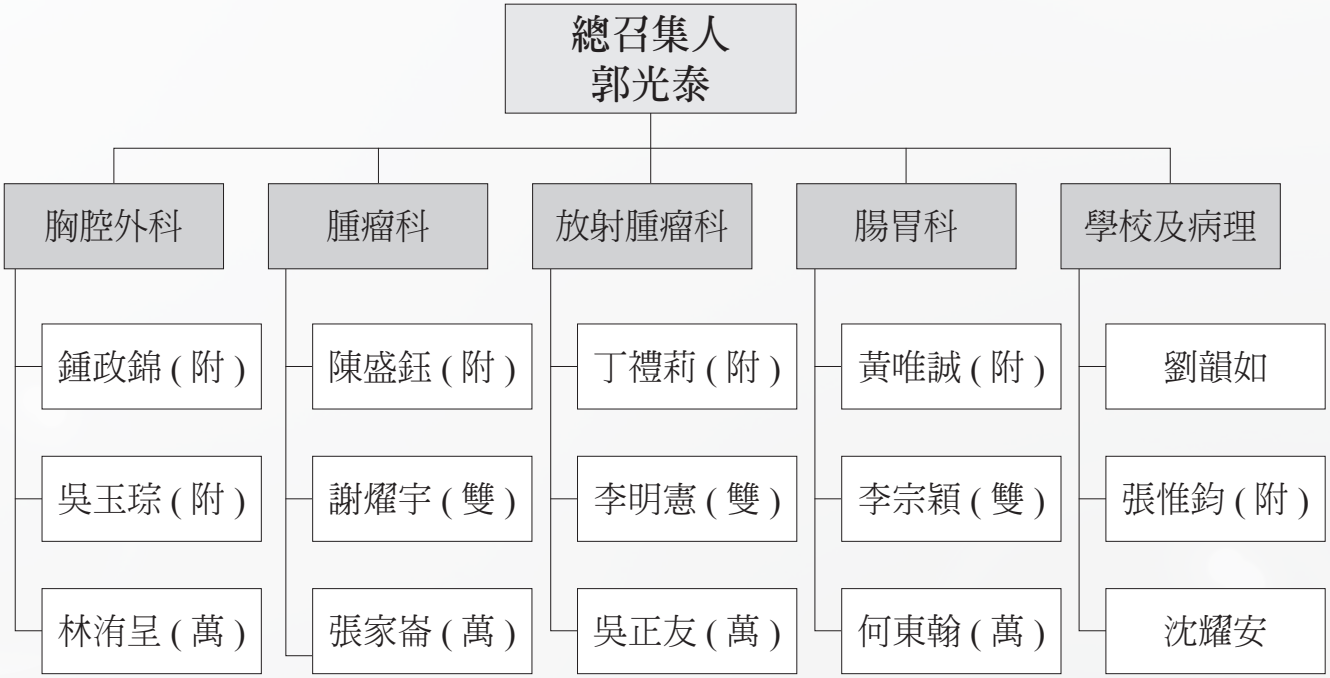
Esophageal and Esophagogastric Junction Cancer Guidelines

食道團隊成員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114 年版與上一版差異：

114 年版	115 年修訂版
I. Imaging and Staging 1. Replace imaging terms with “Abdomen CT” and “Pelvis CT.” 2. Abdomen CT or Chest CT is not required if FDG-PET/CT has been performed. 3. Change the requirement for EUS from “Essential” to “Recommended.”	**I. Molecular Testing for Esophageal Adenocarcinoma** ● The guideline originally included HER2 testing; add CLDN18.2 as an optional flexible testing item.
II. Treatment Staging for Esophageal Squamous Cell Carcinoma (SCC) 1. For T1a, Tis, and T1b, staging should be based primarily on Pathologic staging (P staging). 2. Endoscopic resection (ER) is recommended for accurate staging. 3. Revise the definition of High-risk lesions for cT2, N0 to include only G3 (poorly differentiated).	**II. PD-L1 Testing Before Neoadjuvant Therapy** ● Remove the entire requirement for PD-L1 testing prior to neoadjuvant therapy.
III. Treatment Outcomes and Adjuvant Therapy 1. For R1 or R2 resection, subsequent treatment should follow the NCCN guidelines with 5FU-based chemotherapy. 2. For surveillance, confirm that the use of Nivolumab is classified as Category 1.	**III. Re-staging After Neoadjuvant Therapy** 1. Change PET from “preferred” to “required.” 2. List preoperative upper gastrointestinal endoscopy (UGI/endoscopy) as required to ensure a negative surgical margin; remove “Optional.” 1. Biopsy is not mandatory and should only be performed when suspicious lesions are identified.

114 年版	115 年修訂版
IV. Molecular Testing for Metastatic/Advanced Cancer 1. Revise to: “Perform microsatellite and PD-L1 testing (if not done previously) if metastatic cancer is suspected.” 2. Add the statement: “NGS may be considered via a validated assay.” 3. Include: “HER2 testing for adenocarcinoma.”	**IV. Revision of Treatment Wording for Esophageal Adenocarcinoma** ● Replace “Chemoradiation” in the guideline with “Systemic Therapy.”
V. Follow-up Frequency 1. If asymptomatic: H&P every 3–6 months for years 1–2, then every 6–12 months for years 3–5. 2. Delete the wording “then annually.”	**V. Pathologic Staging for Esophageal Adenocarcinoma** ● Follow the 2025 updated NCCN Guidelines, merging T1 and T2 staging categories for esophageal adenocarcinoma.
VI. Imaging Text Revision 1. Revise “Imaging as clinically indicated” to “Imaging studies as clinically indicated.”	

Pretreatment Workup

Required Evaluations

- Upper GI endoscopy and biopsy
- Chest / abdomen CT
- PET-CT evaluation (skull base to mid-thigh) if no evidence of M1 disease
- Endoscopic ultrasound (EUS) if no evidence of M1 unresectable disease or luminal obstruction
- Bronchoscopy if the tumor is at or above the carina with no evidence of M1 disease
- Complete blood count (CBC) and comprehensive chemistry profile
- HER2-neu testing ± CLDN18.2 testing if metastatic adenocarcinoma is documented or suspected
- Nutritional assessment and counseling
- Family history screening

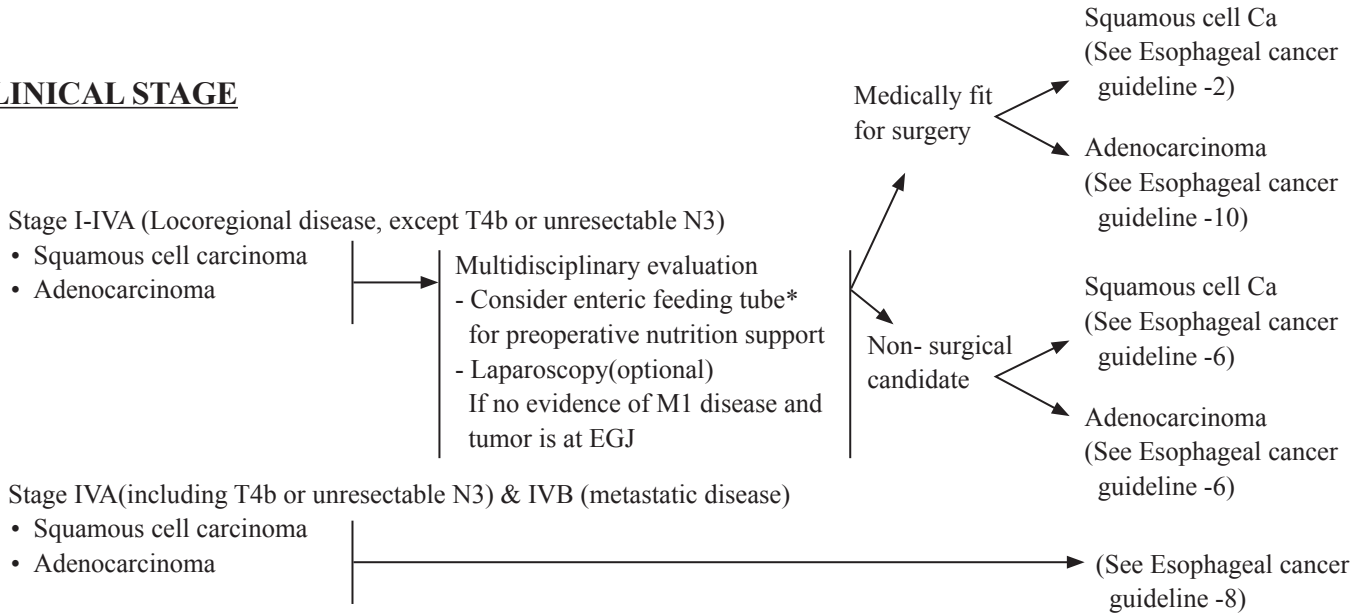
For Carcinoma in situ (Tis)

