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Comprehensive
Cancer
Network[®]

NCCN Clinical Practice Guidelines in Oncology™

Esophageal Cancer

V.1.2007

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This manuscript is being updated to correspond with the newly updated algorithm.

Clinical Trials: The NCCN believes that the best management for any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.

To find clinical trials online at NCCN member institutions, [click here: nccn.org/clinical_trials/physician.html](#)

NCCN Categories of Consensus: All recommendations are Category 2A unless otherwise specified.

See [NCCN Categories of Consensus](#)

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These guidelines are a statement of consensus of the authors regarding their views of currently accepted approaches to treatment. Any clinician seeking to apply or consult these guidelines is expected to use independent medical judgment in the context of individual clinical circumstances to determine any patient's care or treatment. The National Comprehensive Cancer Network makes no representations nor warranties of any kind whatsoever regarding their content, use, or application and disclaims any responsibility for their application or use in any way. These guidelines are copyrighted by National Comprehensive Cancer Network. All rights reserved. These guidelines and the illustrations herein may not be reproduced in any form without the express written permission of NCCN. ©2007.

Summary of the Guidelines Updates

Summary of changes in the 1.2007 version of the Esophageal Cancer guidelines from the 2006 version include:

(ESOPH-1):

- Workup: “Barium swallow” was added
- Included new footnotes “f” and “h” describing Resectable and Unresectable Stage IVA
- Medically fit, resectable section: Revised staging and added footnotes to clarify stages
- Medically unfit for surgery: Deleted phrase “unresectable,” and added “unresectable stage IVA” with footnote “h” to clarify
- Footnote “e” now includes a statement about resectable T1-T3 tumors

(ESOPH-2):

- Primary Treatment; Bottom Branch: Included heading “Preoperative chemotherapy/RT”
- PET/CT scan denoted as category 2B
- Adjuvant treatment for Persistent local disease: Now reads “Esophagectomy *if fit for surgery (preferred)*....”
- Adjuvant treatment for Progressive or metastatic disease: Deleted “endoscopic therapy” and included “Best supportive care”

(ESOPH-5):

- Top Branch: Salvage Therapy:
 - ▶ Deleted “endoscopic therapy” and included “Best supportive care
 - ▶ “Surgery (recurrence limited to anastomosis)” changed to “Surgery (recurrence limited to *local regional*)”

(ESOPH-A):

- A new page entitled, “Principles of Surgery” was added to outline recommended guidelines for esophageal surgery.

(ESOPH-B):

- All category of consensus recommendations for systemic therapies were revised to reflect current data
- Postoperative chemoradiation: First bullet changed to fluoropyrimidine/leucovorin
- “5-FU” was changed to “fluoropyrimidine” throughout page

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WORKUP

- H&P
- Barium swallow (optional)
- Esophagogastroduodenoscopy to visualize entire upper GI tract, if possible
- CBC, SMA-12, Chest/abdominal CT
- If tumor is at or above the carina with no evidence of M1 disease, do bronchoscopy
- Endoscopic ultrasound (EUS), if no evidence of M1 disease, with FNA if indicated
- If no evidence of M1 disease and tumor is at GE junction, laparoscopy is optional
- Suspicion of metastatic cancer confirmed by biopsy
- PET/CT scan if no evidence of M1 disease

CLINICAL STAGE

Stage I–III, IVA^a
(locoregional cancer)

Stage IVB
metastatic cancer

ADDITIONAL EVALUATION
(as clinically indicated)

- Multidisciplinary evaluation is encouraged (mandatory for patients with celiac-positive disease)
- Nutritional assessment (for preoperative nutritional support, consider nasogastric or J-tube [PEG is not recommended])
- Barium enema or colonoscopy if colon inter-position or bypass planned
- Consider arteriogram if performing colon interposition

Medically fit,^b resectable^{c,d} T1–T4,^e N0–1, NX, or Stage IVA^{d,f}

Medically unfit for surgery, unresectable T4,^g unresectable stage IVA^h or Surgery not elected and patient medically able to tolerate chemotherapy

Medically unfit for surgery and patient unable to tolerate chemotherapy

Metastatic cancer

[See Primary Treatment \(ESOPH-2\)](#)

[See Primary Treatment \(ESOPH-4\)](#)

[See Primary Treatment \(ESOPH-4\)](#)

[See Salvage therapy \(ESOPH-6\)](#)

[See Salvage therapy \(ESOPH-6\)](#)

^aCeliac nodal involvement in cancers of the gastroesophageal junction may still be considered for combined modality therapy.

^bMedically able to tolerate major abdominal and/or thoracic surgery.

^cChemoradiotherapy is the preferred modality for cervical esophageal carcinoma.

^d[See Principles of Surgery \(ESOPH-A\)](#).

^eResectable T4: involvement of pleura, pericardium or diaphragm. T1–T3 tumors are resectable even with regional nodal metastases.

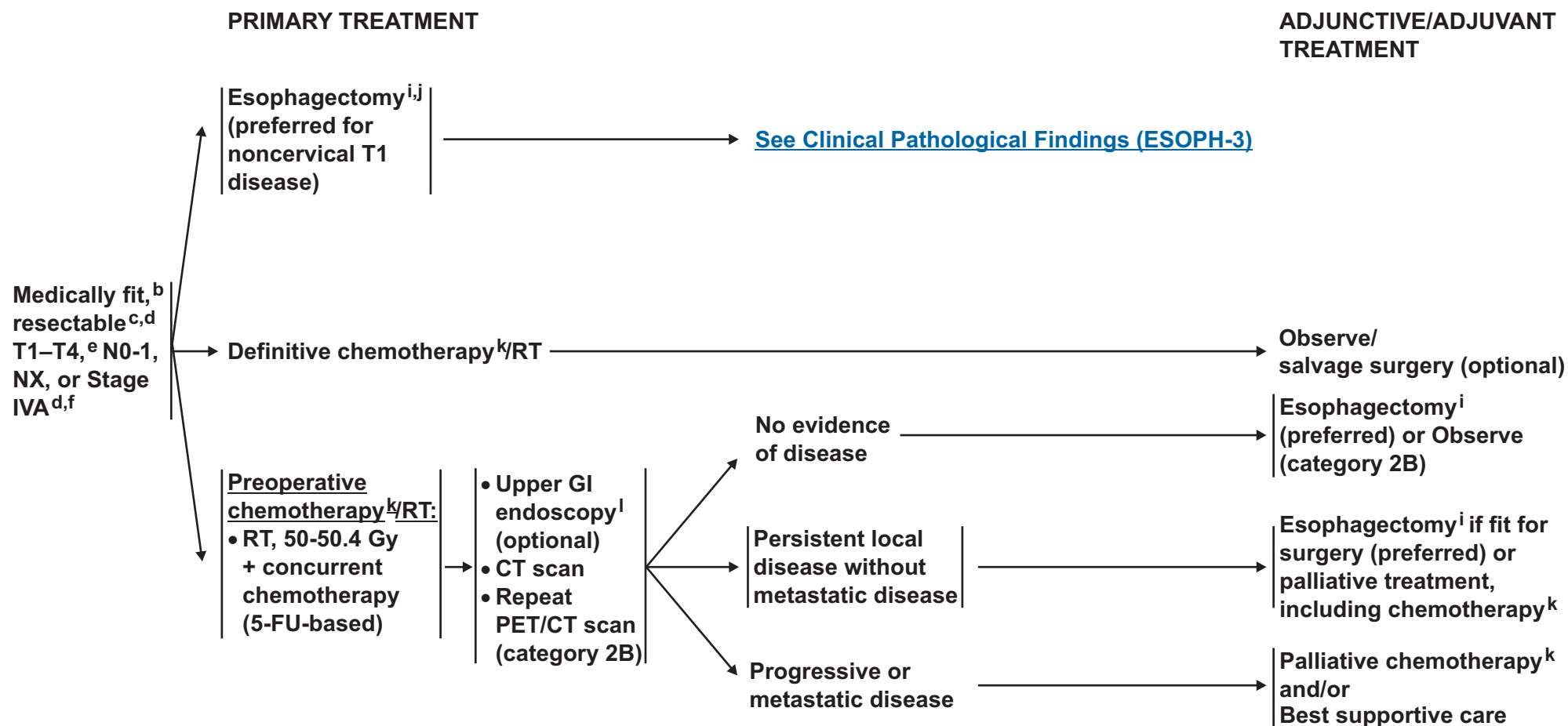
^fResectable Stage IVA: Celiac nodes ≤ 1.5 cm, no involvement of celiac artery, aorta, or other organs.

