Taipei Veterans General Hospital
Practices Guidelines
Oncology

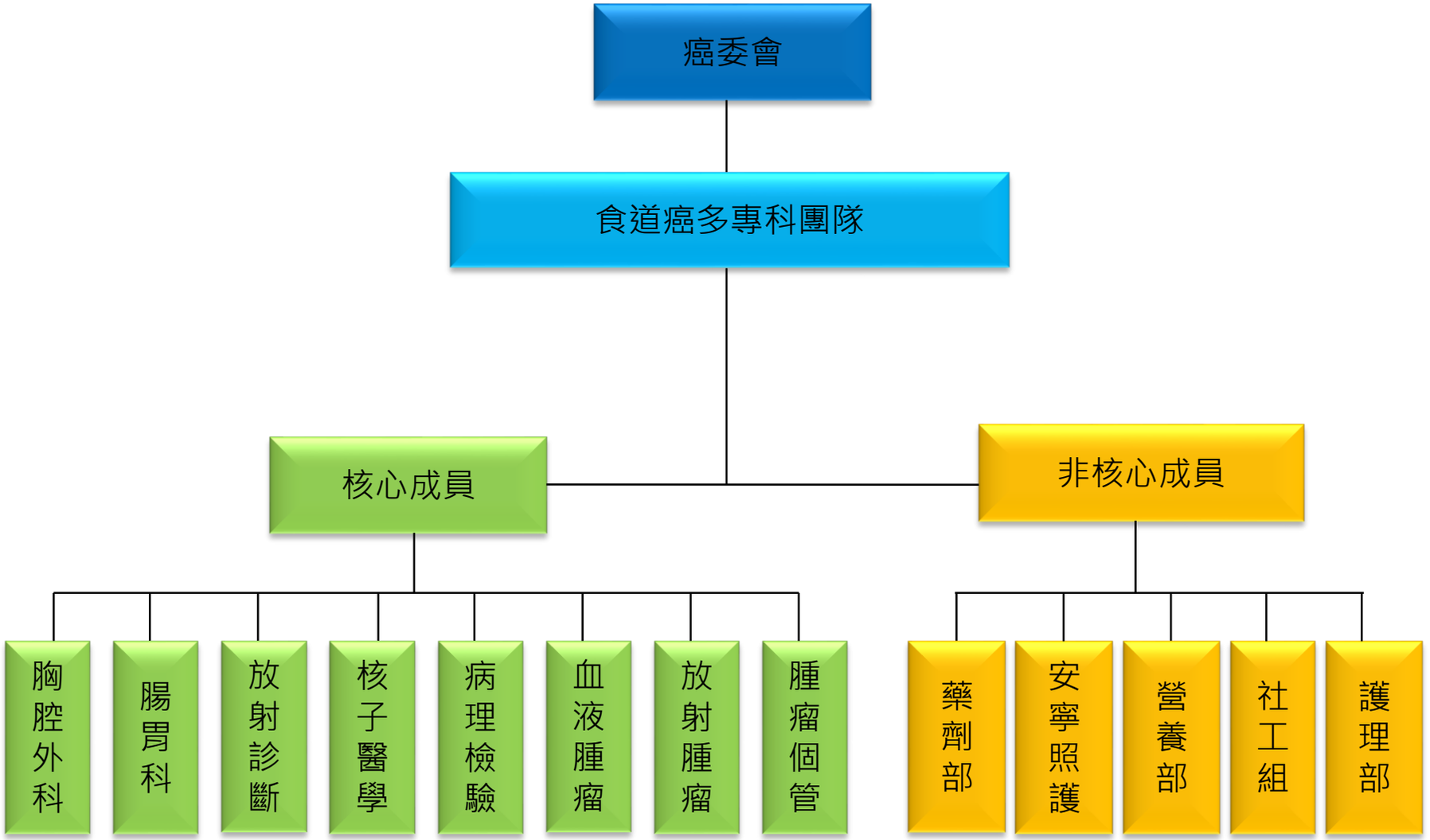
Esophageal Cancer

2020/12/21修訂

Esophageal Cancer

台北榮總食道癌診療共識

食道癌多專科團隊組織架構



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Summary of Guidelines Updates

