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Management of Patients with Early Esophageal Cancer, Dysplastic, and Non-Dysplastic Barrett's Esophagus

Effective Date: February, 2024

Cancer Care Alberta

Clinical Practice Guideline GI-011 – Version 3
www.ahs.ca/guru

Background

Barrett's esophagus is defined by the American Gastroenterological Association (AGA) as a condition in which the stratified squamous epithelium that normally lines the distal esophagus is replaced by metaplastic intestinal columnar epithelium that predisposes to cancer development.[1] The prevalence of Barrett's esophagus in patients who undergo an upper gastrointestinal endoscopy for any reason is 4%; this prevalence rises to 9% in males over the age of 50 years, and to as high as 12-15% in patients with gastroesophageal reflux disease (GERD).[2, 3] However, while up to 44% of the general population experiences GERD, only approximately 10% of these individuals will go on to develop Barrett's esophagus.[4] In addition, approximately 25% of patients with Barrett's esophagus have no symptoms of reflux, therefore making the *overall* prevalence of Barrett's esophagus difficult to estimate.[5] Risk factors for Barrett's esophagus include: male gender, age greater than 50 years, White race, a history of chronic GERD greater than 10 years, a body mass index greater than 30, a family history of Barrett's esophagus or esophageal cancer, the presence of a hiatal hernia, and a waist circumference greater than 35 inches for women or 40 inches for men.[1, 2, 6] A history of heavy alcohol consumption and a history of smoking have been identified as possible risk factors.[7]

The risk of progression from Barrett's esophagus to esophageal adenocarcinoma is difficult to predict accurately; predisposing risk factors include a length of Barrett's esophagus ≥ 6cm, a hiatal hernia greater than 3cm in length, and the presence of dysplasia.[7, 8] Most patients with Barrett's esophagus and no or low-grade dysplasia will not progress to cancer. The incidence of esophageal cancer in patients with non-dysplastic Barrett's esophagus is approximately 1 per 300 patients per year.[9] In a prospective cohort study of 713 patients with Barrett's esophagus and no dysplasia or low-grade dysplasia, Sikkema and colleagues identified several risk factors significantly associated with progression to high-grade dysplasia or esophageal adenocarcinoma, including a duration of Barrett's esophagus greater than 10 years (risk ratio (RR)=3.2; 95% confidence interval (CI) 1.3-7.8), the length of Barrett's esophagus (RR=1.11 per cm increase in length; 95% CI 1.01-1.2), the presence of esophagitis (RR=3.5; 95% CI 1.3-9.5), and the presence of low-grade dysplasia (RR=9.7; 95% CI 4.4-21.5).[10] Wani and colleagues followed 1204 patients with Barrett's esophagus and no dysplasia for over 5 years, and reported that 98.6 and 97.1% of patients had not developed cancer at 5 and 10 years, respectively. A length of Barrett's esophagus ≥6cm was identified as a predictor of progression to adenocarcinoma.[11] In contrast, high-grade dysplasia is frequently found in association with esophageal adenocarcinoma.[12, 13]

The purpose of this guideline and accompanying algorithms is to describe the criteria for the use of endoscopic procedures for adult patients with Barrett's esophagus in Alberta. For a detailed description of treatment modalities for esophageal cancer, please refer to the GI-009 Esophageal Cancer clinical practice guideline.

Guideline Questions

1. What are the recommended treatment options for patients with Barrett's esophagus and early esophageal cancer?
2. In what clinical situations is endoscopic therapy the most appropriate treatment for patients with Barrett's esophagus and early esophageal cancer?

Search Strategy

A review of the literature was conducted by searching journal articles using the PubMed electronic database (January 1 2011 to June 1 2022). The following terms were searched in various combinations: Barrett Esophagus [MeSH Terms], Esophageal Neoplasms [MeSH Terms], Esophageal Diseases [MeSH Terms], Radiofrequency Ablation [MeSH Terms], Cryoablation [All Fields], Endoscopic Mucosal Resection [All Fields], Photodynamic Therapy [All Fields], and Multipolar Electrocoagulation [All Fields]. The results were limited to systematic reviews, meta-analyses, randomized controlled trials, and clinical trials. Articles were excluded from the final review if they: had a non-English abstract, were not available through the library system, were published before the year 2011, the patients did not have early stage disease, the publication was a pathology study only, surgical procedural study, systematic review of retrospective studies only, or photodynamic therapy only. The references and bibliographies of articles identified through the search were scanned for additional sources. A search for practice guidelines published since January 2011 was conducted by accessing the websites and/or print publications of relevant national and international organizations. The full literature search strategy and resulting evidence tables are available upon request.

Target Population

The recommendations in this guideline apply to patients with a history of GERD and either suspected or confirmed Barrett's esophagus.

Recommendations and Discussion

Screening

A single screening endoscopy is suggested for patients with chronic GERD symptoms (>10 years) and/or frequent (weekly or more) symptoms of GERD. All patients must also have 3 or more of the following additional risk factors for Barrett's esophagus: male sex, age >50 years, Caucasian, presence of central obesity (waist circumference > 102 cm for men and 88 cm for women), has undergone a sleeve gastrectomy, current or past history of tobacco smoking, and confirmed family history of Barrett's esophagus or esophageal cancer in a first-degree relative[14] *(level of evidence IV, strength of recommendation C).* For more information on GERD, please refer to the Digestive Health Strategic Clinical Network™ GERD Primary Care Pathway.

Diagnostic endoscopy should be performed using a white-light, high-resolution endoscope[15] *(level of evidence II, strength of recommendation A).*

Repeat surveillance is not recommended for patients who have a negative initial screening by endoscopy. If inflammation and Barrett's esophagus is observed, the patient should be treated with a daily proton pump inhibitor (PPI), and a repeat endoscopy should be performed within 6-12 months.[16, 17] If the patient has columnar mucosa endoscopically but is negative for intestinal metaplasia on histology, a repeat endoscopy in 1-2 years is recommended with biopsies.[14] At this point, the Prague C & M Criteria should be used to assess the presence and extent of suspected Barrett's esophagus[18] *(level of evidence IV, strength of recommendation C).*