^gUnresectable T4: invasion of aorta, trachea, heart, great vessels.

^hUnresectable Stage IVA: Celiac nodes > 1.5 cm or involvement of celiac artery, aorta, or other organs.

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^bMedically able to tolerate major abdominal and/or thoracic surgery.

^cChemoradiotherapy is the preferred modality for cervical esophageal carcinoma.

^d[See Principles of Surgery \(ESOPH-A\).](#)

^eResectable T4: involvement of pleura, pericardium or diaphragm. T1-T3 tumors are resectable even with regional nodal metastases.

^fResectable Stage IVA: Celiac nodes less ≤ 1.5 cm, no involvement of celiac artery, aorta, or other organs.

ⁱTranshiatal or transthoracic, or minimally invasive; gastric reconstruction preferred.

^jFeeding jejunostomy for postoperative nutritional support, generally preferred.

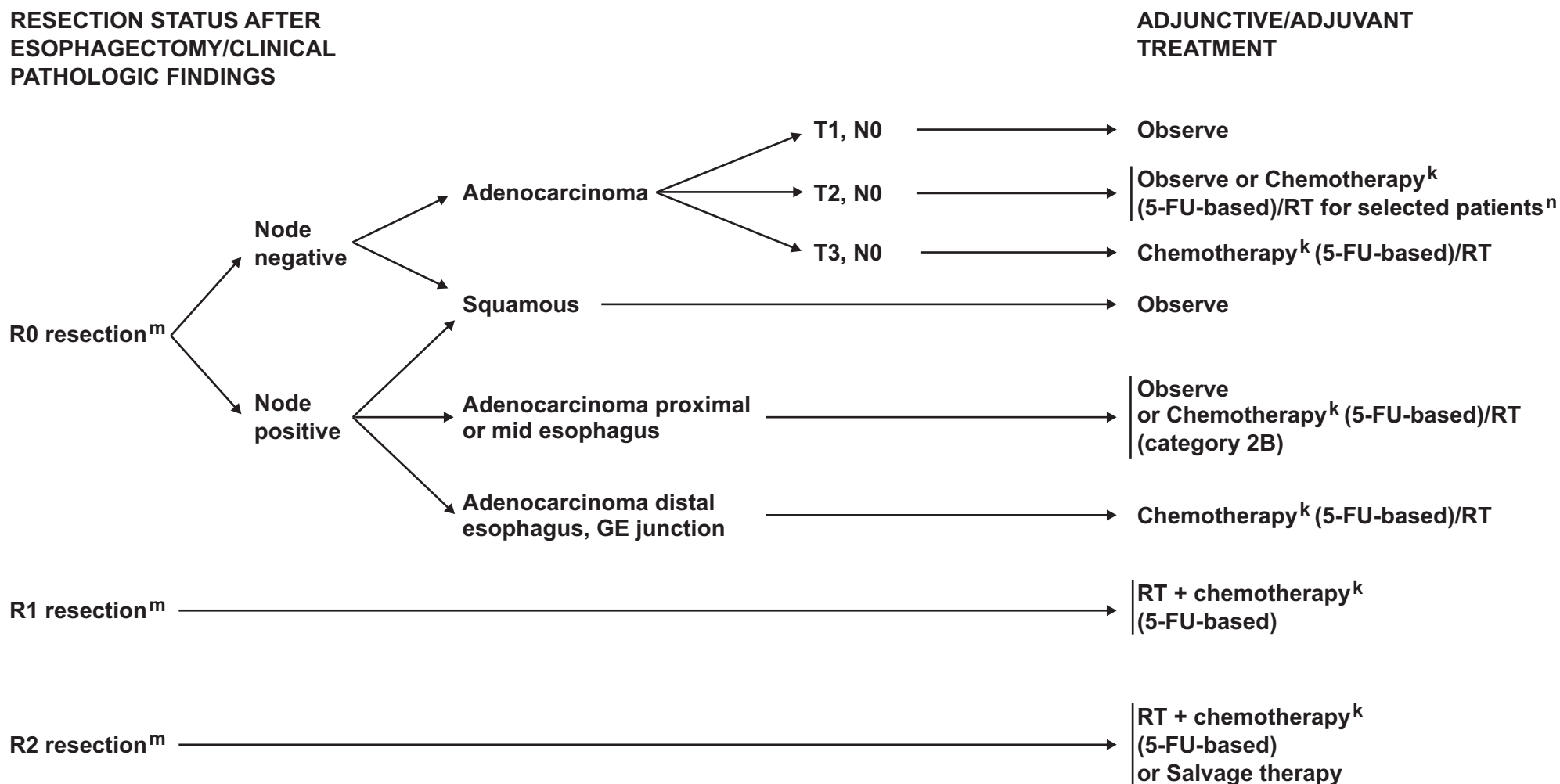
^k[See Principles of Systemic Therapy \(ESOPH-B\).](#)

^lAssessment ≥ 4 weeks, endoscopy with biopsy and brushings.

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[Follow-up](#)
[\(See ESOPH-5\)](#)



^kSee Principles of Systemic Therapy (ESOPH-B).

^mR0= No cancer at resection margins, R1= Microscopic residual cancer, R2= Macroscopic residual cancer or M1B.

ⁿFor higher risk patients such as poorly differentiated histology, lymphovascular invasion, neurovascular invasion or young patients. Limit to lower esophageal or GE junction patients.

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[Follow-up](#)
[\(See ESOPH-5\)](#)

PRIMARY TREATMENT

Medically unfit for surgery, unresectable T4,^g unresectable stage IVA^h or Surgery not elected and patient medically able to tolerate chemotherapy

RT, 50-50.4 Gy + concurrent chemotherapy^k (5-FU-based) (preferred) or Best supportive care

Medically unfit for surgery and patient unable to tolerate chemotherapy

Best supportive care

Best Supportive Care

- Obstruction: Stent, laser, photodynamic therapy, RT (external or brachytherapy)
- Nutrition: Enteral feeding
- Pain control: RT and/or medications
- Bleeding: RT or surgery and/or endoscopic therapy
- Esophageal dilatation

^gUnresectable T4: invasion of aorta, trachea, heart, great vessels.

^hUnresectable Stage IVA: Celiac nodes > 1.5 cm or involvement of celiac artery, aorta, or other organs.

^kSee [Principles of Systemic Therapy \(ESOPH-B\)](#).

