ASGE guideline: the role of endoscopy in the surveillance of premalignant conditions of the upper GI tract

This is one of a series of statements discussing the utilization of gastrointestinal endoscopy in common clinical situations. The Standards of Practice Committee of the American Society for Gastrointestinal Endoscopy prepared this text. In preparing this guideline, a MEDLINE literature search was performed, and 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 appropriate utilization of endoscopy are based on a critical review of the available data and expert consensus. Further controlled clinical studies are needed to clarify aspects of this statement, and revision may be necessary as new data appear. Clinical consideration may justify a course of action at variance to these recommendations.

INTRODUCTION

Cancer of the upper gastrointestinal (UGI) tract may develop in association with several underlying diseases. Surveillance of premalignant UGI conditions refers to endoscopic follow-up of individuals who are at increased risk for malignancy or in whom a neoplastic lesion has been identified and removed. The natural history of many of these premalignant conditions is not well characterized, and published surveillance data are limited by both lead-time and length-time bias. This guideline addresses the following conditions: Barrett's esophagus, achalasia, caustic ingestion, tylosis, upper aerodigestive tract cancer, gastric epithelial polyps, intestinal metaplasia of the stomach, pernicious anemia, postgastrectomy, familial adenomatous polyposis, and hereditary nonpolyposis colorectal cancer syndrome. This review updates the 1998 ASGE guideline on this subject.[1]

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ESOPHAGEAL CANCER

Barrett's esophagus

Barrett's esophagus is defined as specialized intestinal metaplasia of the distal tubular esophagus irrespective of length.[2] The recognition of Barrett's esophagus as the premalignant precursor to adenocarcinoma has led to societal statements and recommendations regarding surveillance endoscopy.[1,3,4] Controversy exists, however, regarding the clinical efficacy of both screening and surveillance, as evidenced by a recent workshop of recognized experts in Barrett's esophagus.[5] Retrospective U.S. published data suggest a survival benefit in patients with Barrett's esophagus who undergo endoscopy at least 1 year before a diagnosis of carcinoma,[6,7] while other surveillance studies demonstrate a shift toward earlier stage tumors and a higher resectability rate.[8,9] Conversely, European investigators demonstrate the lack of an overall mortality benefit in patients undergoing long-term Barrett's surveillance,[10-13] with an observed cancer incidence rate of 1 in 200 patient years.[11] Economic models suggest that screening high-risk individuals (eg, white males, chronic reflux, age >50 years) is cost effective compared to no screening.[14-16] These models, however, conflict with each other regarding the cost effectiveness of further surveillance in patients with Barrett's esophagus who are nondysplastic.[15,16]

An initial screening endoscopy may be appropriate in selected patients with frequent (eg, several times per week), chronic, long-standing GERD (eg, >5 years). Patients at increased risk for Barrett's are typically white males aged >50 years and those with nocturnal reflux. Patients with a normal screening EGD need no further screening examinations.[3]

When Barrett's esophagus is identified, multiple systematic biopsy specimens should be obtained, and a biopsy of any macroscopic lesions in particular should be performed. While the optimal biopsy protocol has not been established, one accepted approach is to obtain 4 quadrant biopsy specimens every 2 cm.[17] The use of maximum capacity ''jumbo'' biopsy forceps may improve the yield and should be considered, especially in patients with dysplasia. Biopsy specimens should be classified as containing carcinoma, high-grade dysplasia (HGD), low-grade dysplasia (LGD), indefinite for dysplasia, or no

dysplasia. The characterization of HGD should be confirmed by an expert GI pathologist.