- Upper GI endoscopy and biopsy
- Chest / abdomen CT

Optional Evaluations

- Pelvic CT with contrast as clinical indicated
- Endoscopic resection (ER) is recommended for the accurate staging of early stage cancers(T1a or T1b). Early-stage cancer can best be diagnosed by ER
- Biopsy of metastatic disease as clinically indicated
- Universal testing for microsatellite instability (MSI) by PCR/next-generation sequencing (NGS) or MMR by IHC is recommended in all newly diagnosed patients as clinically indicated
- Next-generation sequencing (NGS)) should be considered
- Smoking cessation advice, counseling, and pharmacotherapy as indicated
- Biopsy of metastatic disease as clinically indicated

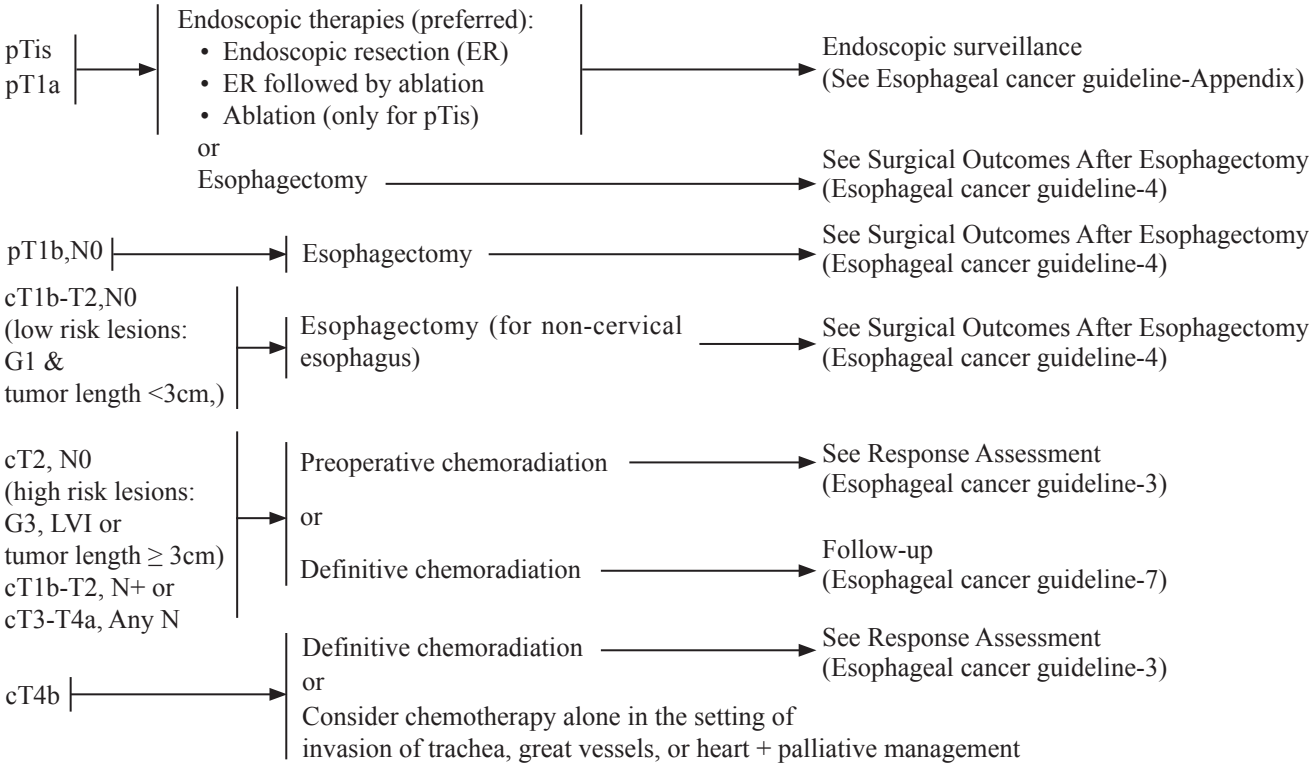
Pretreatment Workup



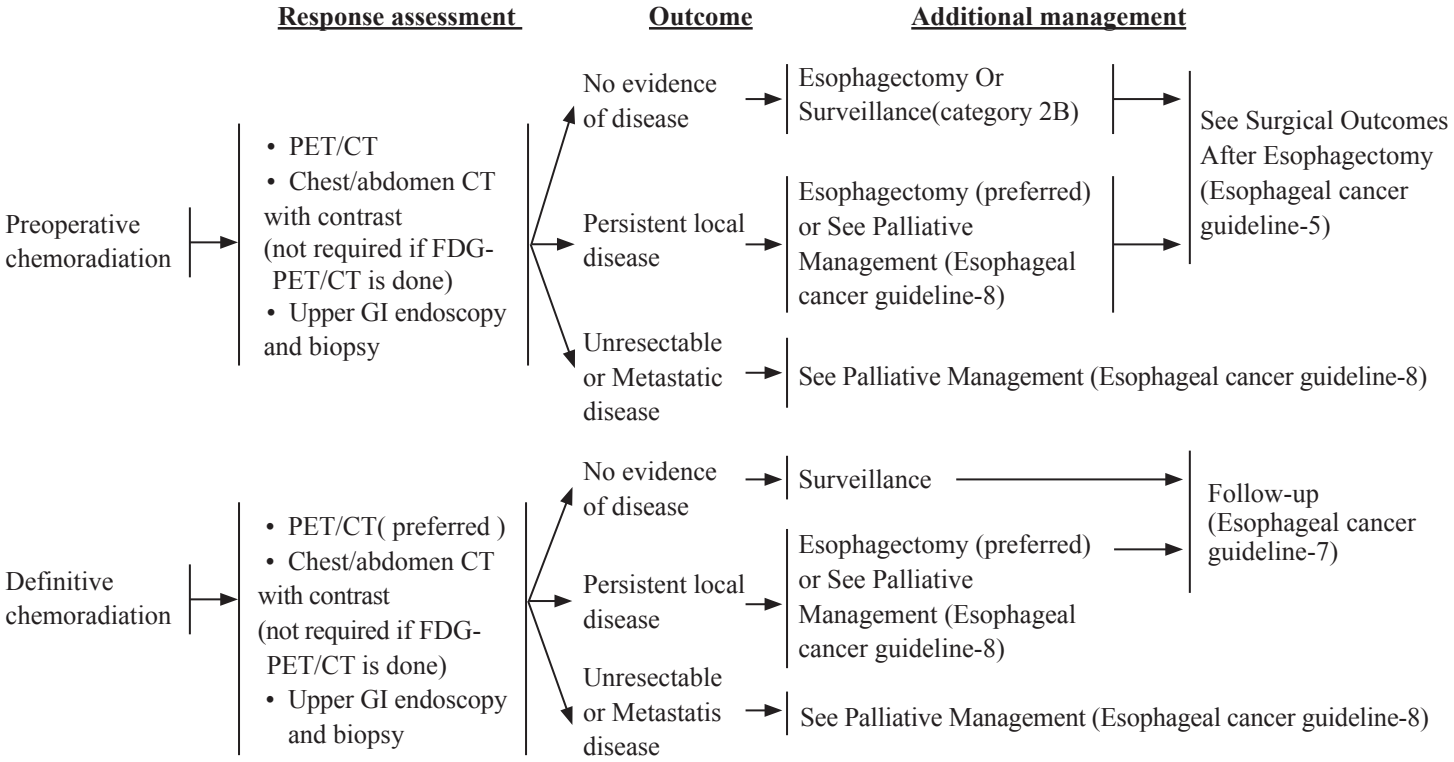
* Percutaneous gastrostomy tube (PCG) may be considered for patient with cervical esophageal tumors receiving definitive chemoradiation or for patients with marginally resectable disease.