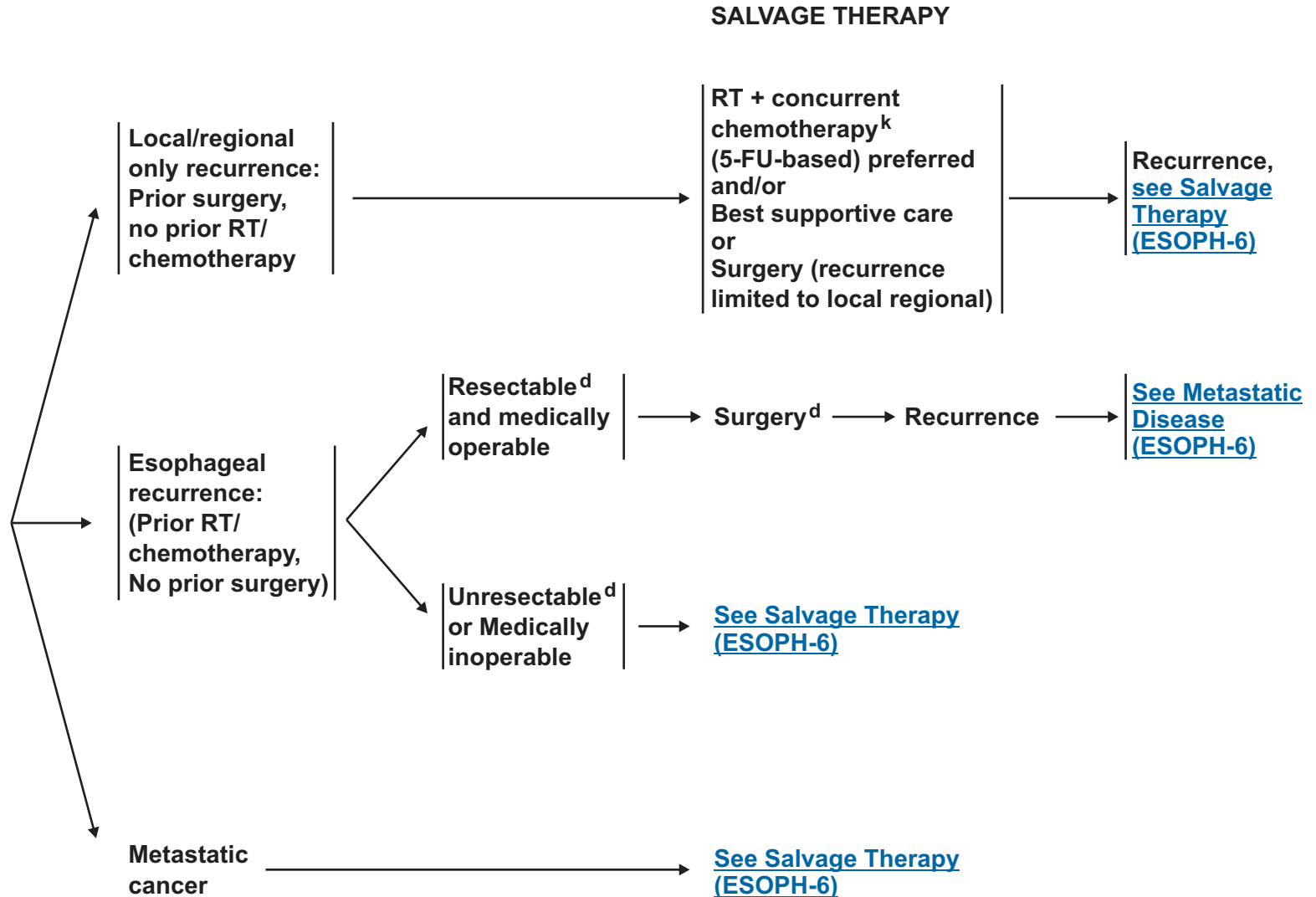
[Follow-up](#)
[\(See ESOPH-5\)](#)

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FOLLOW-UP

- If asymptomatic: H&P every 4 mo for 1 y, every 6 mo for 2 y, then annually
- Chemistry profile + CBC, as clinically indicated
- Chest x-ray as indicated
- Radiology and endoscopy, as clinically indicated (eg, persistent or recurrent dysphagia)
- Dilatation for anastomotic stenosis
- Nutritional counseling



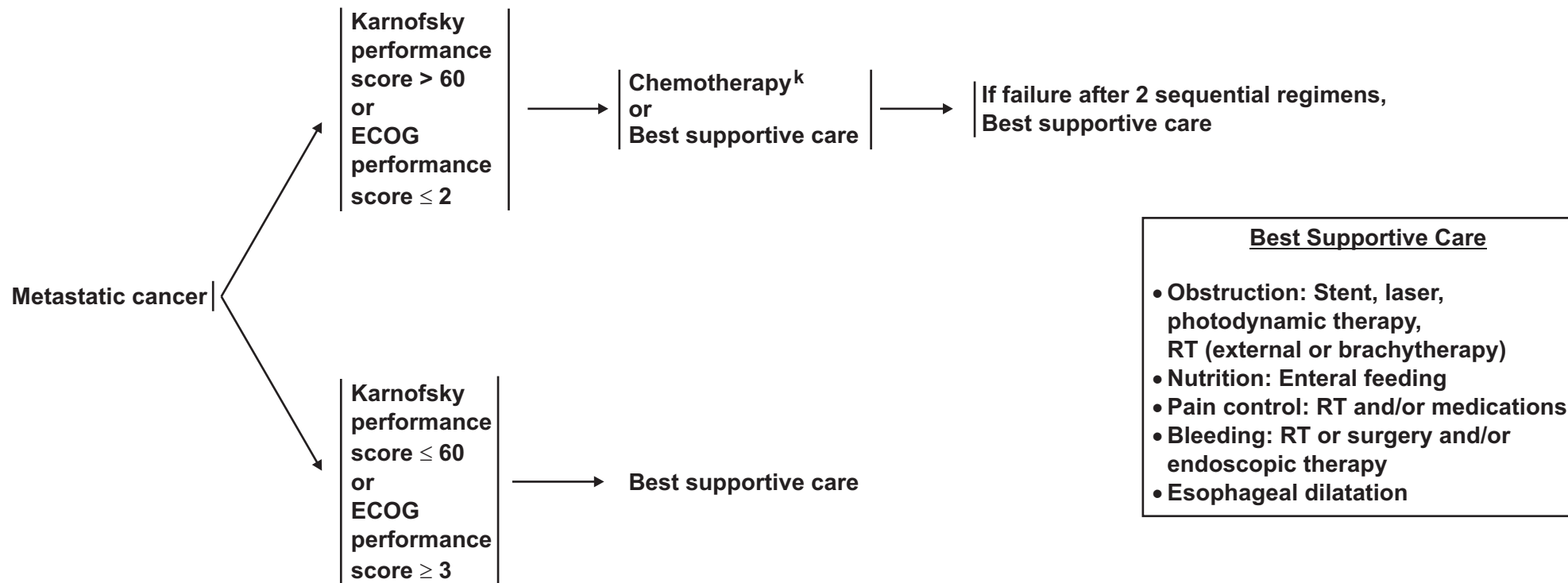
^dSee [Principles of Surgery \(ESOPH-A\)](#).

^kSee [Principles of Systemic Therapy \(ESOPH-B\)](#).

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SALVAGE THERAPY



^kSee Principles of Systemic Therapy (ESOPH-B).

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[Back to Follow-up and recurrence \(ESOPH-5\)](#)

PRINCIPLES OF SURGERY

- Prior to surgery all patients should be assessed for physiologic ability to undergo esophageal resection.¹
- Prior to surgery clinical staging should be performed to assess resectability with endoscopic ultrasound, CT scan chest and abdomen, and CT-PET.
- Esophageal resection should be considered for all physiologically fit patients with localized resectable esophageal cancer in the thorax (> 5 cm from cricopharyngeus).
- Cervical esophageal tumors or thoracic esophageal tumors < 5 cm from the cricopharyngeus should be treated with definitive chemoradiation.
- Resectable thoracic esophageal (> 5 cm from cricopharyngeus) or gastroesophageal junction cancer:
 - ▶ T1-T3 tumors are resectable even with regional nodal metastases (N1)
 - ▶ T1a tumors limited to lamina propria can be considered for endoscopic mucosal resection in experienced centers.
 - ▶ T4 tumors are resectable with involvement of pericardium, pleura or diaphragm only.
 - ▶ Stage IVA is resectable for lower esophagus with celiac nodes ≤ 1.5 cm and no involvement of celiac artery, aorta or other organs.
- Unresectable Esophageal Cancer:
 - ▶ T4 tumors are unresectable with involvement of the heart, great vessels, trachea or adjacent organs including liver, pancreas, lung and spleen.
 - ▶ Stage IVA is unresectable for the lower esophagus with celiac nodes > 1.5 cm, involvement of celiac artery, aorta, or other organs including liver, pancreas, lung, and spleen.
 - ▶ Stage IVB is unresectable with systemic metastases or non-regional lymph nodes.
- The type of esophageal resection is dictated by the surgeon's experience and preference and the patient's preference.

[Continued on next page](#)

¹Steyerberg EW, Neville BA, Kopper LB, Lemmens VE, Tilanus HW, Coebergh JW, Weeks JC, and Earle CC. Surgical mortality in patients with esophageal cancer: development and validation of a simple risk score. J Clin Oncol, 24 (26):4277-84, 2006.