In patients with Barrett's esophagus with no evidence of dysplasia on initial endoscopy, a repeat endoscopy should be performed within the next year. If no dysplasia is confirmed, these patients are considered to be at low risk to have their condition progress and/or develop cancer. Therefore, the interval for additional surveillance has been recommended to be every 3 years.[3] A recent AGA consensus statement, however, has recommended this interval be lengthened to 5 years, on the basis of decision analysis models.[4]

Patients with HGD are at significant risk for having or developing adenocarcinoma.[18] Patients with more diffuse HGD may have an increased cancer risk compared to those with unifocal HGD,[19] although this is debated.[20] Surveillance endoscopy may be acceptable for patients with HGD without carcinoma, particularly in patients with contraindications to or who refuse surgery. In these cases, surveillance should be done at frequent intervals (eg, every 3 months) with an extensive biopsy protocol (eg, 4-quadrant jumbo biopsies every 1 cm with additional biopsies of macroscopic abnormalities).[17,21] If no dysplasia is found on 2 consecutive endoscopies, the interval may be lengthened to, for example, every 6 months for 1 to 2 years and then yearly as long as no dysplasia is reencountered.[21] A wide variety of endoscopic mucosal ablative techniques have been developed for managing HGD.[22] Patients who have undergone endoscopic therapy should continue to have surveillance at intervals appropriate to the highest grade dysplasia pretreatment. The clinical significance of LGD is less well understood, and there is a high degree of interobserver variability in this histologic diagnosis.[23] In one surveillance study of patients with Barrett's esophagus and LGD, 60% of patients regressed to no dysplasia, 12% persisted with stable LGD, and 28% progressed to HGD and/or carcinoma.[23] The rate of progression to HGD or cancer may be higher in those with LGD at baseline endoscopy.[24] Surveillance (eg, every 1 year) has been recommended in Barrett's esophagus with LGD.[3]

Longer segment length of Barrett's appears to moderately increase the risk of developing dysplasia.[25-27] Surgical antireflux procedures do not seem to decrease the incidence of cancer development in patients with Barrett's esophagus.[5,28] Recent retrospective and epidemiological data suggest that PPI and NSAIDs may be chemoprotective.[29] Furthermore, by resolving reflux esophagitis, proton pump inhibitors may be useful to histologically differentiate inflammatory changes from dysplasia.

The use of unsedated endoscopy may be a feasible and cost-saving approach for screening and surveillance but requires a motivated patient who will forgo conscious sedation.[30] The use of chromoendoscopy and enhanced endoscopic imaging to highlight an area for targeted biopsies shows promise,[31,32] but the results appear to be poorly reproducible.[33,34] The use of flow cytometry or other molecular markers to stratify patients with low cancer risk from patients with high cancer risk for further follow-up appears to be promising.[35] EUS may be useful in selected patients with HGD to exclude cancer or in those in whom endoscopic treatments are being considered.[36,37] Capsule endoscopy of the esophagus has recently become available, and a prospective study found comparable sensitivity and specificity to standard endoscopy.[38] The cost effectiveness of capsule endoscopy for Barrett's screening is not yet defined.

Recommendations

1. Screening EGD for Barrett's esophagus should be considered in selected patients with chronic, longstanding GERD. After a negative screening examination, further screening endoscopy is not indicated.
2. The cost effectiveness of surveillance in patients without dysplasia is controversial. Surveillance endoscopy is appropriate for patients fit to undergo therapy, should endoscopic/histologic findings dictate. For patients with established Barrett's esophagus of any length and with no dysplasia, after 2 consecutive examinations within 1 year, an acceptable interval for additional surveillance is every 3 years.
3. Patients with HGD are at significant risk for prevalent or incident cancer. Patients who are surgical candidates may elect to have definitive therapy. Patients who elect surveillance endoscopy should undergo follow-up every 3 months for at least 1 year, with multiple large capacity biopsy specimens obtained at 1 cm intervals. After 1 year of no cancer detection, the interval of surveillance may be lengthened if there are no dysplastic changes on 2 subsequent endoscopies performed at 3-month intervals. High-grade dysplasia should be confirmed by an expert GI pathologist.
4. Surveillance in patients with LGD is recommended. The significance of LGD as a risk factor for cancer remains poorly defined; therefore the optimal interval and biopsy protocol has not been established. A follow-up EGD (ie, at 6 months) should be performed with concentrated biopsies in the area of dysplasia. If LGD is confirmed, then one possible management scheme would be surveillance at 12 months and yearly thereafter as long as dysplasia persists.
5. If the presence or degree of dysplasia is indeterminate and there is evidence of acute inflammation due to gastroesophageal acid reflux, repeat biopsy should be performed after 8 weeks of effective acid-suppression therapy.

