

## The role of endoscopy in the management of premalignant and malignant conditions of the stomach

Prepared by: ASGE STANDARDS OF PRACTICE COMMITTEE

**John A. Evans, MD, Vinay Chandrasekhara, MD, Krishnavel V. Chathadi, MD, G. Anton Decker, MBBCh, MRCP, MHA, Dayna S. Early, MD, Deborah A. Fisher, MD, MHS, Kimberly Foley, RN, BSN, CGRN, SGNA Representative, Joo Ha Hwang, MD, PhD, Terry L. Jue, MD, Jenifer R. Lightdale, MD, MPH, FASGE, NASPGHAN Representative, Shabana F. Pasha, MD, Ravi Sharaf, MD, Amandeep K. Shergill, MD, Brooks D. Cash, MD, Chair, Previous Committee Chair, John M. DeWitt, MD, FASGE, Chair**

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*This is one of a series of statements discussing the use of GI endoscopy in common clinical situations. The Standards of Practice Committee of the American Society for Gastrointestinal Endoscopy (ASGE) prepared this text. In preparing this guideline, a search of the medical literature was performed by using PubMed from January 1980 through March 2014 by using the keyword(s) "gastric tumor," "gastric cancer," "gastric lymphoma," "gastric and adenocarcinoma," "gastrointestinal stromal tumor," "gastrointestinal endoscopy," "endoscopy," "endoscopic procedures," and "procedures." The search was supplemented by accessing the "related articles" feature of PubMed, with articles identified on PubMed as the references. Pertinent studies published in English were reviewed. Additional references were obtained from the bibliographies of the identified articles and from recommendations of expert consultants. When little or no data exist from well-designed prospective trials, emphasis is given to results from large series and reports from recognized experts. Guidelines for the appropriate use of endoscopy are based on a critical review of the available data and expert consensus at the time that the guidelines are drafted. Further controlled clinical studies may be needed to clarify aspects of this guideline. This guideline may be revised as necessary to account for changes in technology, new data, or other aspects of clinical practice. The recommendations were based on reviewed studies and were graded on the strength of the supporting evidence by using the GRADE criteria (Table 1).<sup>1</sup>*

*This guideline is intended to be an educational device to provide information that may assist endoscopists in providing care to patients. This guideline is not a rule and should not be construed as establishing a legal standard*

*of care or as encouraging, advocating, requiring, or discouraging any particular treatment. Clinical decisions in any particular case involve a complex analysis of the patient's condition and available courses of action. Therefore, clinical considerations may lead an endoscopist to take a course of action that varies from these guidelines.*

This revision of the 2006 document "The Role of Endoscopy in the Surveillance of Premalignant Conditions of the Upper GI Tract" has been expanded to include discussion of malignant conditions of the stomach.<sup>2</sup> ASGE documents addressing the role of endoscopy in malignant and premalignant conditions of the esophagus have been recently published.<sup>3,4</sup>

### PREMALIGNANT CONDITIONS OF THE STOMACH

#### Gastric polyps

**Sporadic gastric epithelial polyps.** Gastric polyp histology cannot be reliably distinguished by endoscopic appearance; therefore, biopsy or polypectomy is warranted when polyps are detected.<sup>5</sup> The majority (70%-90%) of gastric epithelial polyps are fundic gland polyps (FGPs) or hyperplastic polyps and are often incidental findings on endoscopy. Sporadic FGPs may develop in association with long-term proton pump inhibitor use and are not associated with an increased risk of cancer in the absence of familial adenomatous polyposis syndrome (FAP).<sup>6-8</sup> In contrast, hyperplastic polyps are associated with an increased risk of gastric cancer. Dysplastic elements and focal cancer have been found in 5% to 19% of hyperplastic polyps,<sup>9-12</sup> and some national guidelines recommend polypectomy of all gastric hyperplastic polyps greater than 0.5 cm to 1 cm.<sup>13</sup> Size greater than 1 cm and pedunculated morphology have been identified as risk factors for dysplasia in hyperplastic polyps.<sup>9</sup> Adenomatous polyps also have

**TABLE 1. GRADE system for rating the quality of evidence for guidelines<sup>1</sup>**

Quality of evidence	Definition	Symbol
High quality	Further research is very unlikely to change our confidence in the estimate of effect.	⊕⊕⊕⊕
Moderate quality	Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.	⊕⊕⊕○
Low quality	Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.	⊕⊕○○
Very low quality	Any estimate of effect is very uncertain.	⊕○○○

malignant potential.<sup>14-16</sup> Adenomatous polyps of the stomach should be endoscopically removed when possible, but recurrence has been reported in up to 2.6% after complete endoscopic excision,<sup>17</sup> and gastric cancer has been found in 1.3% of patients during follow-up.<sup>18</sup> Compared with EMR, endoscopic submucosal resection reduces tumor recurrences, yet increases the risk of procedural adverse events.<sup>19</sup> Endoscopy is recommended 1 year after adenomatous polyp resection, followed by surveillance endoscopy every 3 to 5 years, although this strategy has not been extensively studied. Hyperplastic and adenomatous polyps may occur in the presence of *Helicobacter pylori* (*H pylori*) infection and environmental metaplastic atrophic gastritis, and polypectomy should be performed.