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PRINCIPLES OF SURGERY (continued)

- **Acceptable operative approaches for thoracic esophageal (> 5 cm from cricopharyngeus) or gastroesophageal junction cancer:²**
 - ▶ **Right or left transthoracic with anastomosis in chest or neck**
 - ▶ **Transhiatal with anastomosis in neck**
 - ▶ **Minimally invasive with anastomosis in neck or chest**
- **Acceptable conduits:**
 - ▶ **Gastric (preferred)**
 - ▶ **Colon**
 - ▶ **Short segment jejunum**
 - ▶ **Long segment jejunum with supercharged microvascular anastomosis**
- **Acceptable lymph node dissections:³**
 - ▶ **Standard**
 - ▶ **Extended (En-Bloc)**
- **A minimum of 15 lymph nodes should be removed/evaluated to achieve adequate nodal staging**
- **Patients who develop localized, resectable esophageal recurrence after definitive chemoradiation can be considered for salvage esophagectomy if they do not have distant recurrence.⁴**
- **Esophageal resection should be performed in experienced esophageal centers.⁵**

²de Hoyos A, Litle VR, and Luketich JD. Minimally invasive esophagectomy. Surg Clin North Am. 85 (3): 631-47, 2005.

³Hofstetter WL. Lymph Node Dissection in Esophageal Cancer. Current Therapies in Thoracic and Cardiovascular Surgery, edited by SC Yang and DE Cameron. Mosby, Inc., Philadelphia, Pennsylvania, pp. 360-363, 2004.

⁴Swisher SG, Wynn P, Putnam JB, Mosheim MB, Correa AM, Komaki RR, Ajani JA, Smythe WR, Vaporciyan AA, Roth JA, and Walsh GL. Salvage esophagectomy for recurrent tumors after definitive chemotherapy and radiotherapy. J Thorac Cardiovasc Surg, 123:175-183, 2002.

⁵Birkmeyer JD, Siewers AE, Finlayson EVA, Stukel TA, Lucas FL, Batista I, Welch HG, and Wennber DE. Hospital volume and surgical mortality in the United States. N Engl J Med, 346(15):1128-37, 2002.

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PRINCIPLES OF SYSTEMIC THERAPY

- For localized esophageal carcinoma, only fluoropyrimidine/cisplatin has been studied alone or in conjunction with radiation therapy. However, many participating institutions have developed chemotherapy regimens in the context of phase II studies. Thus, many regimens indicated below represent institutional preferences but they may not be superior to fluoropyrimidine/cisplatin.
- For metastatic esophageal carcinoma: phase III trials have not been performed for more than 15 years. The regimens indicated below represent institutional preferences in the context of phase II trials.
- Postoperative chemotherapy alone has not been studied in phase III trials. The suggestion below is an institutional preference.

Preoperative Chemotherapy:

- Fluoropyrimidine/cisplatin (category 2B)
- Taxane-based regimen (category 2B)

Preoperative or Definitive Chemoradiation:

- Fluoropyrimidine/cisplatin (category 2B)
- Taxane-based (category 2B)
- Irinotecan-based (category 2B)

Postoperative Chemoradiation:

- Fluoropyrimidine/leucovorin (category 2A)
- Fluoropyrimidine/cisplatin (category 2B)

Postoperative Chemotherapy:

- Taxane-based (category 2B)

Metastatic Cancer:

- Fluoropyrimidine-based (category 2B)
- Cisplatin-based (category 2A)
- Oxaliplatin-based (category 2B)
- Taxane-based (category 2A)
- Irinotecan-based (category 2B)

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Staging

Table 1

American Joint Committee on Cancer (AJCC) TNM Classification of Carcinoma of the Esophagus*

Primary Tumor (T)

- TX Primary tumor cannot be assessed
- T0 No evidence of primary tumor
- Tis Carcinoma in situ
- T1 Tumor invades lamina propria or submucosa
- T2 Tumor invades muscularis propria
- T3 Tumor invades adventitia
- T4 Tumor invades adjacent structures

Regional Lymph Nodes (N)

- NX Regional lymph nodes cannot be assessed
- N0 No regional lymph node metastasis
- N1 Regional lymph node metastasis

Distant Metastasis (M)

- MX Distant metastasis cannot be assessed
- M0 No distant metastasis
- M1 Distant metastasis

Tumors of the lower thoracic esophagus:

- M1a Metastasis in celiac lymph nodes
- M1b Other distant metastasis

Tumors of the midthoracic esophagus:

- M1a Not applicable
- M1b Nonregional lymph nodes and/or other distant metastasis

Tumors of the upper thoracic esophagus:

- M1a Metastasis in cervical nodes
- M1b Other distant metastasis

Stage Grouping

Stage 0	Tis	N0	M0
Stage I	T1	N0	M0
Stage IIA	T2	N0	M0
	T3	N0	M0
Stage IIB	T1	N1	M0
	T2	N1	M0
Stage III	T3	N1	M0
	T4	Any N	M0
Stage IV	Any T	Any N	M1
Stage IVA	Any T	Any N	M1a
Stage IVB	Any T	Any N	M1b

Histologic Grade (G)

- GX Grade cannot be assessed
- G1 Well differentiated
- G2 Moderately differentiated
- G3 Poorly differentiated
- G4 Undifferentiated

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Manuscript This manuscript is being updated to correspond with the newly updated algorithm.

NCCN Categories of Consensus

Category 1: There is uniform NCCN consensus, based on high-level evidence, that the recommendation is appropriate.

Category 2A: There is uniform NCCN consensus, based on lower-level evidence including clinical experience, that the recommendation is appropriate.

Category 2B: There is nonuniform NCCN consensus (but no major disagreement), based on lower-level evidence including clinical experience, that the recommendation is appropriate.

Category 3: There is major NCCN disagreement that the recommendation is appropriate.

All recommendations are category 2A unless otherwise noted.

Overview

Upper gastrointestinal (GI) tract carcinomas (those originating in the esophagus, gastroesophageal junction, and stomach) constitute a major health problem around the world. It is estimated that approximately 36,830 new cases of upper GI carcinomas and 25,200 deaths will occur in the United States in 2006.¹ A dramatic shift in the location of upper GI tumors has occurred in the United States.² Changes in histology and location of upper GI tumors have also been observed in some parts of Europe.³⁻⁵ In Western Hemisphere countries, the most common site of esophageal carcinoma is in the lower third of the esophagus, where it often involves the gastroesophageal junction.

Epidemiology of Esophageal Carcinoma

Carcinoma of the esophagus (predominantly squamous cell carcinoma) is the ninth most common malignant cancer around the world. It is endemic in many parts of the world, particularly in the developing nations.⁶ The incidence of esophageal carcinoma represents one of the widest variations, with a 60-fold difference between high- and low-incidence regions.⁷ High prevalence areas include Asia, southern and eastern Africa, and Northern France.^{8,9} In the United States, carcinoma of the esophagus is infrequent, constituting 1% of all malignancies and 6% of all GI cancers. Approximately 14,550 new cases of esophageal carcinoma and 13,770 deaths are estimated to occur in 2006.¹

Although squamous cell carcinoma is most common in the endemic regions of the world, adenocarcinoma is most common in the world's nonendemic areas, such as North America and many western European countries. Squamous cell carcinoma occurs more frequently among men than women, and it is associated with alcohol and tobacco use.¹⁰ In addition, these patients often have a history of head and neck carcinoma. The increasing incidence of esophageal adenocarcinoma may be due to an increasing frequency of gastroesophageal reflux disease (GERD) in the general population. GERD is a common condition that affects up to 30% of the Western population.¹¹ GERD is associated with high body mass index. Patients diagnosed with adenocarcinoma are predominantly white men. About 62% of cases of esophageal carcinoma have evidence of Barrett's esophagus, a metaplastic change in the lining of the esophagus from normal squamous to columnar intestinal epithelium.¹¹

Staging

The modern staging of carcinoma of the esophagus is based on the tumor/node/metastasis (TNM) classification developed by the American Joint Committee on Cancer (see [Table 1](#)).¹² Clearly, patient outcomes are correlated with the initial stage of the cancer at diagnosis, but the best correlation with survival is associated with the surgical pathologic stage. Although surgical pathology yields the most accurate staging, the advent of better imaging techniques, including endoscopic ultrasonography, has improved preclinical staging;¹³ (18)F-fluorodeoxyglucose positron emission tomography (FDG-PET) may be useful for detection of distant lymphatic and hematogenous metastases; PET/CT is even more accurate.¹⁴ In North America and many western European countries, where screening programs for early detection of esophageal cancer are not in use or practical because of low incidence, the diagnosis is often made late in the course of the disease. At diagnosis, nearly 50% of patients have cancer that extends beyond the locoregional confines of the primary. Fewer than 60% of patients with locoregional cancer can undergo a curative resection. Nearly 70% to 80% of resected specimens harbor metastases in the regional lymph nodes. Thus, clinicians are often dealing with advanced-stage carcinoma in newly diagnosed patients.¹