《 Esophageal cancer guideline-2》

Squamous cell carcinoma: primary treatment options for medically fit surgery patients



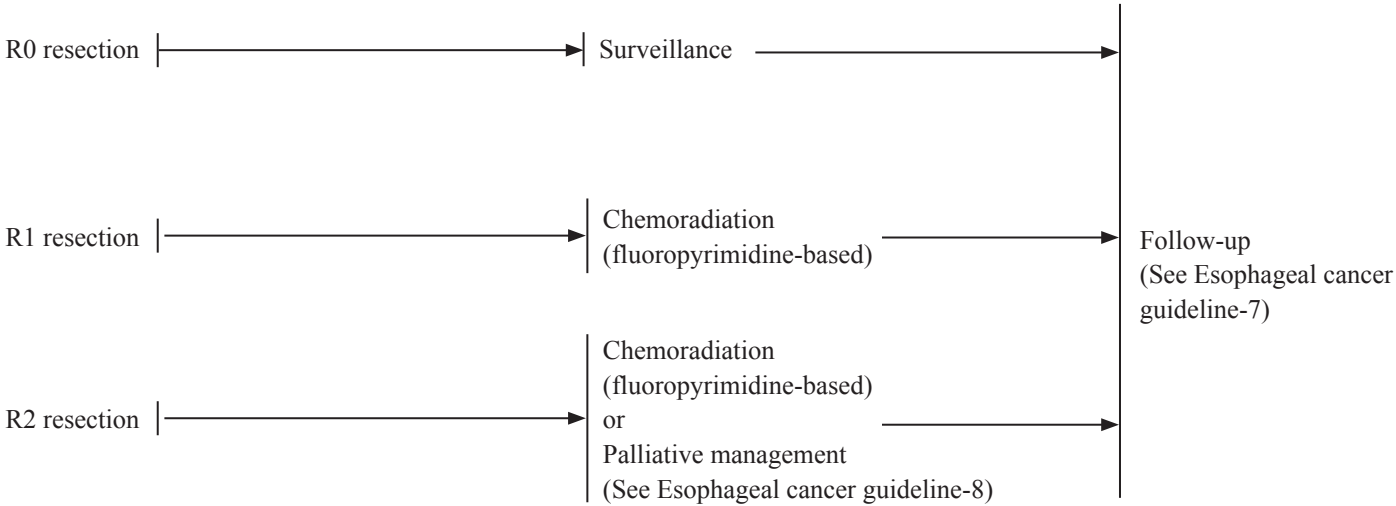
Squamous cell carcinoma: response assessment



《Esophageal cancer guideline-4》

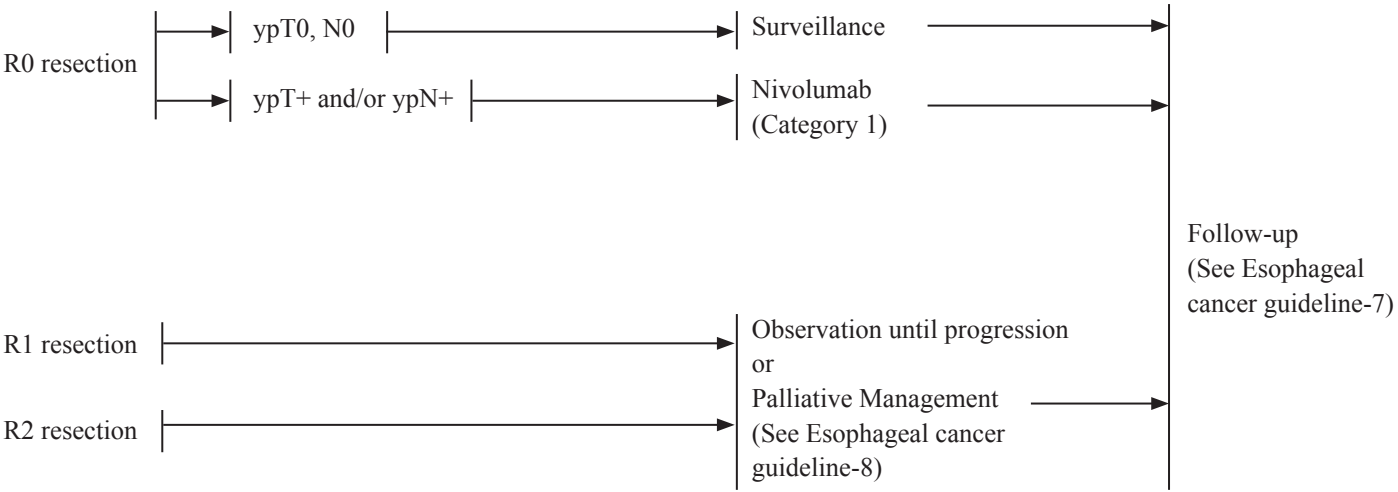
Squamous cell carcinoma: surgical outcomes

Patients **Have Not** Reveived Preoperative Chemoradiation



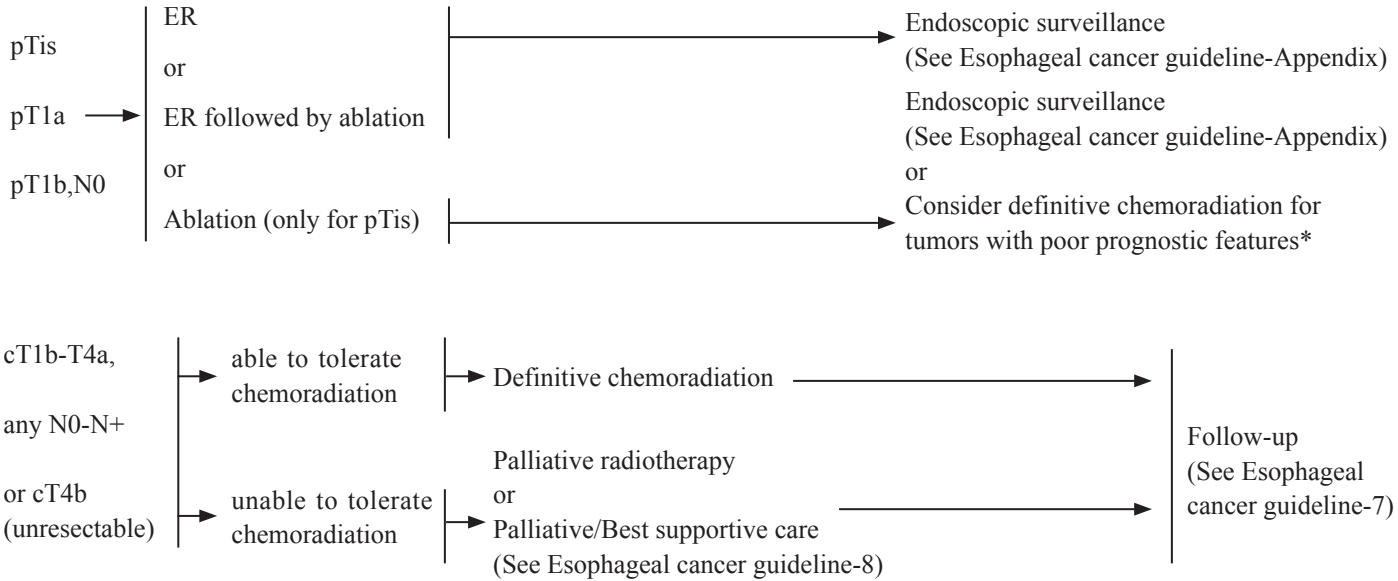
Squamous cell carcinoma: surgical outcomes