Diagnosis

Targeted biopsies of every suspicious lesion, followed by 4-quadrant biopsies every 1cm throughout the entire Barrett's esophagus segment are recommended[14, 19] *(level of evidence IV strength of recommendation B).* Columnar mucosa of at least 1 cm in length is necessary for a diagnosis of Barrett's esophagus, and patients with a normal-appearing Z-line should not undergo a routine endoscopic biopsy[14] *(level of evidence IV, strength of recommendation C).* Biopsies should be submitted in separate jars corresponding to the level from which it was taken. However, if visible mucosal irregularities such as flat or raised nodules that are suspicious for dysplasia or early carcinoma are visualized within the zone of Barrett's during endoscopic surveillance, endoscopic resection is recommended and biopsies of the area are to be avoided. This allows for a larger sample, and therefore more precise assessment of depth of tumour invasion into the mucosa and submucosa[20-22] *(level of evidence IV, strength of recommendation B).*

The grade of dysplasia will determine the most appropriate surveillance interval and management strategy for patients with Barrett's esophagus. Dysplasia is defined microscopically based on cytological and structural changes to the intestinal epithelium severe enough to suggest neoplastic

transformation; the distinction between low- and high-grade is based on the severity of these changes.[21] We recommend that all Barrett's esophagus biopsies revealing any grade of dysplasia (indefinite, low or high grade) be reviewed and confirmed by two pathologists, one of whom should be an expert in interpreting esophageal histopathology[14, 16, 19] *(level of evidence II, strength of recommendation A).*

- For patients with no dysplasia and a Barrett's esophagus segment ≤3 cm, endoscopic surveillance is recommended every 5 years; for patients with no dysplasia and a Barrett's esophagus segment between 3 cm and 10 cm, endoscopic surveillance is recommended every 3 years, with 4-quadrant biopsies every 2 cm.
- Patients with no dysplasia but *any* of the following risk factors should be referred to a tertiary centre for consideration of endoscopic eradication therapy (EET): age younger than 30 years at diagnosis, circumferential Barrett's esophagus segment >10 cm, or family history of Barrett's esophagus or esophageal cancer.
- Patients with biopsies that are indefinite for dysplasia should have twice daily treatment with a proton pump inhibitor (PPI) and a repeat endoscopy every 3 to 6 months, with 4-quadrant biopsies every 1 cm after, until the presence and degree of dysplasia can be determined histologically.
- For patients with a single focus of low-grade dysplasia and no additional risk factors (age ≤30 years at diagnosis, circumferential Barrett's esophagus segment >10 cm, family history of Barrett's esophagus or esophageal cancer) endoscopic surveillance is recommended every 6 to 12 months. Patients with *any* additional risk factors and patients with multifocal or multi-level low-grade dysplasia should be referred to a tertiary centre for consideration of EET.
- Patients with high-grade dysplasia, early esophageal cancer, or invasive cancer should be referred to a tertiary centre for further evaluation. Refer to the GI-009 Esophageal Cancer clinical practice guideline for detailed staging information.

Treatment

Given the complexities in diagnosis and treatment of patients with dysplastic Barrett's esophagus or early esophageal cancer, as well as the risks associated with both over- and under-treatment of Barrett's esophagus, we recommend that these patients are best managed in a tertiary centre, with input from experienced gastroenterologists, surgeons, pathologists, and oncologists[23] *(level of evidence IV, strength of recommendation B).* The goal of treatment for Barrett's esophagus is to control the symptoms of GERD, heal the mucosal inflammation, manage any dysplasia, and prevent progression or improve survival for patients who progress to adenocarcinoma.

Upon diagnosis of Barrett's esophagus, we recommend that all patients should be started on daily therapy with a proton pump inhibitor (PPI)[14, 17]*(level of evidence IV, strength of recommendation C).*

In general, routine endoscopic or surgical treatment for patients with Barrett's esophagus in which there is no dysplasia, is indefinite for dysplasia, or has low-grade dysplasia is not recommended. However, if these patients have one or more additional risk factors, including: i) age younger than 30 years at the time of Barrett's diagnosis, ii) a family history of Barrett's esophagus or esophageal cancer, or iii) a segment of circumferential Barrett's esophagus greater than 10 cm, endoscopic ablative therapy can be considered. If these additional risk factors are not present, patients should continue to be monitored with endoscopic surveillance at the appropriate intervals and the appropriate number of biopsies *(level of evidence IV, strength of recommendation C).*

There is little evidence to demonstrate that patients with Barrett's esophagus treated with anti-reflux surgery procedures have a lower risk of progression to neoplasia than those treated medically, therefore we recommend against the use of anti-reflux surgery as an anti-cancer therapy *(level of evidence IV; strength of recommendation D)*.[14]
Patients with high-grade dysplasia or early esophageal cancer should be referred to a tertiary centre, and an endoscopic ultrasound and/or enhanced computed tomography (CT) scan of the chest should be considered in order to rule out lymphadenopathy as these patients are at risk of lymph node metastasis, although this risk is not well-defined[24] *(level of evidence IV, strength of recommendation C).*

If visible lesions, nodules, or mucosal irregularities are seen during endoscopic surveillance, the patient should first undergo endoscopic resection instead of a standard endoscopic biopsy. This provides a larger tissue sample with better orientation, therefore allowing for more accurate diagnosis, staging, and improved treatment planning.[20] We recommend these samples are pinned flat before fixation and histologic sectioning should be in a "bread loaf" manner to allow for assessment of depth of invasion (see Appendix A). These samples should be handled by a lab and pathologists with expertise in esophageal dysplasia. Samples should be mapped and tagged corresponding as precisely as possible to the location in the esophagus from which it was resected *(level of evidence IV, strength of recommendation B).*

Endoscopic Eradication Therapy:
Endoscopic eradication therapy (EET) offers a minimally invasive treatment approach, avoiding the morbidity and mortality associated with esophagectomy. EET includes endoscopic resection of any visible lesion within the Barrett's esophagus segment, followed by endoscopic ablation to achieve complete eradiation of dysplasia and intestinal metaplasia.[14, 29]

Studies comparing EET to surgery in patients with mucosal (T1a) esophageal adenocarcinoma found no difference in survival and greater complications with surgery.[30, 31] Furthermore, intramucosal tumours are associated with minimal nodal metastases risk,[24] and therefore, may be treatable endoscopically. Specifically, EET as curative therapy is indicated for T1a carcinoma patients if all of the following criteria are met *(level of evidence II, strength of recommendation A)*:

- The patient has been assessed by a multidisciplinary Tumour Board
- The diagnostic specimen has been properly handled by an expert pathologist
- The procedure will be performed by an endoscopist who is an expert in endoscopic resection at a tertiary centre
- The patient does not present with any high-risk features such as tumour size > 2 cm, poor differentiation, or lymphovascular invasion.