Surgery

The incidence of carcinoma of the esophagus, particularly of adenocarcinoma of the distal esophagus, is increasing dramatically.¹ It is hoped that as the incidence of patients with early-stage cancer increases as a result of surveillance programs for columnar-lined epithelium, an increasing number of patients with esophageal cancer are expected to be candidates for resection.¹⁵

Outcomes

One of the major developments in the surgical therapy of esophageal cancer has been the marked reduction in surgical morbidity and mortality as a result of improvements in staging techniques, patient selection, and support systems.¹⁶ Surgical management of patients with esophageal cancer may include staging,¹⁷ resection with curative intent, and palliative techniques. The intent of surgery should be to achieve an R0 resection. Palliative resections should be avoided in patients with clearly unresectable or advanced cancer who can be effectively palliated using nonsurgical modalities.^{18,19} The 5-year survival after an R0 resection is 15% to 20%, and the median survival after R0 resection is approximately 18 months; no difference in survival was observed between groups treated with either surgery alone or induction therapy followed by surgery.^{20,21}

Stage I, II, and III cancer are assumed to be potentially resectable. Modern preoperative staging (including esophageal ultrasound, PET²² or PET/CT (which is more accurate), and molecular biologic techniques²³) may result in improved prognostic stratification, improved patient selection for surgical therapy, and improved overall survival.²⁴ A recent study reported that serum c-reactive protein levels, body weight change, and clinical TNM staging before treatment can be combined in an index to predict the prognosis of patients with esophageal carcinoma.²⁵ C-reactive protein needs to be further investigated before its routine incorporation into initial staging. Pretreatment weight loss is a documented prognostic factor. Selecting patients for surgery includes assessing whether they are medically fit (ie, medically able to tolerate major abdominal and/or thoracic surgery) and the extent of their cancer. Patients with advanced comorbidity, including severe cardiac and pulmonary

disease, cannot undergo resection but may benefit from noninvasive palliative interventions. However, most patients with early-stage cancer can tolerate resection.

Surgical Approaches

Various surgical approaches may be used, depending on the size and location of the primary tumor and on the preferences of the surgeon. The optimal location of the anastomosis has been debated. The advantages of the cervical anastomosis include more extensive resection of the esophagus, possibility of avoiding thoracotomy, less-severe symptoms of reflux, and less-severe complications related to anastomotic leak. Advantages of the thoracic anastomosis include a lower incidence of anastomotic leak and lower stricture rate.²⁶ Although some surgeons prefer the colon interposition, most surgeons use the stomach as the conduit to replace the esophagus after esophagogastrectomy. Colon interposition is usually reserved for patients who have had previous gastric surgery or other procedures that have devascularized the stomach. The use of the gastric conduit simplifies the procedure and is associated with equivalent patient satisfaction and fewer postoperative complications.²⁷

Several approaches are acceptable for esophagogastrectomy. Ivor-Lewis esophagogastrectomy uses abdominal and right thoracic incisions, with upper thoracic esophagogastric anastomosis (at or above the azygos vein).²⁸ Mobilization of the stomach for use as the conduit is performed, with dissection of the celiac and left gastric lymph nodes, division of the left gastric artery, and preservation of the gastroepiploic and right gastric arteries. This approach may be used for lesions at any thoracic location, but margins may be inadequate for tumors in the middle esophagus. Transhiatal esophagogastrectomy is performed using abdominal and left

cervical incisions.²⁹ The mobilization of the stomach for use as the conduit is performed as in the Ivor-Lewis esophagogastrectomy. This procedure is completed via the abdominal incision, and the gastric conduit is drawn through the mediastinum and exteriorized in the cervical incision for the esophagogastric anastomosis. This approach may be used for lesions at any thoracic location; however, transhiatal dissection of large, middle esophageal tumors adjacent to the trachea is difficult and may be hazardous.

Left thoracoabdominal esophagogastrectomy uses a contiguous abdominal and left thoracic incision, through the eighth intercostal space. Mobilization of the stomach for use as the conduit is performed as described previously, and esophagectomy is accomplished via the left thoracotomy. Esophagogastric anastomosis is performed in the left chest, usually just superior to the inferior pulmonary vein, although it may be performed higher if the conduit is tunneled under the aortic arch. This approach may be used for lesions in the distal esophagus.

Minimally invasive esophagectomy is associated with decreased morbidity and shorter recovery times when compared with open procedures.³⁰ A study of minimally invasive surgery in 77 patients by Luketich and colleagues found no operative or hospital mortalities; major and minor complication rates were 27% and 55%, respectively.³¹ Luketich and colleagues recently published a larger study in 222 patients of minimally invasive esophagectomy (mainly using thoracoscopic mobilization). They reported that mortality was only 1.4% and hospital stay was only 7 days, which is less than most open procedures; only 16 patients (7.2%) required conversion to an open procedure.³⁰ However, it is important to note that 62% of their patients had early-stage disease. Minimally invasive esophagectomy is useful for older patients.³² No randomized trials

have assessed whether minimally invasive esophagectomy improves survival when compared with open procedures. Open esophagectomy is still preferred in many settings (eg, large and bulky tumors, concerns about the location of positive margins, concerns that the gastric conduit may not be useable, patient has received multiple previous upper abdominal surgeries). Open surgery should remain the standard for many patients.

Radiation Therapy

Several historical series have reported results of using external-beam radiation therapy (RT) alone. Most of these series included patients with unfavorable features, such as clinical T4 cancer. Overall, the 5-year survival rate for patients treated with conventional doses of RT alone is 0% to 10%.³³⁻³⁵ Shi and colleagues³⁶ reported a 33% 5-year survival rate with the use of late-course accelerated fractionation to a total dose of 68.4 Gy. However, in the Radiation Therapy Oncology Group (RTOG) 85-01 trial, in which patients in the RT-alone arm received 64 Gy at 2 Gy/d with conventional techniques, all patients died of cancer by 3 years.^{37,38} Therefore, the panel recommends that RT alone should generally be reserved for palliation or for patients who are medically unable to receive chemotherapy.

Alternative radiation approaches, such as hypoxic cell sensitizers and hyperfractionation, have not resulted in a clear survival advantage. Experience with intraoperative radiation as an alternative to external-beam radiation is limited.³⁹ Conformal and intensity-modulated RT are currently being investigated.⁴⁰ In the adjuvant setting, randomized trials do not show a survival advantage for preoperative or postoperative RT alone.⁴¹ A meta-analysis from the “Oesophageal Cancer Collaborative Group” also showed no clear evidence of a survival advantage with preoperative radiation.⁴²

Chemoradiotherapy

Multiple modalities have been employed for treatment of esophageal cancer because of the overall poor survival rates of patients who have been treated with resection alone.^{43,44} The only randomized trial that was designed to deliver adequate doses of systemic chemotherapy with concurrent RT was the RTOG 85-01 trial reported by Herskovic et al³⁷ and others.^{38,45} This Intergroup trial primarily included patients with squamous cell carcinoma. Patients received 4 cycles of 5-fluorouracil (5-FU) and cisplatin. RT (50 Gy at 2 Gy/d) was given concurrent with day 1 of chemotherapy. The control arm was RT alone, albeit a higher dose (64 Gy) than in the combined modality therapy arm. Patients who were randomly assigned to receive combined modality therapy had a significant improvement in both median survival (14 versus 9 months) and 5-year survival (27% versus 0%).³⁸ With a minimum follow-up of 5 years, the 8-year survival was 22%.⁴⁵ The incidence of local failure as the first site of failure (defined as local persistence plus recurrence) was also lower in the combined modality arm (47% versus 65%).

The INT 0123 trial was the follow-up trial to RTOG 85-01. In this trial, patients with either squamous cell carcinoma (85%) or adenocarcinoma (15%) who were selected for a nonsurgical approach were randomly assigned to a slightly modified RTOG 85-01 combined modality regimen with 50.4 Gy versus the same chemotherapy with a higher dose of radiation (64.8 Gy). For the 218 eligible patients, no significant difference was observed in median survival (13.0 versus 18.1 months), 2-year survival (31% versus 40%), and local/regional failure or local/regional persistence of cancer (56% versus 52%) between the high-dose and standard-dose RT arms.⁴⁶ Recent trials have used more novel agents, such as

paclitaxel-based chemotherapy,^{47,48} docetaxel-based,⁴⁹ oxaliplatin-based,⁵⁰ or irinotecan-based^{51,52} chemotherapy.