Achalasia

The risk for patients with achalasia developing squamous cell carcinoma of the esophagus appears to be higher than in the general population. Risk estimates in

clinical studies have varied, influenced by patient number, selection, and duration of follow-up.[39] The prevalence of esophageal cancer in achalasia patients has ranged from 0.4% to 9.2% in most series.[40-47] Incidence has ranged from 1 in 2443 to 1 in 173 cancer cases per patient-years of follow-up,[41-43,46,48] although 1 study with limited follow-up found no incident cancers.[49] Most studies have found an increased cancer risk ranging from 7- to 33-fold compared with the general population,[41,43,45,46] with 1 recent prospective surveillance study from Germany reporting a 140-fold risk.[48] It is not clear whether surgical myotomy,[40,45,48,50] balloon dilation,[40,45,48,50] medical treatment with calcium-channel blockers, or injection of botulinum toxin affects the subsequent risk of cancer.[48] Most cases of esophageal cancer are squamous cell carcinoma, although some cases of adenocarcinoma associated with Barrett's esophagus have been reported,[48,51] predominantly after myotomy.

The duration of symptoms of achalasia before the diagnosis of esophageal cancer is usually at least 15 years.[40,41,43,44,47,48] The mean age at diagnosis in most studies is 48 to 71 years. The prognosis of esophageal cancer in achalasia is poor.[48] The role of endoscopic surveillance in achalasia is controversial. Despite the lack of demonstrable cost effectiveness, several authors have advocated periodic endoscopy as reasonable after 15 years of symptoms.[39,43,44,48,50]

Recommendations

1. There are insufficient data to support routine endoscopic surveillance for patients with achalasia.
2. If surveillance were to be considered, it would be reasonable to initiate it 15 years after onset of symptoms, but the subsequent surveillance interval is not defined.

Caustic injury

There appears to be an increased risk of developing squamous cell carcinoma of the esophagus after severe caustic injury to the esophagus, most commonly after lye ingestion. The incidence of cancer in corrosive strictures has been estimated to be 2.3% to 6.2%, and a history of caustic ingestion was present in 1% to 4% of patients with esophageal cancer.[52-55] A single series from Finland found the magnitude of risk was approximately 1000-fold increased compared with a similar population.[52]

Clinical characteristics of patients who developed esophageal cancer after caustic injury include[53-57]: mean age 35 to 51 years; average interval between caustic injury and development of esophageal cancer approximately 40 years; and cancers located in the mid-esophagus. The prognosis in some series appears to be better than that for patients with sporadic esophageal cancer.[52,54,57] There are no data from prospective surveillance programs.

Recommendations

1. Begin endoscopic surveillance 15 to 20 years after caustic ingestion.
2. The time interval of endoscopic surveillance requires study. Generally, endoscopic examination should not be conducted more frequently than every 1 to 3 years. There should be a low threshold to evaluate swallowing problems with endoscopy.

Tylosis

Tylosis is a rare genetic disorder characterized by hyperkeratosis of the palms and soles, transmitted in an autosomal dominant pattern. It is associated with a high incidence of development of squamous cell carcinoma of the esophagus.[58-61] In the initial reports, esophageal cancer was found in 18 of 48 patients with tylosis, and the incidence was estimated at 95% by age 65 years.[58,60] Mean age at onset of esophageal cancer was 45 years, and death from esophageal cancer occurred in patients as young as 30 years. Late onset tylosis (type A), which typically presents between ages 5 and 15 years, has been described in about 10 genealogies and is associated with a mean esophageal cancer incidence of 27%.[62] Early onset tylosis (type B) presents by 1 year of age and is not associated with esophageal malignancy.[59-62] Esophageal malignancies associated with tylosis are predominantly in the distal esophagus.[58] Preliminary results of an endoscopic surveillance program of 1 of the tylosis families reported that 14% of subjects developed dysplasia over a mean follow-up period of 5 years and 1 patient developed squamous cell carcinoma.[63]

Recommendations

1. Begin endoscopic surveillance at age 30 years.
2. The time interval of endoscopic surveillance requires study. Generally, endoscopic examination should not be conducted more frequently than every 1 to 3 years.