Patients **Have** Reveived Preoperative Chemoradiation



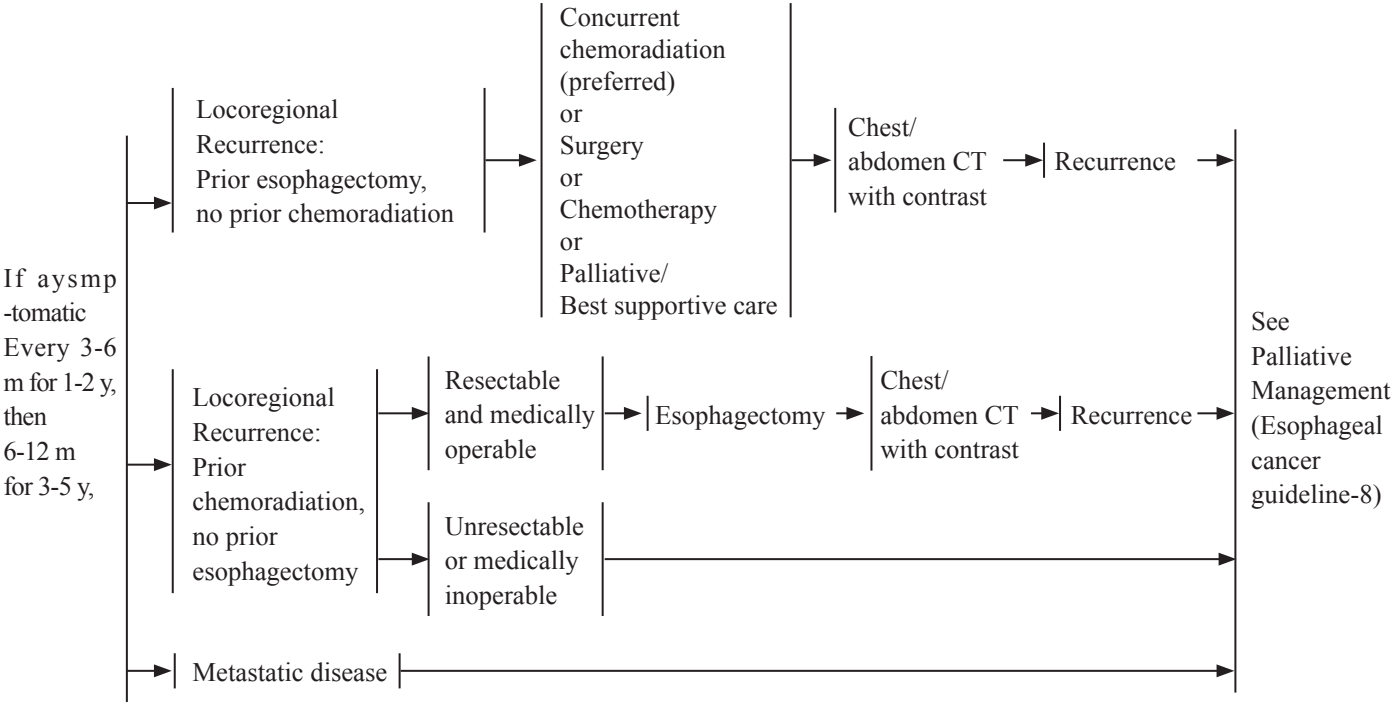
《 Esophageal cancer guideline-6》

Squamous cell carcinoma &adenocarcinoma : non-surgical candidate



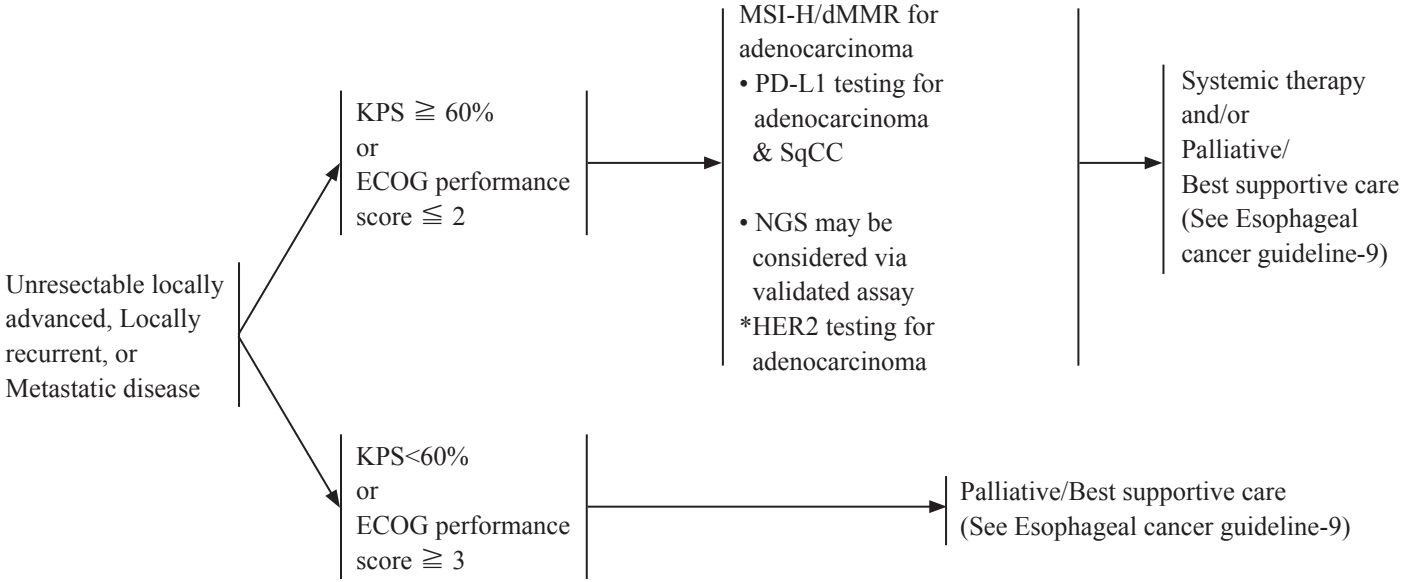
* Poor prognostic features: positive margin(s), max. tumor diameter > 2cm, G2/3, LVI or more

Squamous cell carcinoma & adenocarcinoma follow up – recurrence – palliative management



《 Esophageal cancer guideline-8》

Squamous cell carcinoma & adenocarcinoma : unresectable locally advancer, locally recurrent, or metastatic disease



Principles of Palliative/Best Supportive Care

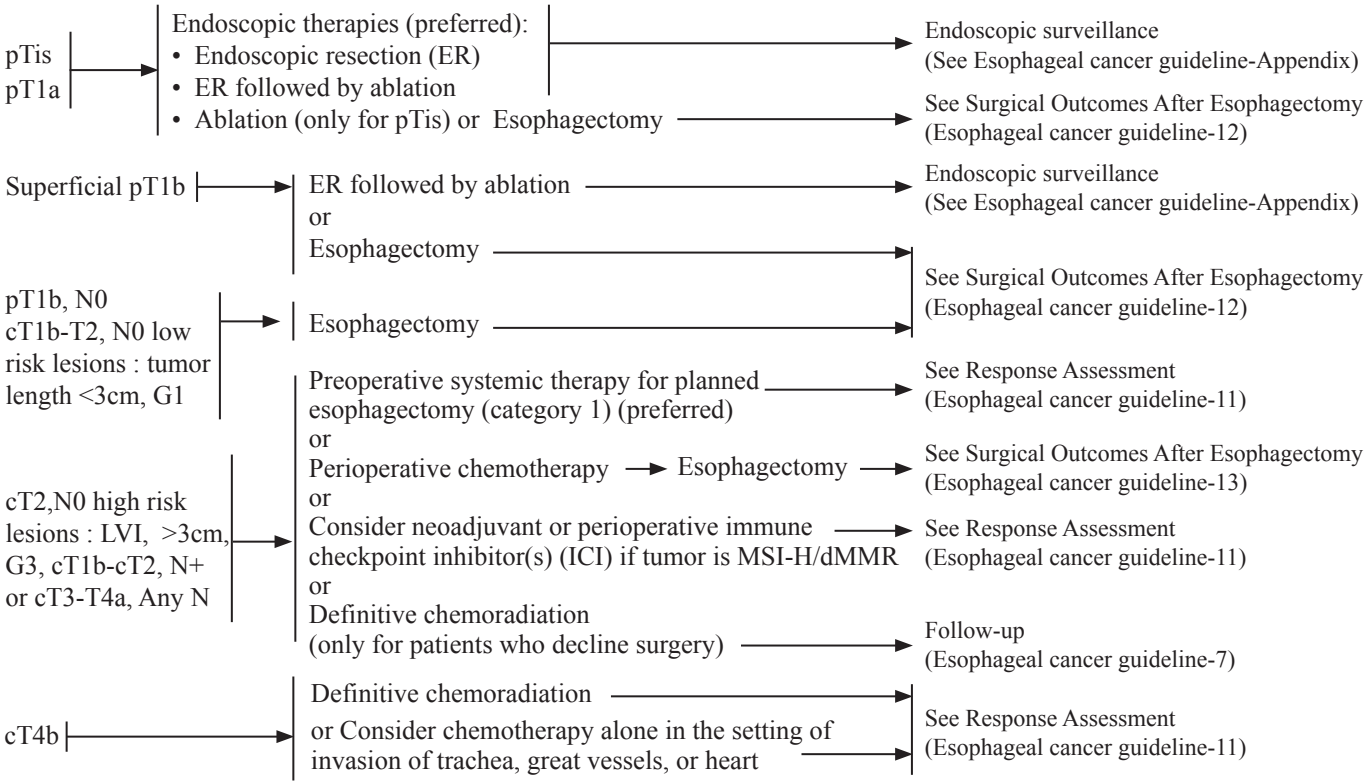
Palliative and Supportive Care: The primary goal of optimal supportive and palliative care is to prevent and relieve suffering and to provide the best possible quality of life for patients and their families, regardless of disease stage or the need for other treatments. For esophageal cancer, interventions aimed at symptom relief may also significantly prolong survival.A multidisciplinary team (MDT) approach is particularly important. Therefore, the use of MDT-based palliative care is strongly encouraged for patients with esophageal cancer.

