time imaging of BE as a key area for new endoscopic technologies and has outlined, in a PIVI document entitled "Imaging in Barrett's Esophagus PIVI," the performance thresholds for an imaging technology with targeted biopsies to eliminate the need for random biopsies during endoscopic surveillance of BE.[14] The performance thresholds established in the PIVI document are (1) imaging technology with targeted biopsies should have a per-patient sensitivity of $\geq$90% and a negative predictive value (NPV) of $\geq$98% for detecting HGD or early EAC, compared with the current standard protocol, and (2) the imaging technology should have a specificity that is sufficiently high (80%) to allow a reduction in the number of biopsies (compared with random biopsies).

These PIVI thresholds were selected based on the fact that despite a marked increase in the incidence of EAC, the incidence of HGD and EAC in patients with BE remains low, with an estimate of 0.6% to 1% per year.[15] Given the low prevalence of HGD and EAC in patients with nondysplastic BE, sensitivity and NPV were selected as important metrics for new imaging technologies seeking to eliminate the need for random biopsies.[14] Prior clinical trials have indicated that the sensitivity of current surveillance biopsy protocols ranges from 28% to 85%.[16-19] In addition, prior analyses assessing cost-effectiveness of BE surveillance have assumed a sensitivity of 85% to 90% for surveillance programs.[20-22] This was the basis for selecting a sensitivity of $\geq$90% as the threshold for replacing the current biopsy protocol with advanced imaging targeted biopsies.[14] To allow a reduction in the number of biopsies compared with random biopsy protocols, a threshold specificity of $\geq$80% was set, because prior clinical trials indicate that the specificity of current biopsy protocols ranges from 56% to 100%.[14,16,19]

The systematic review and meta-analyses were performed by the ASGE Technology Committee to specifically assess whether these PIVI thresholds have been met, based on the existing literature. Input also was sought from the