History of upper aerodigestive tract cancer

There is an association between previous or current squamous cell cancer of the head and neck (oral cavity, oropharynx, hypopharynx, or larynx), lung, or esophagus with synchronous or metachronous squamous cell carcinoma of the esophagus. The incidence of multiple squamous cell carcinomas of the upper aerodigestive tract ranges from 3.7% to 30.0%, probably related to a common exposure to alcohol and tobacco.[39,64,65] Prospective studies of endoscopy in patients with head and neck cancer, predominantly men, have found an incidence of synchronous and/or metachronous esophageal cancer of 2.5% to $>$13.9%.[66-72] Metachronous esophageal cancers have been identified at varying intervals, and the risk does not appear to decrease with time.[64-67,69-72] Studies using Lugol dye staining in endoscopy have demonstrated utility

in detecting early stage esophageal cancer and esophageal dysplasia.[67-69,71,73]

The role of endoscopic screening and surveillance in patients with upper aerodigestive tract cancers is controversial. Despite the lack of demonstrable cost effectiveness or prolonged survival, several authors have advocated periodic endoscopy.[39,69,71,72]

Recommendations

1. There are insufficient data to support routine endoscopic surveillance for patients with previous aerodigestive squamous cell cancer.
2. A single endoscopy may be indicated to identify synchronous esophageal cancer.

GASTRIC CANCER

Gastric epithelial polyps

The majority of gastric epithelial polyps found during endoscopy are incidental and frequently either of hyperplastic or fundic gland histology (70%-90%).[1] These polyps, in particular fundic gland polyps, were thought to be of no malignant potential. Fundic gland polyps may develop in association with long-term proton pump inhibitor use but have not been associated with an increased risk of cancer.[74] Adenomatous polyps have malignant potential, and this risk correlates with size and older patient age.[75] Patients with adenomatous polyps should have complete excision and surveillance endoscopy to ensure no recurrence. Polyp histology cannot be reliably distinguished by endoscopic appearance, and therefore either biopsy or polypectomy is warranted in any suspicious lesion.[76] Hyperplastic polyps may have an increased risk of cancer. The importance of adequate sampling is highlighted by recent reports of dysplastic elements being present in up to 19% of hyperplastic polyps, including some cases of focal cancer,[77-79] leading some authors to recommend polypectomy of all lesions >0.5 cm.[77] Adenomatous and hyperplastic polyps may occur in the presence of chronic gastritis and/or *H pylori* infection. Topographic biopsy ''mapping'' may be useful to detect the presence of gastritis and intestinal metaplasia.

Surveillance of patients in whom gastric polyps have been previously resected has not been extensively studied. Recurrence of adenomatous polyps has been reported in 0.0% to 5.2%.[80,81] Gastric cancer has been found in 1.3% of patients during follow-up.[82]

Recommendations

1. Adenomatous gastric polyps are at increased risk for malignant transformation and should be resected completely. Hyperplastic polyps have a rare malignant potential. Endoscopic polyp appearance cannot differentiate histologic subtypes; therefore biopsy or polypectomy is recommended when a polyp is encountered.
2. Polypoid defects of any size detected radiographically should be evaluated endoscopically, with biopsy and/or removal of the lesions.
3. Polyps should be endoscopically excised wherever feasible and clinically appropriate. If endoscopic polypectomy is not possible, a biopsy of the polyp should be performed, and if adenomatous or dysplastic tissue is detected, referral for surgical resection should be considered. If representative biopsy samples are obtained and the polyp is nondysplastic, no further intervention is necessary. If it is felt that endoscopic biopsy cannot sufficiently exclude the presence of dysplastic elements, referral for surgical resection is reasonable in polyps that cannot be removed endoscopically.
4. When multiple gastric polyps are encountered, a biopsy of the largest polyps should be performed or they should be excised, and representative biopsy specimens should be taken from some others. Further management should be based on histologic results.
5. Surveillance endoscopy 1 year after removing adenomatous gastric polyps is reasonable to assess recurrence at the prior excision site, new or previously missed polyps, and/or supervening early carcinoma. If the results of this examination are negative, repeat surveillance endoscopy should be repeated no more frequently than at 3- to 5-year intervals. Follow-up after resection of polyps with high-grade dysplasia and early gastric cancer should be individualized.
6. No surveillance endoscopy is necessary after adequate sampling or removal of nondysplastic gastric polyps.