Dysphagia

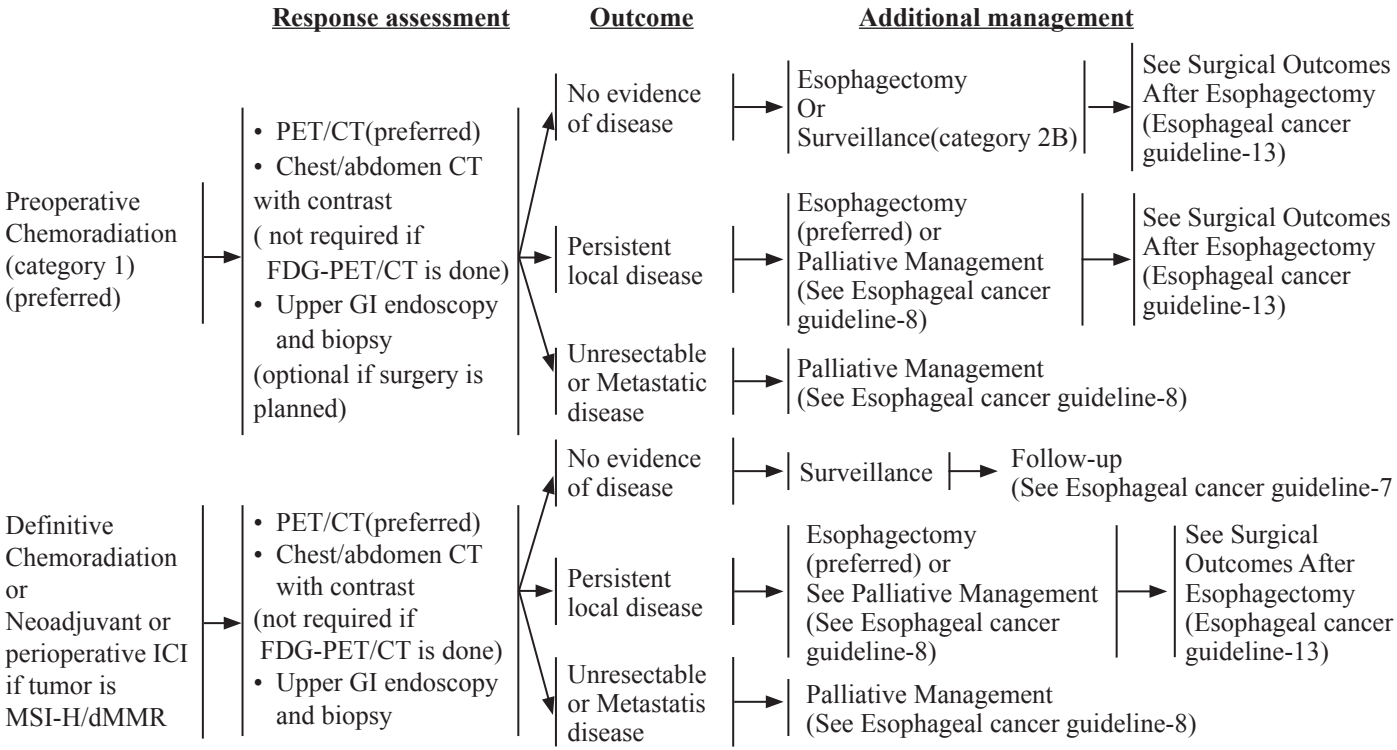
- Assess the extent of disease and the functional degree of swallowing impairment, preferably through a standardized scoring scale and confirm the etiology of dysphagia
- Dysphagia grading scale
  - Grade 0: Able to eat solid food without special attention to bite size or chewing
  - Grade 1: Able to swallow solid food cut into pieces less than 18 mm in diameter and thoroughly chewed
  - Grade 2: Able to swallow semisolid food (consistency of baby food)
  - Grade 3: Able to swallow liquids only
  - Grade 4: Unable to swallow liquids or saliva
- Dysphagia arising from esophageal cancer most often is due to obstruction, but on occasion may be primarily due to tumor-related dysmotility.
- Patients with dysphagia who are not candidates for curative surgery should be considered for palliation of their dysphagia symptoms, based on symptom severity. This can be achieved through multiple modalities, although placement of an esophageal stent is most commonly utilized. In contrast, stent placement is generally not advised in patients who may undergo curative surgery in the future due to concerns that stent-related adverse events may preclude curative surgery in the future.

《Esophageal cancer guideline-10》

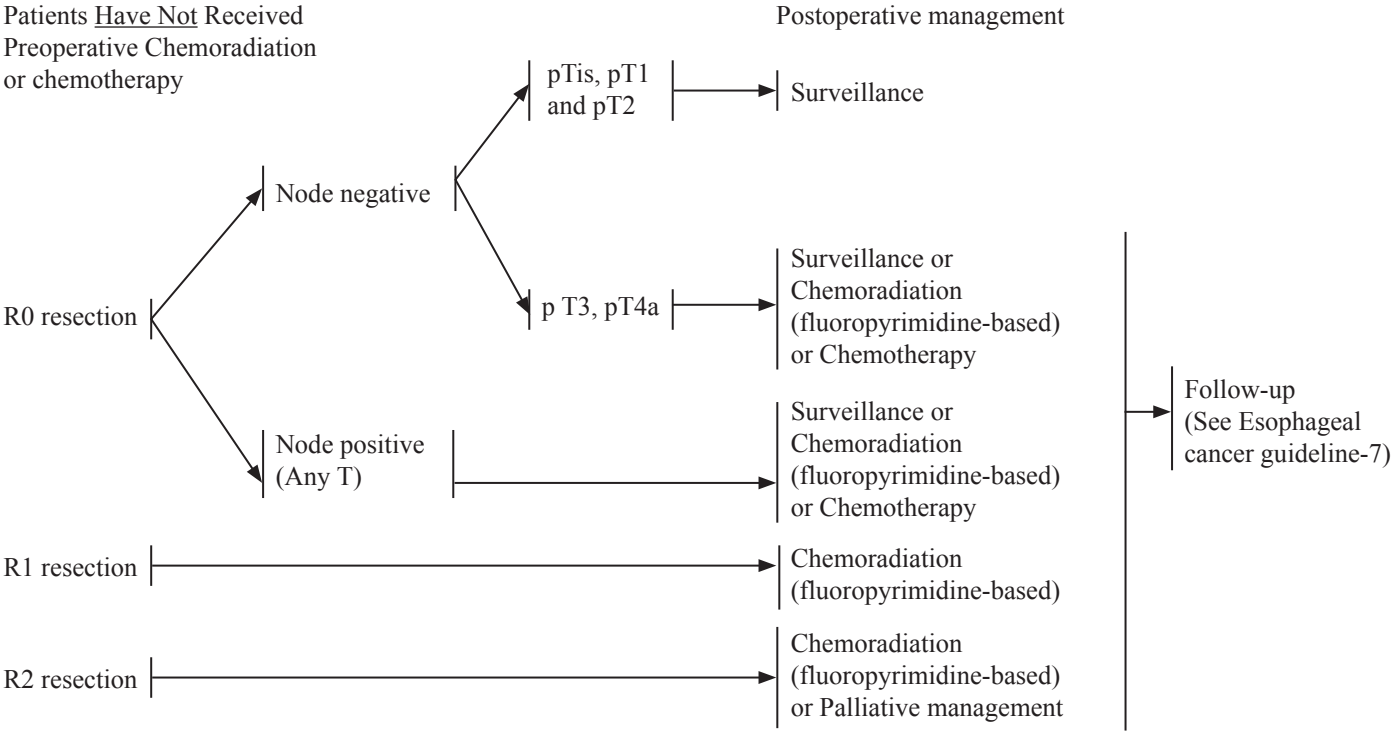
Adenocarcinoma: primary treatment for medically fit surgery patients