The risks and benefits associated with EET should be discussed with patients who are candidates, and patients who do not meet the above criteria should be referred for surgical assessment.

Endoscopic resection. Endoscopic resection is recommended for high grade dysplasia or any visible lesions with mucosal irregularity. Endoscopic resection includes endoscopic mucosal resection (EMR) and endoscopic submucosal dissection (ESD). ESD allows for en bloc resection of lesions, but it is associated with a longer procedure time and a higher risk of complications when compared to EMR.[32-35] EMR involves the use of an endoscope to diagnostically and therapeutically resect mucosal lesions. Current methods of EMR include the lift-and cut cap-assisted technique and the multiband mucosectomy (MBM) technique. A recent systematic review and pooled analysis has reported MBM to be a safe and effective technique for treating visible lesions in Barrett's esophagus.[36] In the context of Barrett's esophagus and early esophageal carcinoma, an endoscopic resection is performed to both accurately diagnose the depth of a visible esophageal lesion and as a potential curative procedure for Tis (high-grade dysplasia) and T1a (tumour invades lamina propria or muscularis mucosa) disease. The evidence suggests that endoscopic resection can be performed with curative intent in intramucosal carcinoma (T1a) under acceptable clinicopathological criteria. In a prospective case series of 349 patients, Pech *et al.* found that complete response was achieved in 96.6% of endoscopically-treated patients; the 5-year survival rate was 84%.[37] A similar study of 100 patients at a single centre found that complete local remission was achieved in 99% of patients treated with endoscopic resection after 1.9 months; the 5-year survival rate was 98%.[38] In a systematic review of the safety and effectiveness of endoscopic approaches, study authors found that complete response following endoscopic resection ranged from 67-100% and recurrence ranged from 0-28%.[39]

Endoscopic ablation. Endoscopic ablation is recommended for patients with high grade dysplasia, or with no/low grade dysplasia with risk factors (age ≤30 years at diagnosis, circumferential Barrett's esophagus segment >10 cm, family history of Barrett's esophagus or esophageal cancer). For patients with high grade dysplasia without evidence of invasive adenocarcinoma, it is recommended that endoscopic resection be followed by non-surgical ablative therapy to the remaining Barrett's esophagus, in order to achieve complete eradication of intestinal metaplasia (CE-IM) *(level of evidence IV, strength of recommendation B).*[29, 40] Non-surgical ablation options for the treatment of Barrett's esophagus with high-grade dysplasia, multifocal low-grade dysplasia, or select patients with no or single focus low-grade dysplasia and additional risk factors are recommended for patients without remnant visible lesions or mucosal irregularities. Among ablative technologies, radiofrequency ablation (RFA) has the highest level of evidence and should be the initial choice, unless there are

clinical, anatomic or endoscopic factors, such as unresponsiveness to RFA, difficult anatomy (tortuous esophagus or across the gastroesophageal junction), strictures, cost, or pain. After initial RFA, cryotherapy, argon plasma coagulation (APC) or multipolar electrocoagulation (MPEC) are alternative modalities that can be used to achieve CE-IM; patient consultation at an expert centre is recommended *(level of evidence II, strength of recommendation A)*.

1. ***Radiofrequency ablation:*** Radiofrequency ablation (RFA) involves the application of direct thermal energy to the lining of the esophagus using an endoscopic platform. The equipment includes balloon- and pad-based probes fixed to the tip of an endoscope to provide circumferential and focal radiofrequency ablation.[24] There is strong evidence to support the use of RFA for the eradication of flat, residual Barrett's esophagus (following endoscopic resection) in patients with high-grade dysplasia,[13, 41, 42] as well as for patients with no or low-grade dysplasia who have additional risk factors.[43-45] In a landmark randomized placebo-controlled trial examining 127 patients with Barrett's esophagus, RFA therapy was associated with significantly higher rates of complete disease eradication compared to the placebo group for patients with both high-grade dysplasia (81.0% versus 19.0%, $p<0.001$) and low-grade dysplasia (90.5% versus 22.7%, $p<0.001$).[13] Patients who achieved complete disease eradication and remained free of Barrett's esophagus at 1 year after RFA had a low risk of recurrence.[46] In a 5-year follow-up to the prospective multi-centre AIM-II trial of patients with Barrett's esophagus and no dysplasia, Fleischer *et al.* reported a complete response-intestinal metaplasia (CR-IM) in 92% of patients treated with RFA;[44] 8% of patients developed focal non-dysplastic Barrett's esophagus at 5 years, and a single session of RFA converted all these to CR-IM. There were no buried glands, dysplasia, strictures, or serious adverse events reported at 5 years. In a study addressing the efficacy of a stepwise regimen of circumferential and focal RFA for the treatment of Barrett's esophagus with either low-grade (N=39) or high-grade (N=24) dysplasia, Sharma and colleagues reported a CR-IM rate of 87%, and a complete response-dysplasia (CR-D) rate of 95% for the low-grade patients, and CR-IM and CR-D rates of 67% and 79% for high-grade patients, respectively.[45] Similarly, in a multicentre randomized trial comparing stepwise radical endoscopic resection versus focal endoscopic resection followed by RFA for patients with Barrett's esophagus and high-grade dysplasia or early esophageal cancer, van Vilsteren *et al.* reported comparably high rates of CR-IM (92% versus 96%) and CR-neoplasia (100% versus 96%) with both procedures.[47] Radical endoscopic resection was associated with a higher number of complications and required more therapeutic sessions, leading the investigators to recommend a combined endoscopic approach of focal endoscopic resection followed by RFA. In a comparison of the neosquamous epithelium of patients with high-grade dysplasia or early esophageal cancer pre- and post-RFA, Pouw and colleagues reported that all patients had normal neosquamous epithelium following ablation, with no persistent genetic abnormalities or buried glands.[42] Adverse effects associated with RFA include chest pain, esophageal hemorrhage, and upper GI bleeding.[13, 42] As a result of these published findings, we recommend RFA as the standard ablative therapy for the treatment of patients with Barrett's esophagus with high-grade dysplasia,

as well as for select patients with no or low-grade dysplasia and additional risk factors *(level of evidence II, strength of recommendation A).*