Gastric intestinal metaplasia and dysplasia

Gastric intestinal metaplasia (IM) is recognized as a premalignant condition that may be the result of an adaptive response to environmental stimuli such as *H pylori* infection, smoking, and high salt intake.[83] Patients with IM may have a >10-fold increased risk of developing gastric cancer,[83] which may be highest in certain geographical areas (eg, Japan) and in patients infected with *H pylori*.

The potential benefits of surveillance have been evaluated in 2 retrospective studies from the UK. Cancer incidence was as high as 11%, and surveillance was associated with both finding more early gastric cancers and improved survival.[84,85]

Patients with confirmed HGD are at significant risk for harboring a prevalent or incident cancer. In both retrospective[86,87] and prospective[88-90] European studies of patients with HGD, the incidence of cancer detection with endoscopic surveillance ranged from 33% to 85%. Early stage gastric cancer was seen in 62% of patients in 1 surveillance cohort.[88]

One recent review of the management of a patient with gastric intestinal metaplasia suggests that for most U.S. patients the risk of progression to cancer is low and

surveillance is not clinically indicated in an ''average risk'' patient.[91] Other reviews suggest that if low grade dysplasia is detected in a patient with IM, then surveillance EGD with a topographic mapping biopsy strategy should be performed every 3 months, at least for the first year. Surveillance should be suspended when 2 consecutive endoscopies show negative results. Patients with confirmed HGD should undergo surgical or endoscopic resection because of the high probability of coexisting invasive adenocarcinoma.[92]

Patients with gastric cancer have a greater prevalence of IM involving the lesser curvature. Topographic biopsy ''mapping'' from the lesser curvature in high-risk patients may yield useful information for the assessment of cancer risk.[93] In addition, if *H pylori* infection is identified, eradication should be considered because it is a class I carcinogen.[94]

Recommendations

1. Endoscopic surveillance for gastric intestinal metaplasia has not been extensively studied in the U.S. and therefore cannot be uniformly recommended.
2. Patients at increased risk for gastric cancer due to ethnic background or family history may benefit from surveillance.
3. Endoscopic surveillance should incorporate a topographic mapping of the entire stomach.
4. Patients with confirmed high-grade dysplasia are at significant risk for progressing to cancer and should be considered for gastrectomy or local (eg, endoscopic) resection.

Pernicious anemia and gastric carcinoid tumors

There may be an increased risk of gastric cancer, as well as gastric carcinoid tumors, in patients with pernicious anemia. The prevalence of gastric neoplasia in patients with pernicious anemia, now considered to be associated with type A atrophic gastritis,[95] is reported to be about 1% to 3% for adenocarcinoma and 1% to 7% for gastric carcinoid.[96] Most studies have shown an increased incidence of gastric cancer in patients with pernicious anemia on the order of 2 to 3 fold,[97-102] 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.[103] The risk seems to be highest within the first year of diagnosis.[98,99]

The benefits of surveillance in patients with pernicious anemia have not been established.[96,104-106] Gastric carcinoma, in addition to gastric carcinoids, has been found in only some prospective series of patients undergoing follow-up endoscopy.[96,105] A recent series from Italy found no gastric carcinoma after an initial follow-up of either 2 or 4 years.[106] Most investigators suggest it would be reasonable to perform endoscopy relatively soon after the diagnosis of pernicious anemia and/or to endoscope patients who develop upper gastrointestinal symptoms.[96,97,103-105]