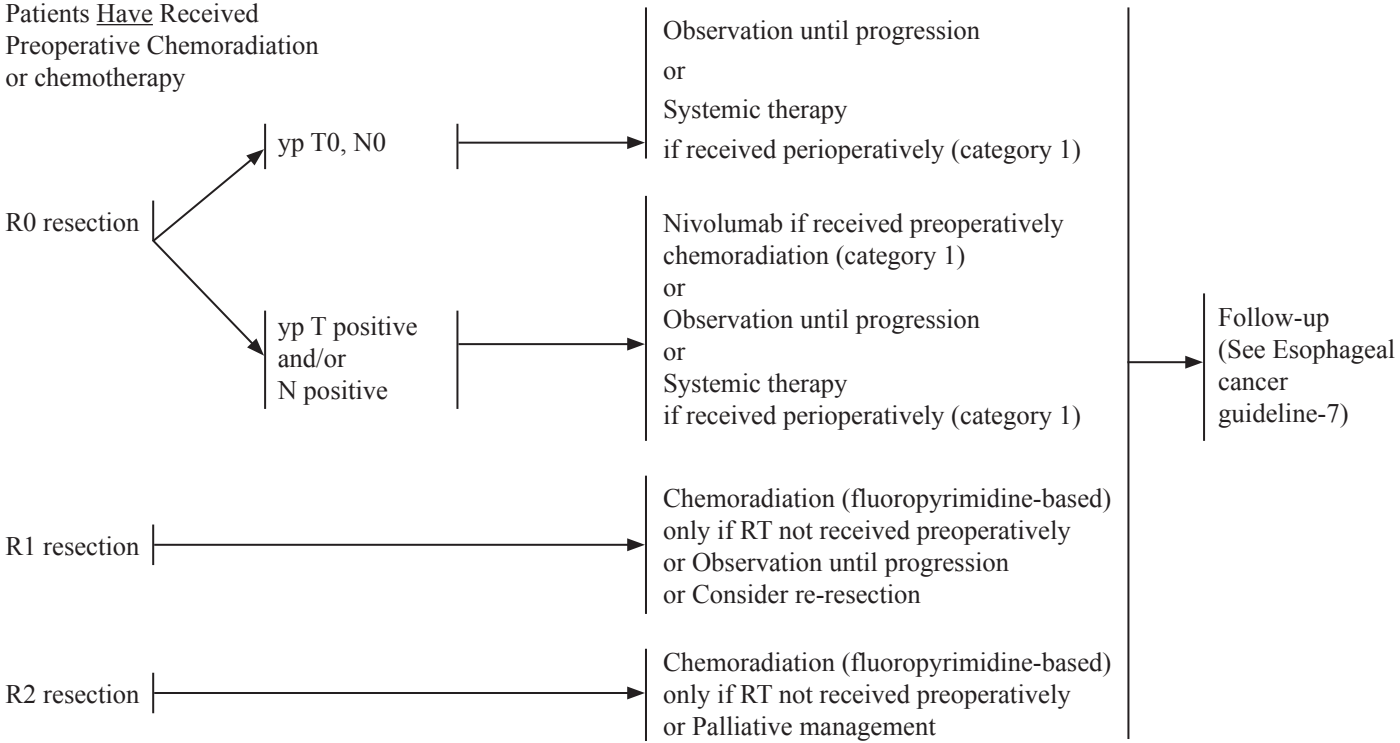
Adenocarcinoma: response assessment



Adenocarcinoma: surgical outcomes



Adenocarcinoma: surgical outcomes



Principles of Endoscopic Staging and Therapy

Treatment of Symptoms

- Esophageal dilation can be performed with the use of dilating balloons or bougies to temporarily relieve obstruction from tumors, or treatment-related strictures. Caution should be exercised to avoid overdilation, to minimize the risk of perforation.
- Long-term palliation of dysphagia can be achieved with endoscopic tumor ablation by Nd:YAG laser, PDT and cryoablation, or endoscopic and radiographic-assisted insertion of expandable metal or plastic stents.
- Long-term palliation of anorexia, dysphagia, or malnutrition may be achieved with endoscopic or radiographic-assisted placement of feeding gastrostomy or jejunostomy. The placement of a gastrostomy in the preoperative setting may compromise the gastric vasculature, thereby interfering with the creation of the gastric conduit in the reconstruction during esophagectomy and should be avoided.

Post-Treatment Surveillance

- Consider deferring assessment endoscopy with biopsy to 6 weeks or later after completion of preoperative therapy in patients whom avoidance of surgery is being considered.
- EUS exams performed after chemotherapy or radiation therapy have a reduced ability to accurately determine the present stage of disease. Similarly, biopsies performed after chemotherapy or radiation therapy may not accurately diagnose the presence of residual disease.
- Endoscopic surveillance following definitive treatment of esophageal cancer requires careful attention to detail for mucosal surface changes, and multiple biopsies of any visualized abnormalities. Strictures should be biopsied to rule out neoplastic cause. EUS-guided FNA should be performed if suspicious lymph nodes or areas of wall thickening are seen on cross-sectional imaging.
- Endoscopic surveillance after ablative therapy or ER of early-stage esophageal cancer should continue after completion of treatment. Biopsies should be taken of the neosquamous mucosa even in the absence of mucosal abnormalities as dysplasia may occasionally be present beneath the squamous mucosa.
- Endoscopic surveillance should also include a search for the presence of Barrett esophagus and four-quadrant biopsies to detect residual or recurrent dysplasia. The ablation of residual or recurrent high-grade and low-grade dysplasia using RFA or cryoablation should be considered.
- Patients who have received therapeutic ER should have endoscopic surveillance.

Principles of Pathologic Review

Pathologic Review Objectives

The purposes of pathologic review include:

- Classification of the tumor
- Determination of the extent of invasion
- Assessment of cancer involvement at surgical margins

All surgical pathology reports should:

- Follow the WHO classification for esophageal cancer
- Stage tumors according to AJCC/UICC TNM, 8th edition

Surgical pathology reports should include the following items:

- Histologic type
- Histologic grade:
  - G1: Well differentiated
  - G2: Moderately differentiated
  - G3: Poorly differentiated
- Microscopic tumor extension
- Margin status

Principles of Pathologic Review

Pathology Report Content According to Specimen Type

The pathology report, depending on the type of specimen, should include the following items:

- Biopsy: invasion, if present; high-grade dysplasia in Barrett esophagus; histologic type; Grade; Presence or absence of Barrett esophagus; Universal testing for MSI by PCR/NGS or MMR by IHC is recommended in all newly diagnosed patients
- Endoscopic resection (ER): include all elements as for biopsy specimen plus the depth of tumor invasion; lymphovascular invasion (LVI), and the status of mucosal and deep margins; Universal testing for MSI by PCR/NGS or MMR by IHC is recommended in all newly diagnosed patients
- Esophagectomy, without prior chemoradiation: include all elements as for ER specimen plus the location of the tumor midpoint in relation to the EGJ, whether the tumor crosses EGJ, lymph node status, and the number of lymph nodes recovered; Universal testing for MSI by PCR/NGS or MMR by IHC is recommended in all newly diagnosed patients, if not previously performed
- Esophagectomy, with prior chemoradiation :
  - the tumor sites should be thoroughly sampled, with submission of entire EGJ or ulcer/tumor bed for specimens without grossly obvious residual tumor
  - For pathology report, include all elements as for esophagectomy without prior chemoradiation, plus assessment of the treatment effect
  - Assessment treatment effect: The modified Ryan scheme in the CAP Cancer Protocol for Esophageal Carcinoma