Randomized trials comparing preoperative combined modality therapy with surgery alone in patients with clinically resectable cancer have shown conflicting results.^{21,53-56} Therefore, although this approach is reasonable, it remains investigational.⁵⁷ In patients with resectable esophageal cancer, chemoradiotherapy plus surgery significantly reduces 3-year mortality compared with surgery alone as shown in a recent meta-analysis; preoperative chemoradiotherapy also downstaged the tumor.⁵⁸ However, postoperative mortality was significantly increased by neoadjuvant chemoradiotherapy. A recent meta-analysis assessed nine randomized controlled trials (> 1000 patients) comparing neoadjuvant chemoradiation and surgery versus surgery alone for esophageal cancer.⁵⁹ This meta-analysis found that neoadjuvant chemoradiation and surgery improved 3-year survival and reduced local-regional cancer recurrence when compared with surgery alone. Such analyses only suggest that preoperative approaches need continued investigations. Another recent trial assessed preoperative chemoradiation with and without surgery in 172 randomly assigned patients with locally advanced esophageal cancer; this study found that overall survival was equivalent in either group, although treatment-related mortality was higher in the surgery group.⁶⁰ The surgical mortality in this trial was unacceptably high.

In the NCCN algorithm, options for preoperative or definitive chemoradiation include 5-FU/cisplatin (category 1), taxane-based regimens (category 3), and irinotecan-based regimens (category 3). For localized esophageal carcinoma, only 5-FU/cisplatin has been studied alone or in conjunction with RT. However, many participating NCCN institutions have developed other chemotherapy regimens in

the context of phase II studies. These regimens represent institutional preferences, but they may not be superior to 5-FU/cisplatin. In the NCCN algorithm, options for postoperative chemoradiation include 5-FU/cisplatin (category 1) and 5-FU--based regimens (category 3).

Brachytherapy

Brachytherapy alone is a palliative modality and results in a local control rate of 25% to 35% and in a median survival of approximately 5 months.⁶¹ In the randomized trial from Sur and colleagues,⁶¹ there was no significant difference in local control or survival with high-dose-rate brachytherapy compared with external beam. In the RTOG 92-07 trial, 75 patients received the RTOG 85-01 combined modality regimen (5-FU/cisplatin/50 Gy) followed by an intraluminal boost.⁶² Local failure was 27%, and acute toxicity included 58% with grade 3, 26% with grade 4, and 8% with grade 5. The cumulative incidence of fistula was 18% per year, and the crude incidence was 14%. Therefore, the additional benefit of adding intraluminal brachytherapy to radiation or combined modality therapy, although reasonable, remains unclear.

Chemotherapy

Chemotherapy can provide transient palliation for some patients with advanced locoregional carcinoma, but other approaches (including combined modality therapy) are more effective for this purpose. Chemotherapy alone has been investigated in the preoperative setting. The preliminary results of an intergroup trial (Intergroup 0113), in which patients with potentially resectable carcinoma of the esophagus of both histologic types were randomly assigned to receive either preoperative chemotherapy with 5-FU plus cisplatin or

surgery alone, did not demonstrate any survival benefit among the patients who received preoperative chemotherapy.²⁰

The Medical Research Council (MRC) published their trial, which involved 802 patients with potentially resectable carcinoma of the esophagus.⁶³ In this trial, patients were randomly assigned to receive either (1) 2 cycles of preoperative 5-FU (1000 mg/m² per day by continuous infusion for 4 days) and cisplatin (80 mg/m² on day 1) repeated every 21 days followed by surgery; or (2) surgery alone. However, this trial had several clinical methodology problems. Nearly 10% of patients received off-protocol preoperative radiotherapy, and patients accrued in China were excluded. At a short median follow-up time of 2 years, there was a 3.5-month survival time advantage (16.8 versus 13.3 months) for the group treated with preoperative chemotherapy. The median survival of the control group is less than expected. A longer follow-up would be necessary to understand whether this advantage in survival time would prevail. The panel does not recommend preoperative or postoperative chemotherapy as standard of care. However, many participating NCCN institutions have developed chemotherapy regimens in the context of phase II studies; these regimens may not be superior to 5-FU/cisplatin.

The list of established chemotherapeutic drugs active against esophageal carcinoma is small. The activity of many agents has only been established against squamous cell histology. Cisplatin is one of the most active agents, with a single-agent response rate consistently in the range of 20% or greater.⁶⁴ Older agents that are active include 5-FU, mitomycin, cisplatin, bleomycin, methotrexate, mitoguanine, doxorubicin, and vindesine (which are all category 3).^{65,66} Newer agents that have shown activity include paclitaxel, docetaxel, vinorelbine, oxaliplatin with 5-FU, lobaplatin, irinotecan, nedaplatin, and gefitinib (which are all category 3).⁶⁷⁻⁷³ In the NCCN algorithm,

preoperative chemotherapy includes 5-FU/cisplatin and taxane-based regimens (category 3); for postoperative chemotherapy, taxane-based regimens (category 3) are also listed.

Combination chemotherapy for metastatic carcinoma of the esophagus continues to evolve. Compared with adenocarcinoma, squamous cell carcinoma appears to be more sensitive to chemotherapy, chemoradiation, or radiotherapy; however, the long-term outcome is not different for patients with the two histologic types.²⁰ The combination of 5-FU plus cisplatin (category 1) is the most investigated and most commonly used regimen for patients with carcinoma of the esophagus. Reported response rates to this combination vary between 20% and 50%.⁶⁶ Paclitaxel combined with 5-FU and cisplatin has demonstrated activity in patients with squamous cell carcinoma and adenocarcinoma.⁷⁴ In addition, the combination of irinotecan (CPT-11) and cisplatin appears to have activity, particularly against squamous cell carcinoma of the esophagus.⁷⁵ A recent phase II trial (35 patients) showed that a carboplatin and paclitaxel regimen was moderately active (43% response rate) in patients with advanced esophageal cancer; however, 52% of patients had neutropenia (grade 3-4).⁷⁶ The Southwest Oncology Group Study conducted a phase II trial of gemcitabine and cisplatin in 64 patients with metastatic esophageal cancer; median survival was 7.3 months.⁷⁷ Another phase II trial assessed gemcitabine and cisplatin in 42 patients with advanced esophageal cancer, yielding a 45% response rate in evaluable patients.⁷⁸ Docetaxel, cisplatin, and irinotecan yielded a 63% response rate (10/16 patients) in a recent phase II study.⁷⁹ Although combination chemotherapy often results in a higher response rate, it can be associated with higher morbidity. For metastatic esophageal carcinoma, phase III trials have not been performed for more than 15 years. The regimens listed in the NCCN algorithm (see [ESOPH-A](#))

represent institutional preferences in the context of phase II trials; these options include 5-FU--based (category 1), and cisplatin-based (category 1), as well as oxaliplatin-based, taxane-based, and irinotecan-based regimens (which are all category 3).

Endoscopic Palliation

Patients with esophageal cancer may benefit from noninvasive techniques that address obstruction, dysphagia, tracheoesophageal fistula, and GI bleeding. In patients with unresectable carcinoma or incurable carcinoma associated with dysphagia, the most realistic goal would be to provide symptomatic relief, which may improve nutritional status, the sensation of well-being, and overall quality of life.⁸⁰

Currently available endoscopic palliative methods to overcome dysphagia include balloon dilatation or bougienage, thermocoagulation (laser), injection of alcohol or chemotherapeutic agents, photodynamic therapy (PDT), intracavitary irradiation, and placement of a plastic or expandable metal prosthesis.⁸¹⁻⁹² The combination of PDT and the self-expanding stents provides the best palliation for most patients with obstruction and unresectable esophageal carcinoma.^{18,19} Patients with tracheoesophageal fistula are usually treated effectively with the placement of a silicone-covered self-expanding metal stent, obviating palliative esophageal exclusion and bypass in most patients. Placement of a gastrostomy or jejunostomy tube may help improve patients' nutritional status.

Treatment Guidelines

Workup

Newly diagnosed patients should undergo a complete history, physical examination, and endoscopy of the entire upper GI tract.