2. ***Cryotherapy*****:** Endoscopic cryotherapy is a thermal ablative modality that uses cycles of rapid cooling and thawing with a cryogen such as liquid nitrogen, carbon dioxide, or nitrous oxide to induce tissue destruction, leading to intra- and extra-cellular damage.[48] Several trials have evaluated cryotherapy in Barrett's esophagus associated neoplasia, and have reported reasonable efficacy rates and a good safety profile, as well as a low rate of recurrence or progression to cancer with long-term follow-up.[49-53] In a recent prospective multicentre trial of 120 patients treated with a nitrous oxide cryoballoon focal ablation system, Canto and colleagues reported rates of complete eradiation-dysplasia (CE-D) and CE-IM rates of 76% and 72% respectively; 12.5% of patients developed strictures requiring dilation, and one patient with high-grade dysplasia progressed to intramucosal adenocarcinoma.[49] In a systematic review of 6 studies of ablation-naïve patients with high-grade dysplasia and/or intramucosal cancer treated with either liquid nitrogen or carbon dioxide based cryotherapy, Hamade *et al.* reported efficacy rates of 69% and 98% for complete eradication of metaplasia and neoplasia, respectively.[54] In a prospective multicentre study from the National Cryospray Registry, Ghorbani *et al.* reported CE-D rates of 91% in patients with low-grade dysplasia and 81% in patients with high-grade dysplasia, and CE-IM rates of 61% in low-grade dysplasia and 65% in high-grade dysplasia;[52] Patients with short-segment Barrett's esophagus with any dysplasia had CE-D and CE-IM rates of 97% and 77%, respectively. Endoscopic cryotherapy may be considered as an alternative ablative therapy in patients who are unresponsive to RFA, patients who experience excessive pain due to RFA, or in settings where anatomy may not allow for RFA *(level of evidence III, strength of recommendation B).*

3. ***Photodynamic therapy:*** Photodynamic therapy (PDT) involves the administration of a photosensitizing drug that accumulates in the dysplastic tissue and causes tissue destruction when it is activated by an endoscopic light source.[55] Several studies have been published showing that PDT is effective in eradicating dysplasia in Barrett's esophagus;[56, 57] it has also been used to treat patients with esophageal cancer and local failure after chemotherapy plus radiotherapy, as well as patients with early stage esophageal tumours who refused or were not candidates for esophagectomy.[58, 59] Patients treated with PDT are extremely photosensitive, and must be cautioned to avoid any exposure to sunlight, in addition, PDT is associated with the formation of strictures in patients with Barrett's esophagus, with some series reporting rates as high as 30%.[56, 60] The cost-effectiveness of PDT has been reviewed in several health technology assessments (HTAs), which concluded that PDT offers relatively poor cost-effectiveness in relation to other endoscopic procedures for Barrett's esophagus and early esophageal cancer, but that all of the endoscopic therapies have similar incremental cost-effectiveness ratios (ICERs) compared to surveillance alone.[61, 62] The HTAs also highlight the additional human resources required for patients treated with PDT, including patient education with a dietician, follow-up care with a nurse

familiar with the PDT procedure, and follow-up appointments with the physician 3 and 6 months after the procedure. PDT is not currently available in Alberta.

4. ***Argon plasma coagulation:*** Argon plasma coagulation (APC) therapy involves the use of a high-frequency monopolar current which is conducted to the tissue by ionized argon gas. In a randomized trial of 76 patients with Barrett's esophagus containing high-grade dysplasia or mucosal adenocarcinoma (T1a), APC showed similar efficacy and safety when compared to RFA;[63] quality of life scores were similar across the two groups of patients, while the cost analysis favoured the APC group. The major complications associated with APC are pain and dysphagia; strictures have been reported in 5-10% of patients.[64] APC is easy to use for small lesions (<4cm), and has a reasonable safety profile; the major concern with this therapy is the heightened risk of buried glands, which may be more common in patients treated with APC versus other ablative techniques.[64] APC should only be performed by experienced clinicians at expert Barrett's esophagus management centres *(level of evidence II, strength of recommendation B).*

5. ***Multipolar electrocoagulation:*** Multipolar electrocoagulation (MPEC) involves the delivery of thermal energy to the abnormal Barrett's mucosa through a probe passed through the endoscope that delivers the current between two or more electrodes. In a study involving 139 patients with Barrett's esophagus and no dysplasia who were followed over 10 years, Allison and colleagues reported a recurrence of Barrett's esophagus in less than 5% of patients, and no adenocarcinoma or high-grade dysplasia of the esophagus developed in any of the patients.[65] The major complications associated with MPEC include painful swallowing, chest pain, fever, gastrointestinal bleeding, and stricture.[66] One of the disadvantages of MPEC is that multiple procedures are required to achieve ablation, and only small amounts of esophageal mucosa can be treated at one time (<4cm). MPEC is not currently available in Alberta.

Surgery:

For patients with carcinoma with any evidence of submucosal invasion (T1b or deeper) or lymph node metastasis, esophagectomy is the most appropriate therapy, and the patient should be referred for surgical evaluation *(level of evidence IV, strength of recommendation B).* [23] Esophagectomy is associated with significant rates of post-operative and long-term complications, with lower morbidity and mortality rates being associated with higher-volume centres and more experienced surgeons.[25-27] It is therefore recommended that patients be referred to a thoracic/upper gastrointestinal (GI) surgeon specializing in the treatment of foregut cancers at a high-volume centre.[15, 23, 28] Any patient with poor prognostic factors should be discussed at a multidisciplinary tumour board, which should include a thoracic/upper GI surgeon. Patients referred to surgery should undergo a full nutritional assessment.

Follow-up

Ongoing ablative therapy should be continued with a goal of eliminating all visible and histologic Barrett's esophagus (CR-IM), allowing for neo-squamous epithelial regrowth. If not possible, then eradication of any Barrett's with dysplasia (CR-D) is a secondary aim. Our recommendations for surveillance are *(level of evidence II, strength of recommendation A)*:

1. For patients with nondysplastic, indefinite, or low-grade dysplasia Barrett's esophagus who achieve CR-IM or CR-D with ablation, follow-up should include surveillance endoscopy plus a 4-quadrant biopsy every 1cm of the entire previous Barrett's esophagus segment at 1 year, 3 years, and every 2 years thereafter, with continuance based on clinical judgment and the individualized plan of care for each patient.

2. For patients with high-grade dysplasia or early esophageal cancer who achieve CR-IM or CR-D with ablation, follow-up should include surveillance endoscopy plus a 4-quadrant biopsy every 1cm of the entire previous Barrett's esophagus at 3, 6, and 12 months, and annually thereafter, with continuance based on clinical judgment and the individualized plan of care for each patient.