Description	Tumor Regression Score
No viable cancer cells (complete response)	0
Single cells or rare small groups of cancer cells (near complete response)	1
Residual cancer with evident tumor regression, but more than single cells or rare small groups of cancer cells (partial response)	2
Extensive residual cancer with no evident tumor regression (poor or no response)	3

Principles of Biomarker Testing

- HER2 status, microsatellite instability (MSI) testing, programmed death-ligand 1 (PD-L1) expression, and NTRK gene fusion testing are used to guide clinical treatment selection for patients with locally advanced, unresectable, or metastatic esophageal cancer and esophagogastric junction (EGJ) adenocarcinoma.
- Assessment of overexpression or amplification of Her2 in Esophageal and EGJ Cancer
  - For patients with inoperable locally advanced, recurrent, or metastatic adenocarcinoma of esophagus or EGJ for whom trastuzumab therapy is being considered
  - Immunohistochemical criteria for scoring HER2/neu expression

	Surgical Specimen Expression Pattern, Immunohistochemistry	Biopsy Specimen Expression Pattern, Immunohistochemistry	HER2 Overexpression Assessment
0	No reactivity or membranous reactivity in <10% of cancer cells	No reactivity or no membranous reactivity in any cancer cell	Negative
1+	Faint or barely perceptible membranous reactivity in ≥10% of cancer cells; cells are reactive only in part of their membrane	Cluster of five or more cancer cells with a faint or barely perceptible membranous reactivity irrespective of percentage of cancer cells positive	Negative
2+	Weak to moderate complete, basolateral or lateral membranous reactivity in ≥10% of cancer cells	Cluster of five or more cancer cells with a weak to moderate complete, basolateral, or lateral membranous reactivity irrespective of percentage of cancer cells positive	Equivocal
3+	Strong complete, basolateral, or lateral membranous reactivity in ≥10% of cancer cells	Cluster of five or more cancer cells with a strong complete, basolateral, or lateral membranous reactivity irrespective of percentage of cancer cells positive	Positive

  - HER2 IHC is performed first, followed by FISH methods in cases showing 2+ (equivocal) expressions by IHC. Cases with HER2: CEP17 ratio >=2 or an average HER2 copy number >=6.0 signals/cell are considered positive by FISH.

Principles of Biomarker Testing

◆ *Microsatellite Instability (MSI) or Mismatch Repair (MMR) Testing:*

- All newly diagnosed esophageal and esophagogastric junction (EGJ) cancers should undergo universal microsatellite instability (MSI) testing via polymerase chain reaction (PCR), next-generation sequencing (NGS), or immunohistochemistry (IHC) for mismatch repair (MMR) proteins. According to the CAP DNA Mismatch Repair Biomarker Reporting Guidelines, results are interpreted as MSI-high (MSI-H) or mismatch repair deficient (dMMR).Testing must be performed in Clinical Laboratory Improvement Amendments (CLIA)-approved laboratories.Patients with MSI-H or dMMR tumors should be referred to a genetics counselor for further evaluation in the appropriate clinical context.
- MMR Interpretation
  ◊ No loss of nuclear expression of MMR proteins: No evidence of dMMR (low probability of MSI-H)
  ◊ Loss of nuclear expression of one or more MMR proteins: dMMR
- MSI Interpretation
  ◊ MSI-stable (MSS)
  ◊ MSI-low (MSI-L)
  – 1%–29% of the markers exhibit instability
  – 1 of the 5 National Cancer Institute (NCI) or mononucleotide markers exhibits instability
  ◊ MSI-H
  – ≥ 30% of the markers exhibit instability
  – 2 or more of the 5 NCI or mononucleotide markers exhibit instability

$$\text{CPS} = \frac{\text{\# of PD-L1-positive cells (tumor cells, lymphocytes, macrophages)}}{\text{Total \# of tumor cells}} \times 100$$

◆ *PD-L1 Testing:*

- PD-L1 IHC testing may be considered on locally advanced, recurrent, or metastatic esophageal and EGJ cancer in patents who are candidate for treatment with PD-1 inhibitors
- Assessment of PD-L1 Protein Expression
  - Pembrolizumab as a second-line treatment option for esophageal SCC with PD-L1 expression levels by combined positive score (CPS) of >=10, and as a third-or subsequent-line treatment option for EGJ adenocarcinoma with PD-L1 expression levels by CPS >=1, as determined by an FDA-approved companion diagnosed test
  - CPS is determined by

Principles of Biomarker Testing

◆ *Next-Generation Sequencing ,NGS:*

- Currently, multiple targeted therapies—including trastuzumab, pembrolizumab/nivolumab, entrectinib/larotrectinib, selpercatinib, and dabrafenib/trametinib—have been FDA-approved for esophageal and esophagogastric junction (EGJ) cancers.Trastuzumab use is based on HER2 overexpression testing.Selection of immune checkpoint inhibitors is guided by MSI testing via PCR, MMR status via IHC/NGS, PD-L1 expression by immunohistochemistry, or high tumor mutational burden (TMB) detected by NGS.The FDA has approved TRK inhibitors for NTRK fusion-positive solid tumors, selpercatinib for RET fusion-positive tumors, and dabrafenib/trametinib for tumors harboring BRAF V600E mutations.When tissue for testing is limited or the patient cannot undergo a traditional biopsy, sequential single-biomarker testing or small molecular diagnostic panels can rapidly exhaust available samples.In these scenarios, comprehensive genomic profiling using validated NGS in a CLIA-approved laboratory can identify HER2 amplification, MSI status, MMR deficiency, TMB, NTRK fusions, RET fusions, and BRAF V600E mutations.IHC/ISH or targeted PCR should be considered first, with NGS testing performed as clinically indicated.

◆ *Liquid Biopsy*:

- The genomic alterations of solid cancers may be identified by evaluating circulating tumor DNA (ctDNA) in the blood, hence a form of "liquid biopsy." Liquid biopsy is being used more frequently in patients with advanced disease, particularly those who are unable to have a clinical biopsy for disease surveillance and management. The detection of mutations/alterations in DNA shed from esophageal and EGJ carcinomas can identify targetable alterations or the evolution of clones with altered treatment response profiles. Therefore, for patients who have metastatic or advanced esophageal/esophagogastric cancers who may be unable to undergo a traditional biopsy or for disease progression monitoring, testing using a validated NGS-based comprehensive genomic profiling assay performed in a CLIA-approved laboratory may be considered. A negative result should be interpreted with caution, as this does not exclude the presence of tumor mutations or amplifications.

Principles of Biomarker Testing

◆ Assessment of *NTRK* gene fusions:

- The FDA granted approval for the use of select TRK inhibitors for *NTRK* gene fusion-positive solid tumors
- A two-step approach is used, which includes IHC first and confirmation of any positivity detected with IHC by Next generation sequencing (NGS)
- TRK IHC as a screening tool:
  - IHC negative: No TRK expression
  - IHC positive: Detection of TRK expression, confirmation by NGS

◆ When only a limited biopsy specimen is available for testing multiple biomarkers, clinicians are advised to indicate the required tests on the pathology request form.For the same pathology tissue block, in addition to H&E staining, reserve unstained slides to prevent excessive tumor cell depletion from repeated processing of the paraffin block.

Principles of Endoscopic Staging and Therapy

1. Initial Endoscopic EvaluationPatients with esophageal SCC must undergo a comprehensive upper gastrointestinal (GI) endoscopy at initial diagnosis, performed by an endoscopist skilled in image-enhanced endoscopy (IEE).Purpose: to confirm the presence or absence of synchronous mucosal cancers or precancerous lesions. (workup)
2. Preoperative Nutritional PlanningAll patients with esophageal cancer should have a consultation with a gastroenterologist prior to surgery or concurrent chemoradiotherapy (CCRT) to discuss whether endoscopic or surgical enteral access (e.g., feeding tube) is needed to maintain nutritional status before and after treatment. (principle of surgery)
3. Endoscopic Ultrasound (EUS) AssessmentPrior to treatment, patients should undergo EUS staging, except for those with confirmed M1 disease on imaging (CT or PET scan). (workup)
4. Early Esophageal Cancer – Endoscopic Resection CriteriaAbsolute indications for endoscopic resection: tumor invasion limited to m1 or m2 layers and LN-negative.Relative indications: tumor invasion limited to m3 or sm1 layers and LN-negative. Diagnostic endoscopic submucosal dissection (ESD) may be considered if the depth of invasion or nodal status is uncertain.
5. NGS TestingIf sufficient tissue remains after the above assessments, a second round of NGS testing may be considered.
6. Lymph Node AssessmentIf EUS detects positive lymph nodes (LN+), FNA/FNB may be optionally performed.
7. Re-staging Post-CCRTOptional EUS may be performed for re-staging after CCRT. (optional)
8. Palliative Endoscopic InterventionsPalliative procedures (e.g., metal stent placement, argon plasma coagulation for local ablation) should be discussed in a multidisciplinary esophageal cancer team meeting prior to execution.