Gastric carcinoids can be classified as type 1 (associated with type A chronic atrophic gastritis), type 2 (associated with Zollinger-Ellison syndrome and MEN-1), and type 3 (sporadic gastric carcinoids). Type 1 is the most common type of gastric carcinoid encountered in clinical practice (68%-83%)[107,108] and usually has a benign clinical course, although occasionally it may be symptomatic or metastasize. Clinical management is not well defined.[107-109] Endoscopic evaluation should include carcinoid size, number, and extent. Management options include endoscopic surveillance alone, endoscopic removal of smaller lesions (<1 cm) if few (3-5), and surgical excision. Antrectomy may result in regression of smaller gastric lesions. Subsequent surveillance is indicated. EUS may be useful when there is diagnostic doubt or to determine depth of involvement before resection.[110,111] Total gastrectomy is indicated for invasive tumors, failure of antrectomy to control disease, or refractory GI bleeding.[107,108,112]

Recommendations

1. A single endoscopy should be considered to identify prevalent lesions (gastric cancer, carcinoid tumors) in patients with pernicious anemia, but there are insufficient data to support routine subsequent endoscopic surveillance for these patients.
2. Surveillance of carcinoid tumors is controversial and should be individualized to the patient.

Postgastric surgery

There may be an increased risk of gastric cancer in patients previously operated on for benign gastric or duodenal ulcer. Reported frequencies of gastric remnant carcinoma vary from 0.8% to 8.9%.[113-124] Endoscopic follow-up studies have detected gastric cancer in 4% to 6% of these patients, and the dysplasia to carcinoma sequence has been described.[116,119-121,124] Other population-based studies have not confirmed an increased risk.[115,125] The risk appears to increase 15 to 20 years after the initial surgery.[114,117-119,122-124,126]

Recommendations

1. There are insufficient data to support routine endoscopic surveillance for patients with previous partial gastrectomy for peptic ulcer disease.
2. Because gastric surgeries are performed for peptic ulcer disease, an index endoscopy should be performed to establish the presence of *H pylori* infection, chronic gastritis, and/or intestinal metaplasia.
3. If surveillance is considered, it should be initiated after an interval of 15 to 20 years. Multiple biopsies from the anastomosis and gastric remnant should be taken. The threshold should be low in order to endoscopically evaluate upper gastrointestinal symptoms.

FAMILIAL ADENOMATOUS POLYPOSIS AND HEREDITARY NONPOLYPOSIS COLORECTAL CANCER

Upper gastrointestinal polyps are common in individuals with familial adenomatous polyposis (FAP).[127-137] Gastric polyps are most often fundic gland polyps (FGPs) and are found in up to 88% of children and adults with FAP.[129,138] Dysplasia is found in FGPs in 45% of adults and 31% of children at a mean of 14.4 years.[138] The malignant potential of dysplastic FGP appears negligible given the high prevalence of disease; however, cases of gastric adenocarcinoma associated with FGPs have been described.[139,140] Adenomas occur in the stomach of individuals with FAP with a prevalence ranging from 2% to 50%.[141-144] When present, they are usually solitary, sessile, and located in the antrum.[128] Gastric cancer is uncommon; it occurred in 0.6% of patients in one series,[145] and in a U.S. study it was not significantly increased.[130] In contrast, Japanese series have shown a relatively higher incidence of gastric cancer in FAP patients.[146,147]

Duodenal adenomas occur in up to 90% of adult FAP patients, with a prevalence of 41% for those in their mid teens.[137,138] Duodenal adenomas occur primarily on the major duodenal papilla or in the periampullary region.[128] A classification of duodenal polyposis (Spigelman classification) based on polyp number, size, histology, and severity of dysplasia has been used to identify a high-risk group.[128,134,135] Adenomatous change of the papilla may not be apparent without biopsy, with adenomatous changes found in 50% of patients in some series.[129,131] Pancreatitis has been reported after biopsies of the papilla. Jejunal and ileal polyps, usually small, may also be present and have been detected in 50% to 90% of patients undergoing push-enteroscopy or capsule endoscopy in small series,[148-150] although in one study a significantly increased rate of development of adenocarcinoma was not found.[130] Capsule endoscopy has been used to assess polyposis in FAP and can detect duodenal and distal intestinal polyps but is not useful for assessing the papilla.[150-152]

