Communication from the ASGE Standards of Practice Committee

GUIDELINE

Role of endoscopy in the staging and management of colorectal cancer

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. Additional references were obtained from the bibliographies of the identified articles and from recommendations of expert consultants. When limited or no data exist from well-designed prospective trials, emphasis is given to results from large series and reports from recognized experts. Guidelines for 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 (Table 1).[1] 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.

Colorectal cancer (CRC) is the third most commonly diagnosed cancer in American men and women and the second leading cause of cancer death.[2] This updated ASGE guideline focuses on the role of endoscopy in the staging and treatment of CRC. Recommendations for CRC screening and surveillance are discussed in previous documents by the Multi-Society Task Force endorsed by the ASGE.[3,4]

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PRESURGICAL LOCALIZATION

Colonoscopy has an important role in the localization of malignant lesions for subsequent identification at the time of surgery. Preoperative endoscopic marking can be helpful in localizing flat, small, or subtle colonic lesions that may be difficult to identify by inspection or palpation during surgery. Marking techniques currently available include endoscopic tattooing and metallic clip placement.[5-7] Tattoos with India ink are visible at surgery for up to 5 months.[5] No guidelines exist on the optimal placement of tattoos or metallic clips; therefore, close communication with surgical colleagues involved in the subsequent resection is important.

STAGING OF CRC

CRC is staged according to the TNM system established by the American Joint Committee on Cancer (Table 2).[8] The primary clinical impact of staging CRC is to differentiate T1N0 or T2N0 disease from T3 or TxN1-2 disease, for which chemoradiation is recommended in addition to surgical resection.[9] Several meta-analyses have evaluated the staging accuracy of EUS,[10-13] and some have compared the accuracy of EUS with that of magnetic resonance imaging (MRI) and CT.[10,11] In general, EUS was found to exhibit high sensitivity (80%-96%) and specificity (75%-98%) for the staging of T0 to T3 disease.[10-13] EUS may have higher T-staging accuracy than other cross-sectional imaging tests,[10] but nodal staging accuracy was modest for EUS (67% sensitivity, 78% specificity) and not statistically different among the 3 imaging modalities.[10,11] MRI may also have a role in guiding surgery because it shows the anatomic relationship between rectal tumors and the pelvic floor and sacrum. Correctly differentiating benign from malignant perirectal lymphadenopathy by EUS is difficult because inflammatory nodes may be present in the setting of rectal cancer; however, EUS-guided FNA (EUS-FNA) of perirectal lymph nodes may be helpful when the presence of nodal metastasis would change patient management.[14] The accuracy of EUS may be subject to publication bias and should be viewed with some caution.[15] In clinical practice, other imaging modalities may have comparable staging accuracy. A 2011 prospective study of 90 subjects found a T2 staging accuracy of 76% to 77% for both EUS and MRI and T3 staging accuracy of 76% for EUS and 83%

TABLE 1. GRADE system for rating the quality of evidence for guidelines[1]

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	⊕◯◯◯

TABLE 2. TNM staging classification of colorectal cancer

Primary tumor (T)	
TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
Tis	Carcinoma in situ: intraepithelial or invasion of lamina propria
T1	Tumor invades submucosa
T2	Tumor invades muscularis propria
T3	Tumor invades through the muscularis propria into the subserosa or into nonperitonealized pericolic or perirectal tissues
T4	Tumor directly invades other organs or structures and/or perforates visceral peritoneum
Regional lymph nodes (N)	
NX	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1	Metastasis in 1-3 regional lymph nodes
N2	Metastasis in ≥4 regional lymph nodes
Distant metastasis (M)	
MX	Distant metastasis cannot be assessed
M0	No distant metastasis
M1	Distant metastasis

for MRI ($P > .05$). MRI did not visualize any T1 tumors, and EUS understaged all T4 tumors in that series.[16] The finding of a nontraversable malignant stricture in the rectum may be predictive of advanced tumor stage (T3, T4, or Tx, N1 or 2) and should be locally staged by radiographic cross-sectional imaging.[17,18] The reported accuracy of EUS restaging after neoadjuvant chemoradiation has been modest to poor: 38% to 75% for T staging and 57% to 84% for N staging.[19-25] A prospective study of 90 subjects comparing CT, MRI, and EUS for T and N staging after neoadjuvant therapy found similarly low accuracy for all 3 modalities. T staging accuracy was 37% by CT, 34% by MRI, and 27% by EUS. N staging was 62% by CT, 68% by MRI, and 65% by EUS.