Histologic confirmation of carcinoma is required. For patients in whom the upper GI tract cannot be visualized, a double-contrast barium study of the upper GI tract is optional. A complete blood count, multichannel serum chemistry analysis, coagulation studies, and computed tomographic (CT) scan of the chest and abdomen should also be performed. PET/CT scans are useful if there is no evidence of M1 disease. Combined (integrated) CT/PET scans are emerging and appear to be useful for restaging patients and monitoring response after neoadjuvant therapy (see "Primary Therapy").⁹³ If the carcinoma is located at or above the carina, bronchoscopy (including biopsy of any abnormality and cytology of the washings) should be performed.

At this point, if metastatic cancer is not evident, endoscopic ultrasonography (with fine-needle aspiration [FNA] if indicated) is recommended. In addition, if the carcinoma is located at the gastroesophageal junction, laparoscopic staging of the peritoneal cavity is optional. Suspicions for metastatic cancer should be confirmed by biopsy. This workup enables patients to be separated into two groups: (1) patients with apparent locoregional carcinoma (stages I to III, IVA), and (2) those with obvious metastatic carcinoma (stage IVB).

Esophagogastric Junction

Cancer of the esophagogastric junction has been characterized by Siewert and colleagues.^{94,95} If the tumor center or more than 66% of the tumor mass is located more than 1 cm above the anatomic gastroesophageal junction, then the tumor is classified as an adenocarcinoma of the distal esophagus, type I. If the tumor center or tumor mass is located within 1-cm oral and 2-cm distal to the anatomic gastroesophageal junction, this adenocarcinoma is classified as type II. If the tumor center or more than 66% of the

tumor mass is located more than 2 cm below the anatomic gastroesophageal junction, these adenocarcinomas are classified as a court of tumors (adenocarcinoma of the gastroesophageal junction, type III).⁹⁴

In 2000, the classification changed slightly. Patients whose tumors have a center that is 5-cm proximal or distal to the anatomic cardia are classified as having adenocarcinomas of the esophagogastric junction. These tumors include type I adenocarcinoma, which may infiltrate the esophagogastric junction from above; type II adenocarcinoma, which arises from the esophagogastric junction; and type III adenocarcinoma, or subcardial gastric carcinoma, which infiltrates up to the esophagogastric junction from below.⁹⁵

Siewert and colleagues note that the description of these types of tumors is purely morphologic based on the anatomic location of the epicenter of the tumor or the location of the tumor mass.⁹⁵ Various techniques used to make this determination can include barium esophagraphy, esophagoscopy, and CT. An individualized therapeutic approach may be preferred for specific patients and for specific tumor locations, based on thorough pretreatment staging. Therapeutic decisions may be refined by taking into account the location of the individual tumor and the specific requirements for local control.

Additional Evaluation

For patients with apparent locoregional carcinoma, additional evaluations may be warranted to assess their medical condition; these evaluations are mandatory for patients with celiac-positive disease. These evaluations may include pulmonary function studies, cardiac testing, and nutritional assessment. For preoperative nutritional support, a nasogastric or jejunostomy tube should be

considered; percutaneous endoscopic gastronomy (PEG) is not recommended. Moreover, evaluation of the colon by barium x-ray or colonoscopy may be warranted if colon interposition is planned as part of the surgical procedure. A superior mesenteric artery angiogram should be considered only in selected cases when colon interposition is planned. Because the management of esophageal cancer requires the expertise of several disciplines---thoracic surgery, radiation oncology, medical oncology, nutritional and pulmonary support, and endoscopy---multidisciplinary evaluation is encouraged.

Primary Therapy

Medically fit patients with a resectable (T1-T3 or resectable T4, N0-1, NX, or IVA) carcinoma have three initial options: (1) esophagectomy (preferred for noncervical T1 disease) followed by further adjuvant therapy; (2) RT (50-50.4 Gy) plus concurrent chemotherapy (5-FU--based) followed by esophagectomy in certain settings; or (3) definitive chemotherapy/RT followed by observation/salvage surgery (optional). Note that resectable T4 tumors involve the pleura, pericardium, or diaphragm; unresectable T4 tumors invade the aorta, trachea, heart, or great vessels. The choice of surgical procedure (ie, transhiatal, transthoracic, or minimally invasive esophagectomy) depends on the preferences of the participating institution. However, surgery is recommended for patients whose carcinoma is below the level of the carina and for whom a procedure involving gastric reconstruction is preferred. Chemotherapeutic agents, other than 5-FU plus cisplatin used concurrently with radiotherapy, remain investigational. Many combinations have been studied;^{48,52,96,97} however, none can be recommended for routine use because of the lack of comparative data. Chemoradiotherapy is the preferred modality for cervical esophageal carcinoma.

After esophagectomy, patients with R0 resection and no nodal metastases who have adenocarcinoma have three options: (1) those with T1, N0 should be observed, and no further therapy may be recommended in the absence of evident cancer; (2) those with T2, N0 may be observed or selected patients can receive chemoradiotherapy (5-FU--based)/RT; and (3) those with T3, N0 may receive chemoradiotherapy (5-FU--based)/RT. Selected higher risk patients---defined as those with T2, N0 cancer but who (1) have a poorly differentiated adenocarcinoma histology, lymphovascular invasion, or neurovascular invasion; or (2) are younger than 40 years---may receive postoperative adjuvant chemoradiation on an individualized decision basis. Patients with R0 resection and negative nodes who have squamous carcinoma should be observed. Patients with R1 resections should be offered radiotherapy with 5-FU--based chemotherapy. Patients with R2 resections should be treated with chemoradiation (RT plus 5-FU--based) or salvage therapy, depending on the extent of the cancer.

For patients found to have positive nodes after surgery (R0 resection), follow-up treatment is based on the location and histology of the lesion. Patients with adenocarcinoma of the distal esophagus or gastroesophageal junction should receive postoperative adjuvant chemotherapy (5-FU--based) and RT.⁹⁸ Patients with adenocarcinomas of the thoracic proximal- or thoracic mid-esophagus may be observed or can receive chemotherapy (5-FU--based)/RT, although comparative data for this recommendation are lacking (category 2B). Patients with R0 resection who have squamous cell carcinoma can be observed. Note that the R classification refers to the amount of residual cancer remaining after tumor resection: R0 indicates no macroscopic or microscopic cancer at resection margins (ie, negative margins); R1 indicates microscopic residual cancer (ie, positive margins); and R2 indicates

gross (macroscopic) residual cancer or M1B (ie, positive margins) but not distant disease.²⁰

In medically fit, resectable patients who have been treated with RT plus concurrent chemotherapy, CT and repeat PET/CT scans are recommended. A recent study in patients with esophageal cancer reported that combined (ie, integrated) FDG-PET/CT scans are more accurate than esophageal ultrasound-FNA and CT scan for predicting nodal status and complete responders after neoadjuvant therapy.⁹³ When used alone, FDG-PET/CT and CT suggest targets for biopsy; however, false-positive results are common. A follow-up upper GI tract endoscopy 4 to 6 weeks after the patient completes therapy is optional. If there is no evidence of disease, the patient may be offered esophagectomy (preferred) or may be observed (category 2B). If persistent local disease (without metastatic disease) is evident; however, the patient can be offered esophagectomy or other methods of palliation (ie, chemotherapy, endoscopic therapy). Patients with progressive or metastatic disease can be offered palliative chemotherapy and/or endoscopic therapy.

Patients with unresectable carcinoma (including T4), those who are medically unfit for surgery, or those who do not choose to undergo surgery may be treated with 50 to 50.4 Gy of radiotherapy plus concurrent chemotherapy (5-FU--based) (preferred) if they are medically able to tolerate chemotherapy. Other combinations---such as taxane/cisplatin or irinotecan/cisplatin^{48,52}---have been used and studied only in phase II settings and are not recommended outside protocol because of the lack of comparative data. Best supportive care is a reasonable alternative in patients with inoperable cancers and is the recommended treatment if the patient cannot tolerate chemotherapy and is medically unfit for surgery. Note that unresectable T4 tumors invade the aorta, trachea, heart, or great

vessels; resectable T4 tumors involve the pleura, pericardium, or diaphragm.