#### Gastric polyps in FAP and Lynch syndrome.

Gastric polyps are common in individuals with FAP.<sup>20-30</sup> These are most often FGPs and are found in up to 88% of children and adults with FAP.<sup>23,31</sup> Adenomas also occur in the stomach of individuals with FAP.<sup>32-35</sup> When present, they are usually solitary and sessile and located in the antrum.<sup>30</sup> Cases of gastric adenocarcinoma associated with FGP have been described in patients with familial polyposis syndromes.<sup>36,37</sup> The risk of gastric cancer in FAP is incompletely characterized. Several multinational series have shown a higher incidence of gastric cancer in FAP patients,<sup>37-39</sup> whereas a U.S. study concluded that the risk was not significantly increased.<sup>28</sup>

There are also conflicting data regarding the risk of gastric cancer in individuals with Lynch syndrome.<sup>38,39</sup> In a Korean cohort of patients, the relative risk of the development of gastric cancer was 2.1-fold higher than in the general population.<sup>40</sup> Conversely, a Finnish cohort of Lynch syndrome patients did not have a higher prevalence of gastric cancer relative to the general population.<sup>41</sup> A recent prospective cohort study demonstrated a standardized incidence ratio of 9.78 (95% confidence interval [CI], 1.18-35.3) for the development of gastric cancer in subjects with a mismatch repair gene mutation over sex- and age-matched unaffected relatives.<sup>42</sup>

#### Gastric intestinal metaplasia and dysplasia

Patients with gastric intestinal metaplasia (GIM) may have a greater than 10-fold increased risk of gastric cancer than the general population.<sup>43</sup> GIM is recognized as a

pre-malignant condition that may be the result of an adaptive response to environmental stimuli such as *H pylori* infection, smoking, and high salt intake.<sup>43</sup> The potential benefits of surveillance were evaluated in 2 retrospective studies from the United Kingdom.<sup>44,45</sup> The incidence of gastric cancer was reported to be as high as 11%.<sup>45</sup> Endoscopic surveillance was associated with earlier stage cancer detection and improved survival.<sup>44,45</sup> Additionally, patients with GIM and high-grade dysplasia (HGD) were at significant risk of harboring a prevalent or incident cancer.<sup>45</sup> In both retrospective<sup>46,47</sup> and prospective<sup>48-50</sup> European studies of patients with GIM and HGD, the cancer detection rate with endoscopic surveillance ranged from 33% to 85%. A review of the management of patients with GIM suggests that for most U.S. patients, the risk of progression to cancer is low, and surveillance is not clinically indicated unless other risk factors for gastric cancer are present, such as a family history of gastric cancer and Asian heritage.<sup>51</sup> A recent European consensus statement suggested that if low-grade dysplasia is detected in a patient with GIM, a repeat surveillance EGD with a topographic mapping biopsy strategy should be performed within 1 year.<sup>52</sup> The optimal frequency of subsequent endoscopic evaluation is not known. Surveillance may be suspended when 2 consecutive endoscopies are negative for dysplasia. Patients with confirmed HGD should undergo surgical or endoscopic resection due to the high probability of coexisting invasive adenocarcinoma. Twenty-five percent of patients with HGD will progress to adenocarcinoma within a year.<sup>53</sup> If *H pylori* infection is identified, eradication should be performed. It remains controversial whether empiric *H pylori* treatment should be administered when GIM is diagnosed.

#### Pernicious anemia

The prevalence of gastric adenocarcinoma in patients with pernicious anemia, now considered to be associated with type A atrophic gastritis,<sup>54</sup> is reported to be 1% to 3%.<sup>55</sup> Most studies have shown a 2- to 3-fold increased incidence of gastric cancer in patients with pernicious anemia,<sup>56-61</sup> although a large U.S. population-based cohort study found an incidence of gastric cancer of 1.2%, similar to that of the general population.<sup>62</sup> The risk seems to be highest within the first year of diagnosis.<sup>56,58</sup> The benefits of endoscopic surveillance in patients with pernicious

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