Adenocarcinoma developing from duodenal adenomas, particularly in the periampullary region, is well recognized and a leading cause of death in patients with FAP who have had colectomy.[128,131] The risk of duodenal cancer is related to the stage of duodenal polyposis. The overall risk of duodenal cancer in FAP is 5%, but individuals with the most advanced stage disease (Spigelman III-IV) have a 7% to 36% risk of developing cancer at a median age of 52 to 68 years versus a risk of $\leq$2% for those with earlier stage disease.[134,135,137] Duodenal adenocarcinoma has been estimated to be $>$100-fold increased compared with the general population.[130] The adenoma-carcinoma sequence has been established, although in large series of duodenal polyposis, progression in patients with FAP has been variable.[131,134,135,137,153,154] Adenocarcinoma development has been reported in patients undergoing surveillance.[131,134,135,137] Recent prospective surveillance studies found a high rate of duodenal polyposis progression and cumulative risk of late stage (Spigelman stage IV) duodenal polyposis, with an estimated cumulative risk of 50% at age 70 years.[137,154]

The efficacy of surveillance programs and appropriate intervals have not been determined. Recommendations for surveillance are based on prospective cohort studies and expert opinion. Treatment options for patients with advanced adenomas or dysplasia include endoscopic modalities and surgery.[137,155,156,159] Endoscopic papillectomy in FAP for papillary adenomas has been reported with long-term success rates in up to 67% of patients, and complications (including pancreatitis, bleeding, cholangitis, and, rarely, death) have been reported in up to 25% of patients.[157,158,160] Options besides snare polypectomy are endoscopic ablative techniques including multipolar electrocoagulation, laser, and argon plasma coagulation. The high risk of recurrence of duodenal and periampullary polyposis with local therapy makes it an unattractive option for control of disease, and often it is followed by surgical therapy for definitive treatment.[157,161,162] The frequency and extent of endoscopic resections required to make an impact in downstaging patients with FAP often obviates its benefit. The use of local therapies, whether endoscopic or surgical, should be tempered by the realization that recurrence is frequent and ultimately will not downstage patients with Spigelman III and IV. These local therapies should be selected carefully for patients with intermediate Spigelman stage with a dominant lesion. A study of the use of celecoxib therapy has shown it to be mildly effective in decreasing duodenal polyposis,[163] but long-term results are not available and there is potential for adverse events.

There is a lack of strong evidence to support the benefit of surveillance for the detection of early duodenal cancer or prevention of death from duodenal cancer, and individuals with FAP under surveillance develop invasive cancer.[164,165] Currently, the impetus for endoscopic surveillance is to detect advanced benign duodenal disease and refer for early surgical intervention before cancer develops. Prophylactic, pancreas-sparing duodenectomy to prevent duodenal/periampullary cancer is recommended when advanced duodenal polyposis (stage IV) is detected.

Cancers of the small bowel and stomach are significantly increased in individuals with hereditary nonpolyposis colorectal cancer (HNPCC) syndrome wherein family members at high risk for carrying the deleterious gene are shown to have 25 times and 4 times the expected number of diagnoses of these tumors, respectively.[166] The degree of risk of gastric cancer in patients with HNPCC is variable. Gastric cancer has been reported to be the second most common extracolonic cancer, after endometrial cancer.[167] In a Korean cohort of patients with

HNPCC, the relative risk of developing gastric cancer was 2.1-fold higher than in the general Korean population.[168] Patients at particular risk were younger patients in their thirties (11.3-fold risk) and forties (5.5-fold risk). Conversely, a Finnish cohort of patients with HNPCC was not found to have a higher prevalence of gastric cancer versus a population control.[169] Less common cancers that occur in excess in HNPCC families include small-bowel cancer.[170] HNPCC-associated small-bowel cancer may present at a young age (median age 39), may be the first tumor manifestation, and occurs with decreasing frequency from duodenum to ileum, with about 50% of occurrences in the duodenum.[171] It has been suggested that upper endoscopy or push-enteroscopy starting at age 30 years might be beneficial for early detection of proximal small-bowel cancer.[171] Although no surveillance data for gastric or small-bowel cancer is available to make recommendations for patients with HNPCC, endoscopic surveillance should be considered.