Follow-up

All patients should be followed systematically. For asymptomatic patients, follow-up should include a complete history and physical examination every 4 months for 1 year, then every 6 months for 2 years, and annually thereafter. A complete blood count, multichannel serum chemistry evaluation, and a chest radiograph should be obtained as clinically indicated. Endoscopy and other radiologic studies can also be done if clinically indicated (eg, persistent or recurrent dysphagia). In addition, some patients may require dilatation of an anastomotic or a chemoradiation-induced stricture. Nutritional counseling may be extremely valuable.⁹⁹

Salvage Therapy

Salvage therapy can range from aggressive intervention with curative intent in patients with locoregional relapse to therapy intended strictly for palliation in patients for whom cure is not a possibility. For patients with local or regional relapse only who have not received RT or chemotherapy, RT plus concurrent chemotherapy (5-FU--based) is preferred; other options include endoscopic therapies or surgery. For example, re-resection can be done in selected patients with anastomotic recurrences. For patients who develop a resectable locoregional relapse after chemoradiotherapy but have not had surgery, the clinician should determine whether the patient is medically fit for surgery and if the relapse is technically resectable. If both of these criteria are met, surgery remains an option. If the patient has another relapse after surgery, the

carcinoma is assumed to be incurable and the patient should receive palliative therapy. Medically unfit patients or those who develop an unresectable relapse after chemoradiotherapy may be offered brachytherapy, laser therapy, PDT, or any other components of best supportive care including esophageal dilatation, pain control, enteral feeding, and/or therapy to control bleeding.

For patients with metastatic carcinoma, only palliative care is appropriate. Whether to offer best supportive care alone or together with chemotherapy should be based on the patient's performance status. Patients should be offered only best supportive care if they have either a Karnofsky performance score of 60 or less or a Eastern Cooperative Group (ECOG) score of 3 or more. Patients with better performance status may be offered best supportive care alone or with chemotherapy. If chemotherapy is selected for palliation, patients should be encouraged to enroll in available clinical trials. Outside of a clinical trial, a patient's chemotherapy may consist of a 5-FU--based (category 1), cisplatin-based (category 1), oxaliplatin-based (category 3), taxane-based (category 3), or irinotecan-based (category 3) chemotherapy. Randomized clinical data on chemotherapy combinations are sparse. Patients may be offered two sequential regimens.

Best Supportive Care

The constituents of best supportive care depend on the patient's symptoms. In the case of esophageal obstruction, the patient may be offered a stent placement, laser therapy, PDT, radiotherapy, or a combination of these methods, as appropriate. Esophageal dilatation may also be useful. For patients requiring nutritional support, enteral feeding may be warranted. Pain control may be achieved with the use of radiotherapy plus pain medications.

Similarly, surgery or radiotherapy and/or endoscopic therapy may be indicated in patients with brisk bleeding from the carcinoma.

Barrett's Esophagus

Barrett's esophagus, the most important risk factor in the development of adenocarcinoma of the esophagus, is a metaplastic condition in which the normal squamous epithelium of the esophagus is replaced by columnar or glandular epithelium. The estimated prevalence of adenocarcinoma in columnar-lined esophagus ranges from 10% to 64% in the biomedical literature, which represents a 40-fold increase relative to the general population.¹⁰⁰ Risk factors associated with development of malignancy include age, male sex, Caucasian race, specialized epithelial type, body mass index, and history of GERD.^{101,102}

Management

The medical management of patients with Barrett's esophagus is based on the symptomatic control of gastroesophageal reflux using histamine-receptor antagonists or proton pump inhibitors. Endoscopy is performed on patients with severe symptoms of gastroesophageal reflux, especially those with a family history of Barrett's esophagus or esophageal cancer. Endoscopic surveillance is performed to evaluate progression from metaplasia to low-grade dysplasia (LGD), high-grade dysplasia (HGD), or adenocarcinoma; however, controversy exists when recommending a surveillance schedule for patients with Barrett's metaplasia. Once the diagnosis of metaplasia is established, routine endoscopic screening with 4-quadrant biopsy every 1 to 3 years is indicated (see [Table 2](#)).¹⁰³ The screening interval is decreased to 6 to 12 months if LGD is present. For patients with metaplasia or LGD, control of acid reflux is

achieved with histamine-receptor antagonists or proton pump inhibitors (omeprazole, esomeprazole, lansoprazole, rabeprazole, or pantoprazole).

If HGD is discovered during surveillance, pathologic confirmation by a second pathologist should be obtained. Among patients found to have HGD, cancer is actually present in approximately 50%. In a study of 15 patients with a preoperative diagnosis of HGD who underwent esophagogastrectomy, the final pathologic study demonstrated carcinoma-in-situ in 3 patients (20%) and invasive carcinoma in 8 patients (53%).¹⁵ A meta-analysis of published results of 119 patients undergoing resection demonstrated an operative mortality of 2.6%, an incidence of invasive cancer of 47%, and a 5-year survival in patients with invasive carcinoma of 82%.¹⁵ Thus, a substantial percentage of patients with HGD already have invasive carcinoma at the time of diagnosis; surgical resection is the treatment of choice for these patients.

Alternative strategies for patients with HGD include mucosal ablation or further surveillance every 3 months. Mucosal ablation can be achieved with PDT, argon beam coagulation, thermal laser ablation, or endoscopic mucosal resection (EMR).¹⁰⁴ Of these methods of mucosal ablation, PDT is superior for achieving ablation of metaplastic and dysplastic epithelium as well as for obviating the need for further interventions.¹⁰⁵ However, lifelong surveillance with deep biopsies is still required for patients with HGD who are treated with PDT or EMR. For patients who are at high risk for cancer or who refuse EMR, continued surveillance every 3 months is an option if definitive therapy would be offered for patients who develop adenocarcinoma. However, approximately 50% of patients with documented HGD actually have occult adenocarcinoma.

Summary

Esophageal cancer is a major health hazard in many parts of the world. The incidence of adenocarcinoma is increasing in white men, particularly in the nonendemic areas, such as North America and many western European countries. Barrett's metaplasia, gastroesophageal reflux, hiatal hernia, and obesity are thought to play a role in these cases. In addition, the most common location of esophageal carcinoma has shifted to the lower third of the esophagus.

Unfortunately, esophageal carcinoma is often diagnosed late; therefore, most therapeutic approaches are palliative. Advances have been made in staging procedures and in therapeutic approaches. The NCCN Esophageal Cancer Guidelines emphasize that palpable advances have been made in the treatment of locoregional esophageal carcinoma. Similarly, endoscopic palliation of esophageal carcinoma has improved substantially because of improving technology. New chemotherapeutic agents are on the horizon including antireceptor agents, vaccines, gene therapy, and antiangiogenic agents. The panel expects numerous advances in the treatment of esophageal carcinoma in the future.

Disclosures for the NCCN Esophageal Cancer Guidelines Panel

At the beginning of each panel meeting to develop NCCN guidelines, panel members disclosed the names of companies, foundations, and/or funding agencies from which they received research support; for which they participate in speakers' bureau, advisory boards; and/or in which they have equity interest or patents. Members of the panel indicated that they have received support from the following: AstraZeneca; Berlex Inc; Bristol Myers-Squibb; Discovery Laboratories, Inc; Exelixis; Genentech Inc; ImClone; Introgen Therapeutics, Inc; National Cancer Institute; OSI Pharmaceuticals, Inc; Pfizer Inc; Sanofi-Aventis; and U.S. Surgical. Some panel members do not accept any support from industry. The panel did not regard any potential conflicts of interest as sufficient reason to disallow participation in panel deliberations by any member.

Table 2**Management of Patients with Barrett's Esophagus**

Condition	Surveillance*	Therapy
Metaplasia (no dysplasia)	Annually x 2, then every 2-3 years	Medical therapy for GERD†
LGD	Every 6 months x 2, then every 12 months	Medical therapy for GERD†
HGD	Proceed with therapeutic option (preferred) or Every 3 months in a patient at high risk for esophagectomy	Esophagectomy (preferred) or Mucosal ablation‡

GERD, gastroesophageal reflux disease; HGD, high-grade dysplasia; LGD, low-grade dysplasia.

*Surveillance includes endoscopic screening with 4-quadrant biopsy.

†Therapy includes omeprazole, esomeprazole, lansoprazole, rabeprazole, or pantoprazole.

‡Mucosal ablation using photodynamic therapy, argon beam coagulation, thermal laser ablation, or endoscopic mucosal resection.

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