Notes

1. Endoscopic Equipment and TechniqueUpper GI endoscopy should include magnifying endoscopes, Lugol's solution, diluted acetic acid, and image-enhanced light sources (e.g., NBI, BLI).Procedures should be performed by an endoscopist trained in

early cancer detection, with documentation of findings. ◦

2. Barrett's Esophagus SurveillancePatients with Barrett's esophagus should undergo routine comprehensive upper GI endoscopy to detect malignant transformation.With dysplasia: at least once per year.Without dysplasia: at least once every three years.）
3. Multidisciplinary Consensus RecommendationsThe Esophageal Cancer Consensus Committee should provide recommendations to multidisciplinary cancer teams at affiliated hospitals.For patients with oral cavity cancer (including tongue), head and neck cancer, hypopharyngeal, and laryngeal cancers, comprehensive upper GI endoscopy by an IEE-skilled endoscopist is recommended at initial diagnosis and at least annually postoperatively to identify coexisting esophageal cancer or precancerous lesions.

Principles of Surgery

- Preoperative Clinical StagingClinical staging prior to surgery should include: 1.Chest and abdominal computed tomography (CT) 2. Positron emission tomography-computed tomography (PET-CT) 3. Endoscopic ultrasound (EUS). Purpose: to assess resectability.
- All patients should consult a thoracic surgeon for evaluation of physiologic suitability for esophagectomy.
- Patients who are physiologically fit for esophagectomy and have locally resectable thoracic (≤ 5 cm above cricopharyngeus) or abdominal esophageal cancer should be considered for surgical resection.
- Esophagogastric Junction (EGJ) Adenocarcinoma – Siewert Classification
  - Siewert Type I: adenocarcinoma of the lower esophagus with the epicenter location located within 1cm to 5 cm above the anatomic EGJ
  - Siewert Type II: true carcinoma of the cardia with the tumor epicenter within 1 cm above and 2 cm below the EGJ
  - Siewert Type III: subcardial carcinoma with the tumor epicenter between 2 cm and 5 cm below the EGJ, which infiltrates the EGJ and lower esophagus from below
- Siewert Types I and II tumors should follow esophageal and EGJ cancer treatment guidelines.Siewert Type III tumors are considered gastric cancer and should follow gastric cancer treatment guidelines, with partial esophagectomy added in selected cases to achieve adequate resection margins.
- Laparoscopy can detect occult metastatic disease not visible on radiologic imaging, particularly for Siewert Types II and III tumors.
- Positive peritoneal cytology is associated with poor prognosis and should be considered M1 disease.Patients with advanced tumors (clinical T3 or N+) should be considered for laparoscopic staging with peritoneal washings.
- Patients with cervical esophageal cancer or tumors ≤ 5 cm above the cricopharyngeus should be treated with definitive chemoradiation.

Principles of Surgery

◆ Resectable Esophageal Cancer Stage I-IVA(Locoregional disease, except T4b or unresectable N3)

- Tis or T1a tumors: Endoscopic management with EMR + ablation or surgery may be considered.
- T1b tumors: Surgical resection is generally indicated.
- T1–T3 tumors:Even if regional lymph nodes are involved, surgical resection can be considered.Multi-station or bulky lymph node metastases represent relative contraindications for surgery.Resectability should also take into account patient age, performance status, and treatment response.
- T4a tumors: Tumor invades pleura, pericardium, or diaphragm.

◆ Unresectable Esophageal Cancer Stage IVA(including T4b or unresectable N3) & IVB(metastatic disease)

- cT4b tumors: Tumor invades heart, great vessels, trachea, or adjacent organs (including liver, pancreas, lung, or spleen).
- Multi-station or bulky lymph node involvement is generally considered unresectable, but individual factors (age, performance status, treatment response) may influence decision-making.
- EGJ tumors with supraclavicular lymph node metastases should be considered unresectable.
- Stage IV metastatic disease, including non-regional lymph node metastases, is considered unresectable.

◆ Choice of esophagectomy technique depends on: 1.Tumor location 2.Available reconstructive organs 3.Surgeon experience and preference 4.Patient preference.

◆ Patients unable to maintain oral intake during the preoperative period may consider esophageal dilation or jejunostomy (J-tube). Jejunostomy is preferred over gastrostomy, as gastrostomy may compromise the stomach for future reconstruction.

Principles of Surgery

◆ Acceptable Surgical Procedures for Esophageal and Esophagogastric Junction (EGJ) Tumors
- Ivor Lewis esophagogastrectomy
- McKeown esohagogastrectomy
- Minimally invasive Ivor Lewis esophagogastrectomy
- Minimally invasive McKeown esophagogastrectomy
- Transhiatal esophagogastrectomy
- Robotic minimally invasive esophagogastrectomy
- Left transthoracic or thoracoabdominal approaches with anastomosis in chest or neck

◆ Acceptable Esophageal Reconstruction Options
- Stomach (preferred)
- Colon
- Jejunum

◆ Acceptable Lymphadenectomy Approaches
- Standard lymphadenectomy
- Extended lymphadenectomy (en-bloc resection).

◆ At least 15 lymph nodes should be removed or evaluated to achieve adequate nodal staging.For patients who received preoperative chemoradiotherapy, the optimal number of nodes is not precisely defined; however, it is still recommended to remove or assess ≥ 15 nodes.

◆ Patients with resectable local tumor and no distant metastasis after definitive chemoradiation may be considered for esophagectomy.

◆ Esophagectomy, endoscopic mucosal resection (EMR), and other ablative procedures should be performed in high-volume esophageal treatment centers by experienced surgeons or endoscopists.

Reference for principles of surgery

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Follow-up

- **History and Physical Examination**
  - Every 3–6 months for the first 1–2 years.
  - Then every 6–12 months for years 3–5.

- **Clinical and Laboratory Assessments**
  - Biochemical tests and complete blood count as clinically indicated.
  - Imaging studies as clinically indicated.
  - Upper GI endoscopy and biopsy based on clinical need.
  - Dilation of esophageal anastomotic strictures as indicated.
  - Nutritional assessment and counseling.

【Radiotherapy guideline for esophageal cancer】

一、Treated area

1. Esophageal tumor
2. Regional lymphadenopathy
3. High risk lymphatic region

二、Total dose / fractions

▲ Post-operative adjuvant therapy

1. Total dose
   (a) Residual tumor / Primary tumor bed：50~50.4 GyE *
   (b) High risk area：45~50.4 GyE
   (c) Irradiated fractions：25~28 fx)

▲ Definitive radiotherapy

1. Total dose
   (a) Tumor：50~50.4 GyE *
   (b) High risk area：45~50.4 GyE
   (c) Irradiated fractions：25~28 fx

* Cervical esophageal cancer may increased dose up to 60~66 GyE；middle to lower esophageal cancer may increased dose up to 60 GyE。

▲ Pre-operative neoadjuvant radiotherapy

1. Total dose
   (a) Tumor：45~50.4 GyE
   (b) High risk area：45~50.4 GyE
   (c) Irradiated fractions：25~28 fx

or

2. Total dose
   (a) Tumor：41.4 GyE
   (b) High risk area：41.4 GyE
   (c) Irradiated fraction：23 fx

▲ Definitive proton therapy (no surgery)

1. Total dose
   (a) Tumor：60~70 GyE
       Irradiated fractions：30~35 fx
   (b) High risk area：36~40 GyE
       Irradiated fractions：20 fx

▲ Brachytherapy (After External beam radiotherapy)

Surface dose 3Gy x 4fx. or 5Gy x 3fx.

三、Irradiation technique :

Using intensity modulated radiotherapy, volumetric modulated arc therapy, tomotherapy or proton therapy and cooperation with image guide radiotherapy. High dose area may be treated concomitantly or sequentially.

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