ENDOSCOPIC MANAGEMENT OF MALIGNANT COLONIC OBSTRUCTION

Endoscopic management of malignant obstruction is discussed in a recent ASGE Standards of Practice document.[26] Endoscopic alternatives to surgical decompression include placement of a self-expandable metal stent (SEMS), tumor debulking, and placement of a decompression tube. Even with successful endoscopic decompression, early surgical consultation is recommended because patients may deteriorate rapidly. Endoscopy should not be performed in patients with peritoneal signs or suspicion of perforation. Colonic SEMS may also be used as a "bridge to surgery" for patients with malignant obstruction who are surgical candidates. The success rate of single-stage elective surgery after colonic SEMS placement for decompression is 60% to 85%.[27] The major adverse events associated with colonic SEMS placement include obstruction, migration, and perforation.[28] In addition, dilation after colonic SEMS placement should be avoided because of the associated risk of perforation.[28]

ENDOSCOPIC RESECTION OF COLORECTAL NEOPLASIA

In general, flat and polypoid lesions found at the time of colonoscopy should be removed.[29] Pedunculated lesions are usually removed by using standard snare polypectomy. Pedunculated polyps with cancer confined to the submucosa and without evidence of unfavorable histological factors have a 0.3% risk of cancer recurrence or lymph node metastasis after complete endoscopic removal, and surgery is not necessary.[30]

For pedunculated polyps with unfavorable histological features (<1 mm cancer-free margin, poor histological differentiation, vascular or lymphatic invasion), invading the submucosa of the bowel wall below the polyp's stalk, or extending through the submucosa into the deeper wall

layers, surgery is recommended because endoscopic removal is unlikely to be curative.[31-33] The site of resection of such polyps should be inked with a tattoo to facilitate identification during surgery. In all cases of potential surgical referral, the risk of recurrent disease should be weighed against the operative risk in individual patients.

Endoscopic removal of larger sessile or flat lesions may require more advanced techniques. EMR and endoscopic submucosal dissection (ESD) are reviewed in a 2008 ASGE Technology Status Evaluation Report.[34] EMR is indicated for sessile or flat neoplastic lesions confined to the mucosa or submucosa of the colon. Lesions that are 2 cm or smaller can often be removed en bloc, whereas larger lesions may require piecemeal resection. Typically, a solution is injected into the submucosa to lift the lesion for easier removal and to provide a cushion to help protect the deeper layers of the bowel wall from mechanical or electrocautery damage. The inability to raise the base of a polyp after submucosal solution injection can indicate the presence of cancer invading deep into the submucosa and precludes endoscopic resection of the lesion.[35,36] Lesions that do not lift can be technically difficult to remove by EMR even if the cause of the nonlifting sign is not invasive malignancy (eg, from fibrosis from a previous biopsy or previous attempts at endoscopic resection).[37] Therefore, EMR should be attempted only if complete resection of neoplastic lesions is anticipated.

ESD was developed for en bloc resection of larger lesions (ie, >2 cm). After submucosal injection of a fluid cushion, the lesion is dissected from the deep layers of the bowel wall by using electrocautery knives. The adverse events of EMR and ESD in the removal of colorectal lesions are reviewed in a previous ASGE document.[28] The major adverse events are the same as those for standard polypectomy (ie, bleeding and perforation); however, the rate is higher.[28] The role of ESD for colorectal lesions is not well established. Compared with its use for gastric lesions, ESD in the colon is more technically challenging because of less space, difficult positioning, thinner bowel wall, and the presence of colonic folds.[34] EMR is widely used to remove benign flat neoplastic lesions in the colon including those with high-grade dysplasia. EMR can also be definitive treatment for intramucosal (T1mN0) CRC in which the risk of lymph node involvement is negligible.[31,33,38,39]