It is reasonable to cease endoscopic surveillance in patients who are no longer fit for repeated endoscopy or who cannot tolerate endoscopic, surgical, or oncologic intervention for esophageal neoplasia.[14]

Treatment Algorithms

Figure 1. Initial Management

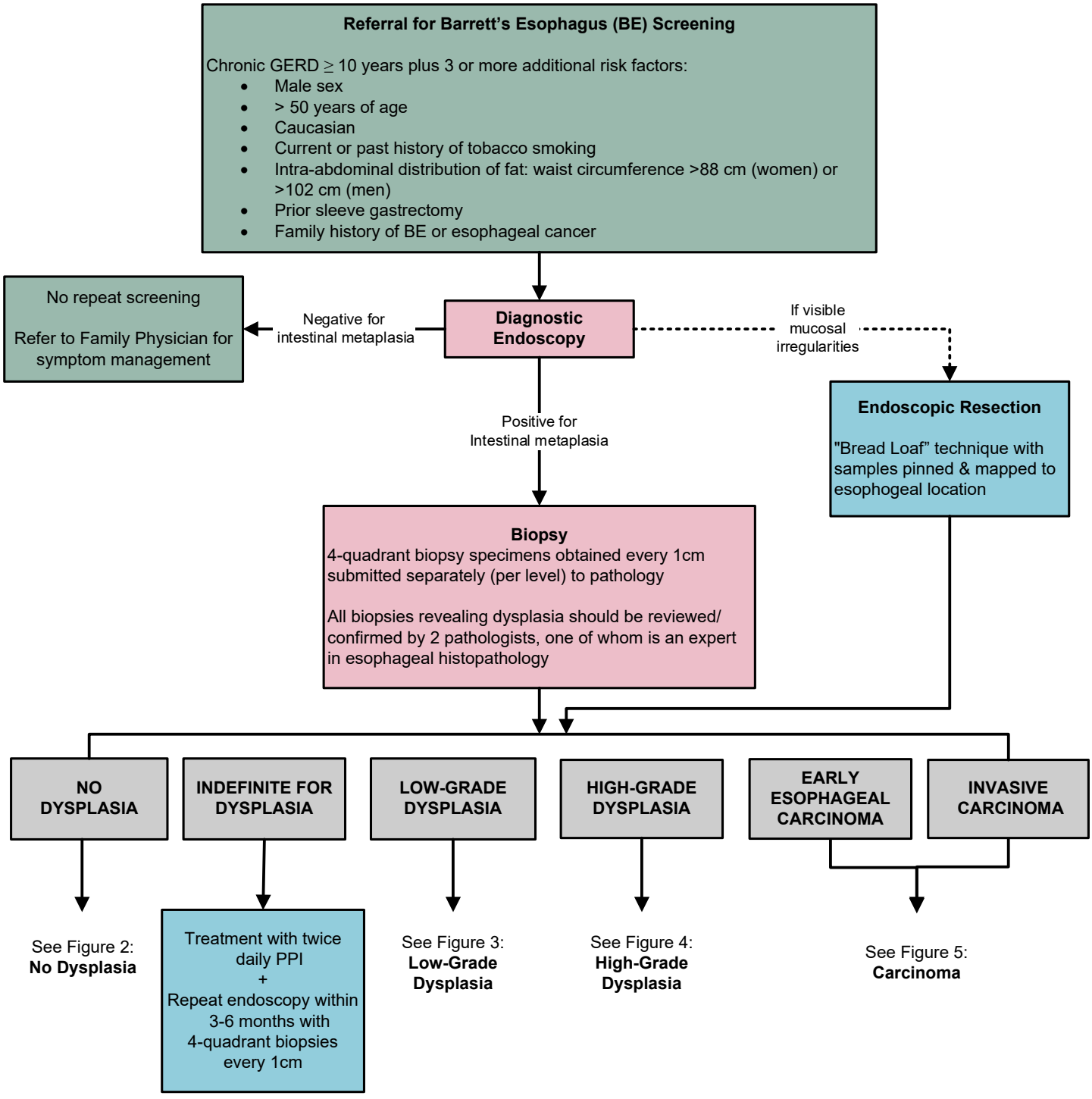


Figure 2. No Dysplasia

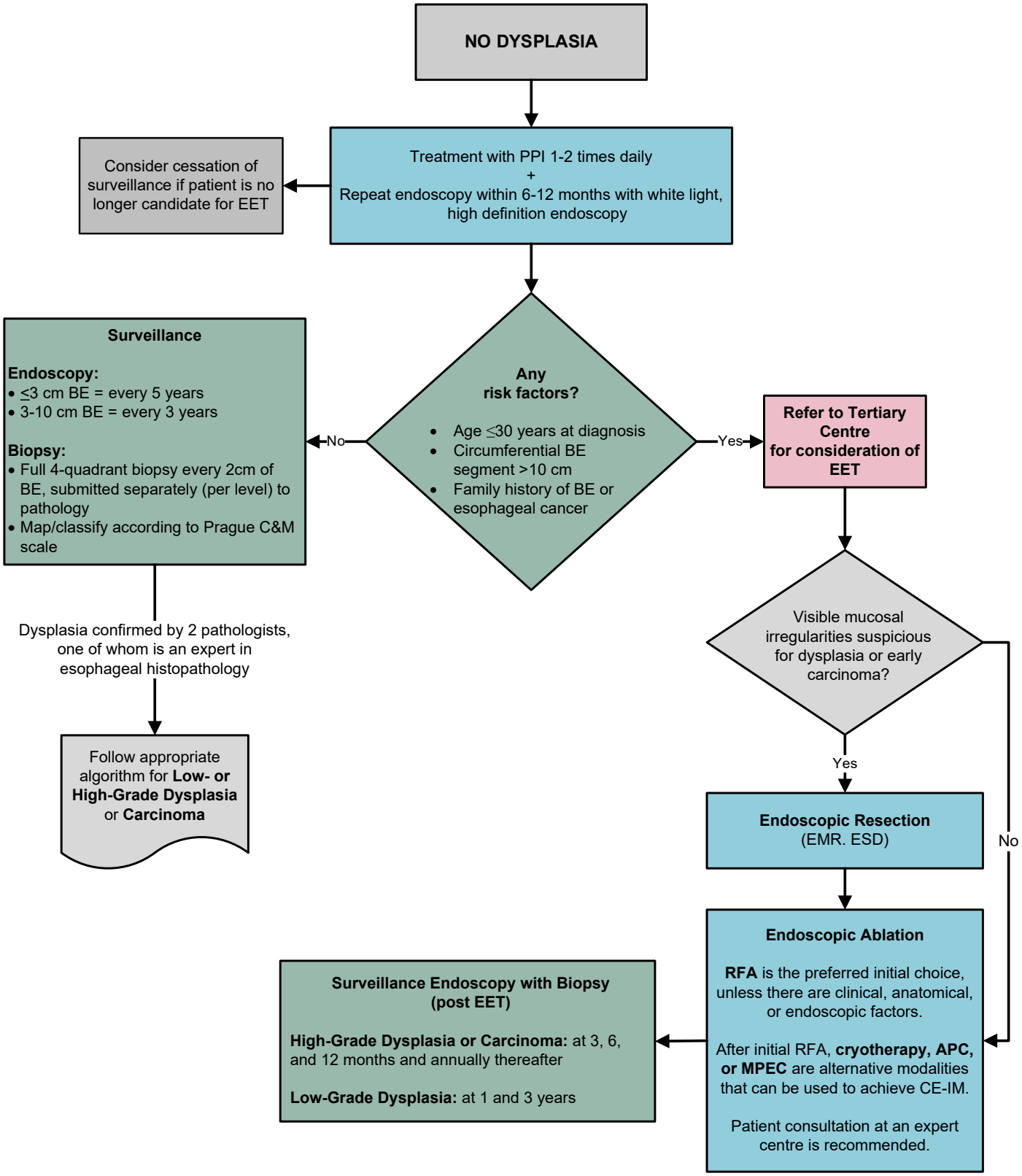