Recommendations

1. Patients with FAP should undergo upper endoscopy with both end-viewing and side-viewing instruments. The optimal timing of initial upper endoscopy is unknown, but could be performed around the time the patient is considered for colectomy, or early in the third decade of life. If no adenomas are detected, another exam should be performed in 5 years because adenomatous change may occur later in the course of the disease.
2. For patients with duodenal and periampullary adenomas, surveillance endoscopy and biopsy should be performed at intervals based on stage of disease. Endoscopic treatment of papillary adenomas may be appropriate in selected patients. If excision is complete, one approach is for follow-up endoscopy and multiple biopsies every 6 months for a minimum of 2 years, with endoscopy thereafter at 3-year intervals.
3. A biopsy of the duodenal polyps should be performed or sampled at the time of initial discovery and on each subsequent examination to determine the stage of duodenal polyposis. The frequency of exams and referral for prophylactic surgery are determined on the basis of duodenal polyp stage.
4. Biopsies of gastric polyps in patients with FAP may be performed to confirm that they are fundic gland polyps and to assess for dysplasia. Antral polyps are usually adenomas and should be resected.
5. Surgical consultation should be obtained for those patients with advanced (stage IV) duodenal polyposis in an effort to prevent periampullary/duodenal carcinoma. Management of high-grade dysplasia in the periampullary region (surgery/ablative therapy vs. more frequent surveillance) is controversial and must be individualized.
6. Patients with HNPCC are at increased risk for the development of gastric and small-bowel cancer. Although there is insufficient data to show a benefit for upper endoscopic surveillance in patients with HNPCC, endoscopic surveillance should be considered.

SUMMARY

- Patients with chronic GERD at risk for Barrett's esophagus should be considered for endoscopic screening (*B*).
- In patients with Barrett's esophagus without dysplasia, the cost effectiveness of surveillance endoscopy is controversial. If surveillance is performed, an interval of 3 years is acceptable (*C*).
- Although an increased cancer risk has not been established in patients with Barrett's esophagus and low grade dysplasia, endoscopy at 6 months and yearly thereafter should be considered (*C*).
- Patients with Barrett's esophagus with confirmed HGD should be considered for surgery or aggressive endoscopic therapy (*B*). Patients with HGD who elect endoscopic surveillance should be followed-up closely (ie, every 3 months) for at least 1 year. If no further HGD is confirmed, then the interval between follow-ups may be lengthened (*B*).
- There are insufficient data to recommend routine surveillance for patients with achalasia (*C*).
- Patients with a severe caustic esophageal injury should undergo surveillance every 1 to 3 years beginning 15 to 20 years after the injury (*C*).
- Patients with tylosis should undergo surveillance endoscopy every 1 to 3 years beginning at age 30 years (*C*).
- There are insufficient data to support routine endoscopic surveillance for patients with previous aerodigestive squamous cell cancer (*C*).
- Adenomatous gastric polyps should be resected because of the risk for malignant transformation (*B*). Adenomatous polyps may recur in synchronous and metachronous sites, and surveillance endoscopies should be performed at 3- to 5-year intervals (*C*).
- Endoscopic surveillance for gastric intestinal metaplasia has not been extensively studied in the U.S. and therefore cannot be routinely recommended (*C*). However, there may be a subgroup of high-risk patients who will benefit from endoscopic surveillance (*B*).
- Patients with confirmed gastric high-grade dysplasia should be considered for gastrectomy or local resection because of the high incidence of prevalent carcinoma (*B*).
- Patients with pernicious anemia may be considered for a single screening endoscopy, particularly if symptomatic, but there are insufficient data to recommend ongoing surveillance (*C*).

- There are insufficient data to support routine endoscopic surveillance in patients with previous partial gastrectomy for peptic ulcer disease (*C*).
- Patients with FAP should undergo regular surveillance endoscopy using both end-viewing and side-viewing endoscopes, starting around the time of colectomy or after age 30 years (*B*).
- Patients with HNPCC have an increased risk of gastric and small-bowel cancer (*B*). Surveillance should be strongly considered (*C*).

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