The optimal technique to minimize the risk of residual neoplasia during piecemeal EMR is evolving. Residual polyp tissue may have contributed to previous reports of interval cancers after colonoscopy with polypectomy.[4,40] In general, the most important principle is to maximize potential for complete eradication on the initial resection attempt. This may necessitate referral to a center with expertise in advanced polypectomy. All visible adenomatous tissue should be endoscopically resected or ablated if snare excision is not feasible. Techniques to minimize residual polyp tissue include taking a small margin of surrounding mucosa at the polyp edges[41] or tissue ablation. Tissue ablation has been described both prophylactically at the resection margins after a piecemeal removal and for the treatment of endoscopically visible residual polypoid tissue. Ablation techniques have been primarily described with argon plasma coagulation (APC),[42-44] with 1 report of diathermy ablation with the snare tip.[41] Estimates of short-term (2-6 months) residual/recurrence rates after piecemeal EMR are broad, ranging from 0% to 55%.[45] Late recurrence (after 12 months) is less common, occurring in less than 5% in 1 study.[45] A small, randomized study evaluating the use of prophylactic APC at piecemeal polypectomy sites where complete excision was thought to be achieved by the endoscopist produced a lower risk of recurrence in the APC group (1/10 vs 7/11, $P = .02$), that was statistically significant.[42] In a larger, more recent study of 479 patients with 514 colonic lesions evaluating the safety and efficacy of EMR, use of APC was an independent predictor of recurrence after presumed effective EMR.[41] The authors of this study reported a 20% recurrence rate and did not prophylactically treat the polyp edges with APC, reserving APC for visible tissue not amenable to snare excision.

Regardless of the technique used, close surveillance after piecemeal polypectomy is mandatory given the potential for recurrence. To facilitate surveillance, tattooing should be considered for polyps that cannot readily be identified by anatomic landmarks. A detailed review of endoscopic tattooing is available in a 2010 ASGE Technology Status Evaluation Report.[5] Ideally, the tattoo should be distinct from the polypectomy site to avoid fibrotic tissue reaction that can be associated with tattooing agents. No guidelines exist on the optimal placement of a tattoo, but some experts have suggested standardizing a tattoo injection to 3 cm downstream from the lesion.[41] Photodocumentation of the polypectomy site in relation to the area of tattoo may be helpful during subsequent surveillance examinations to allow for accurate identification of the scar site if no visible tissue is found. Guidelines recommend a follow-up colonoscopy in 2 to 6 months after piecemeal EMR of large sessile lesions, with both endoscopic and pathological assessments to ensure complete removal.[4,40] One retrospective study found that on the first follow-up surveillance endoscopy, a normal endoscopic appearance of the polypectomy site and negative scar biopsy specimens were predictive of long-term eradication in 97.9% of such cases.[45]

Surgery should be considered for sessile lesions removed piecemeal that are found to be malignant because the adequacy of the resection margin cannot be determined.[46] Malignant lesions with submucosal invasion are associated with a 6% to 12% risk of lymph node metastasis and should also be managed surgically.[47-51] EMR should not be used for ulcerated lesions or lesions that do not lift.[34]

RECOMMENDATIONS

- We recommend removal of suspected neoplastic lesions at the time of colonoscopy when not contraindicated and as technical expertise allows. ⊕⊕⊕⊕
- We recommend EUS in the preoperative locoregional staging of CRC to guide therapy. ⊕⊕⊕○
- We recommend weighing the risk of recurrence against the individual's operative risk in all cases in which surgery is being considered as a treatment for CRC. ⊕⊕⊕○
- We recommend surgical management of all malignant polyps with unfavorable histological features if the patient is an appropriate surgical candidate. ⊕⊕⊕○
- We recommend that pedunculated polyps found to contain cancer confined to the submucosa of the polyp or stalk and with favorable histological features be managed endoscopically. ⊕⊕⊕○
- We recommend surgery for sessile or flat colonic neoplasia that demonstrates submucosal invasion if the patient is an appropriate surgical candidate. ⊕⊕⊕○
- We suggest surgical management for sessile or flat colonic neoplasia that is determined to be malignant after piecemeal endoscopic resection if the patient is an appropriate surgical candidate. ⊕⊕○○
- We recommend EMR only be attempted if complete resection of neoplastic lesions is anticipated. ⊕⊕⊕○

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Abbreviations: APC, argon plasma coagulation; CRC, colorectal cancer; ESD, endoscopic submucosal dissection; EUS-FNA, EUS-guided FNA; MRI, magnetic resonance imaging; SEMS, self-expandable metal stents.

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