Figure 3. Low-Grade Dysplasia

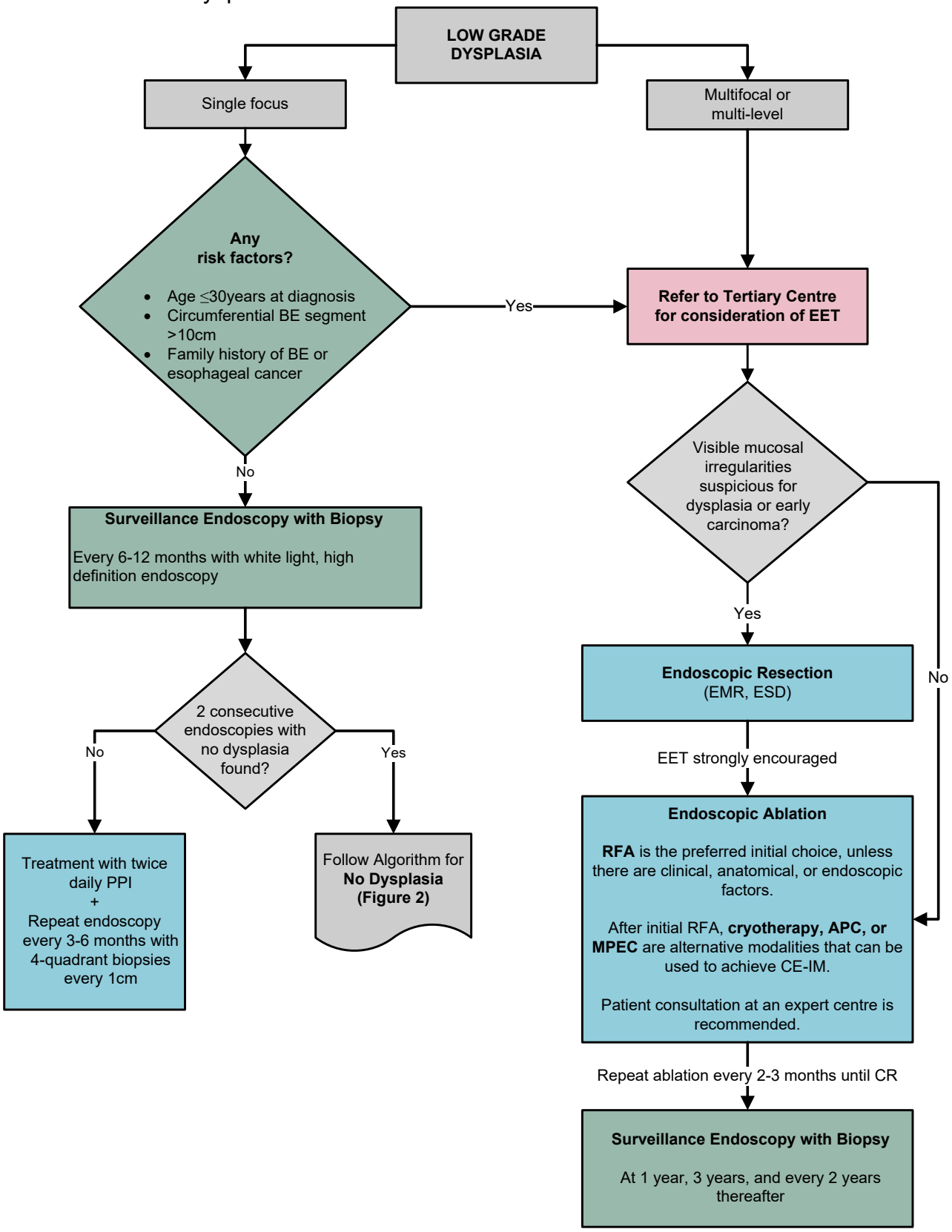


Figure 4. High-Grade Dysplasia

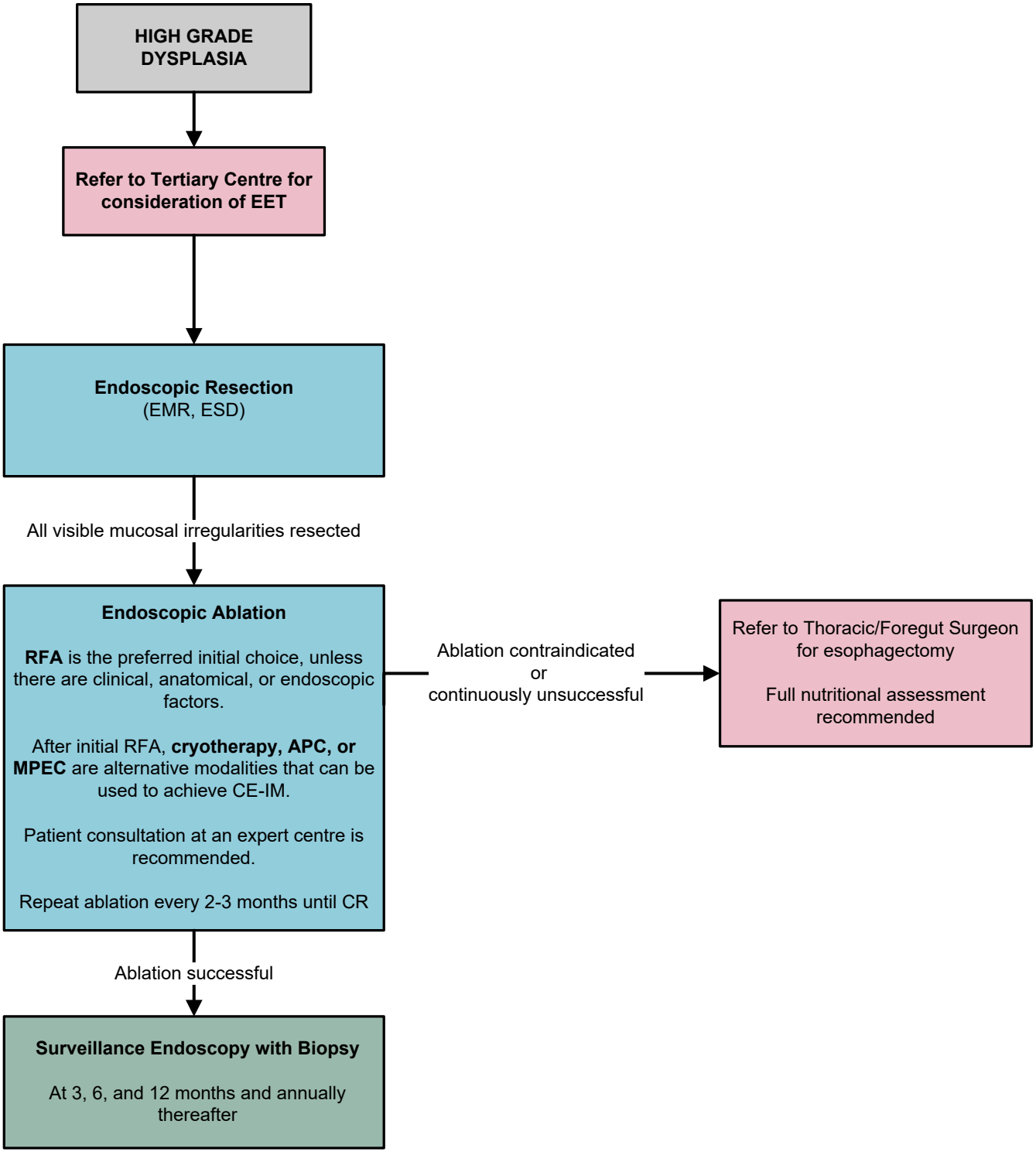
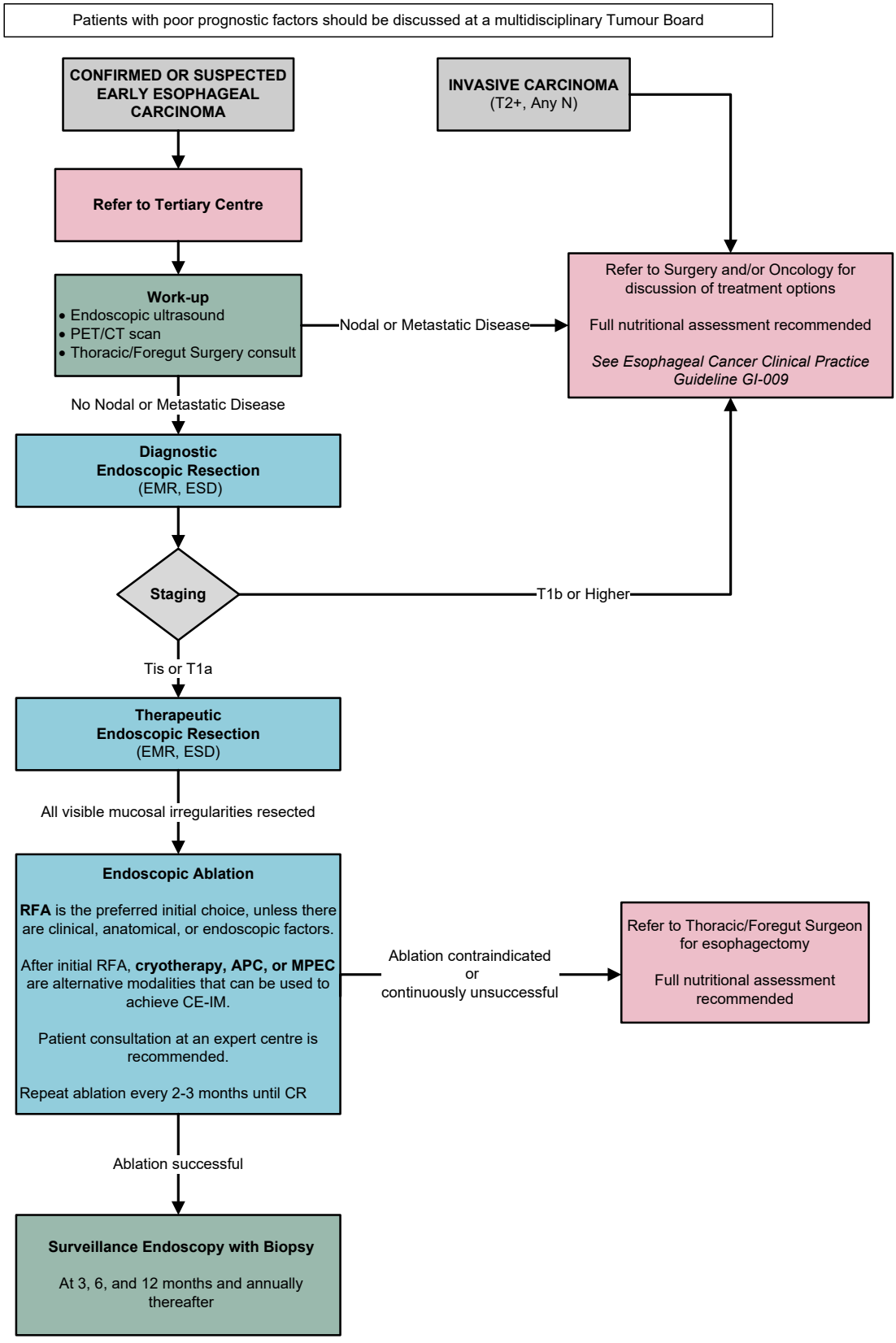


Figure 5. Early Esophageal Cancer or Invasive Carcinoma



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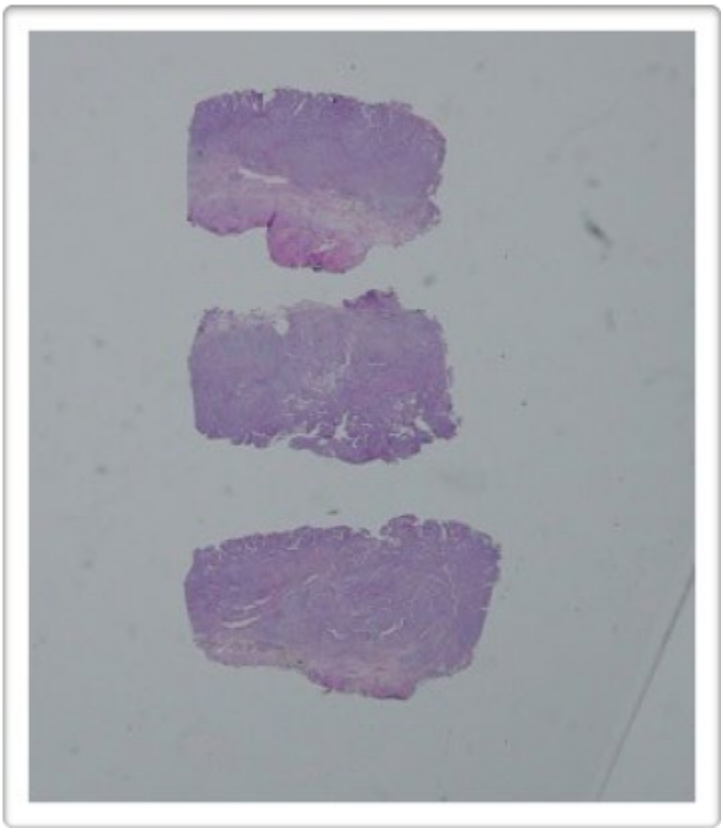
Appendix A: – EMR Specimen Handling (“Bread Loaf” Technique)



Images courtesy of Dr. R. McLean

Development and Revision History

This guideline was developed by a multidisciplinary working group comprised of gastroenterology content experts and a methodologist from the Guideline Resource Unit. The draft guideline was externally reviewed and endorsed by members of the Alberta Gastrointestinal Tumour Team who were not involved in the guideline's development, including surgical oncologists, radiation oncologists, medical oncologists, nurses, pathologists, and pharmacists. A detailed description of the methodology followed during the guideline development process can be found in the Guideline Resource Unit Handbook.

This guideline was originally developed in February 2013 and was revised in March 2014 and February 2024.

Levels of Evidence

I	Evidence from at least one large randomized, controlled trial of good methodological quality (low potential for bias) or meta-analyses of well-conducted randomized trials without heterogeneity
II	Small randomized trials or large randomized trials with a suspicion of bias (lower methodological quality) or meta-analyses of such trials or of trials with demonstrated heterogeneity
III	Prospective cohort studies
IV	Retrospective cohort studies or case-control studies
V	Studies without control group, case reports, expert opinion

Strength of Recommendations

A	Strong evidence for efficacy with a substantial clinical benefit; strongly recommended
B	Strong or moderate evidence for efficacy but with a limited clinical benefit; generally recommended
C	Insufficient evidence for efficacy or benefit does not outweigh the risk or the disadvantages (adverse events, costs, etc.); optional
D	Moderate evidence against efficacy or for adverse outcome; generally not recommended
E	Strong evidence against efficacy or for adverse outcome; never recommended

Maintenance

A formal review of the guideline will be conducted in 2028. If critical new evidence is brought forward before that time, however, the guideline working group members will revise and update the document accordingly.

Abbreviations

AGA, American Gastroenterological Association; APC, argon plasma coagulation; BE, Barrett's esophagus; CI, 95% confidence interval; CE-D, complete eradication-dysplasia; CE-IM, complete eradication-intestinal metaplasia; CR-D, complete response-dysplasia; CR-IM, complete response-intestinal metaplasia; CT, computed tomography scan; EET, endoscopic eradication therapy; EMR, endoscopic mucosal resection; ESD, endoscopic submucosal dissection; ESEM, endoscopically suspected esophageal metaplasia; GERD, gastroesophageal reflux disease; GI, gastrointestinal; HTA, health technology assessment; ICER, incremental cost effective ratio; MBM, multiband mucosectomy; MPEC, multipolar electrocoagulation; PDT, photodynamic therapy; PET, positron emission tomography scan; PPI, proton pump inhibitor; RFA, radiofrequency ablation; RR, risk ratio.

Disclaimer

The recommendations contained in this guideline are a consensus of the Alberta Provincial Gastrointestinal Tumour Team and are a synthesis of currently accepted approaches to management, derived from a review of relevant scientific literature. Clinicians applying these guidelines should, in consultation with the patient, use independent medical judgment in the context of individual clinical circumstances to direct care.

Funding Source

Financial support for the development of Cancer Care Alberta's evidence-based clinical practice guidelines and supporting materials comes from the Cancer Care Alberta operating budget; no outside commercial funding was received to support the development of this document.

All cancer drugs described in the guidelines are funded in accordance with the Outpatient Cancer Drug Benefit Program, at no charge, to eligible residents of Alberta, unless otherwise explicitly stated. For a complete list of funded drugs, specific indications, and approved prescribers, please refer to the *Outpatient Cancer Drug Benefit Program Master List*.

Conflict of Interest Statements

Dr. Paul Belletrutti reports an honorarium from Pentax for an educational event, an honorarium from Pendopharm /Pharmascience Inc. for a speaker's bureau, and support for travel from Pentax.

Dr. Milli Gupta reports support for travel from Pentax.

Dr. Clarence Wong reports payment or honoraria for lectures, presentations, speaker's bureaus, manuscript writing or educational events from the Canadian Association of Gastroenterology and Pendopharm, and support for attending meetings or travel from the University of Calgary and Alberta Health Services.

Xanthoula Kostaras has nothing to disclose.

Citation

Wong C, Belletrutti P, Gupta M, Kostaras X. Cancer Care Alberta, Alberta Health Services (2024). Clinical Practice Guideline on Management of Patients with Early Esophageal Cancer, Dysplastic, and Non-Dysplastic Barrett's Esophagus, Version 3. Accessed [Month, Year]. Available from: www.ahs.ca/guru