- **術前評估 (MDT) ：Reference 新增 2021 ASO 文章.**
- **Page 22**
- **Adenocarcinoma, cT2 difference with low risk & high risk.**
- **Page 25**
- **Adenocarcinoma, Post surgery, R0 resection: if yPT+ or N+, add Nivolumab option.**

Principles of pathological review

- **Pathology review 的目的包括：**
  - Classification of tumor
  - Determine the extent of invasion
  - Establish status of cancer involvement of surgical margins
- **所有手術病理報告都應該依照食道癌 WHO 分類**
- **所有手術病理報告都應該依 AJCC/UICC TNM 7th edition 分期**
- **手術病理報告應包括下列項目**
  - Histologic type
  - Histologic grade (G1: well differentiated; G2: moderately differentiated; G3: poorly differentiated)
  - Microscopic tumor extension
  - Margin status

Pretreatment Workup

WORKUP

- H &P
- Upper GI endoscopy and biopsy
- Chest/ abdominal CT with oral and IV contrast
- PET-CT evaluation if no evidence of M1 disease
- CBC and Chemistry profile
- Endoscopic ultrasound(EUS), if no evidence of M1 disease
- Endoscopic mucosal resection is essential for the accurate staging of early stage cancers(T1a or T1b)
- Biopsy of metastatic disease as clinically indicated
- HER2-neu testing if metastatic adenocarcinoma is documented/ suspected
- Bronchoscopy, if tumor is at or above the carina with no evidence of M1 disease
- Nutritional assessment and counseling
- Assign Siewert category

Pretreatment Workup

CLINICAL STAGE

Stage I-III(locoregional disease)

- Squamous cell carcinoma
- Adenocarcinoma

Stage IV(metastatic disease)

- Squamous cell carcinoma
- Adenocarcinoma

Pretreatment Workup

Squamous cell carcinoma

Stage I-III(locoregional disease)

→ Multidisciplinary evaluation: Consider nasogastric or J-tube for preoperative nutrition support）

- Medically fit for surgery
- Non- surgical candidate

Adenocarcinoma

Stage I-III(locoregional disease)

→ Multidisciplinary evaluation: Consider nasogastric or J-tube for preoperative nutrition support

- Medically fit for surgery
- Non- surgical candidate

Taipei Veterans General Hospital
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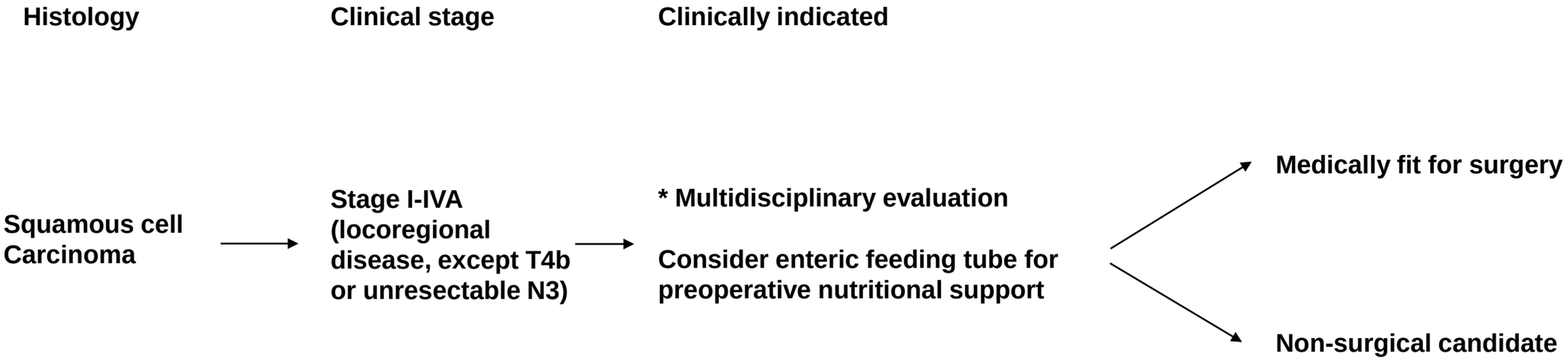
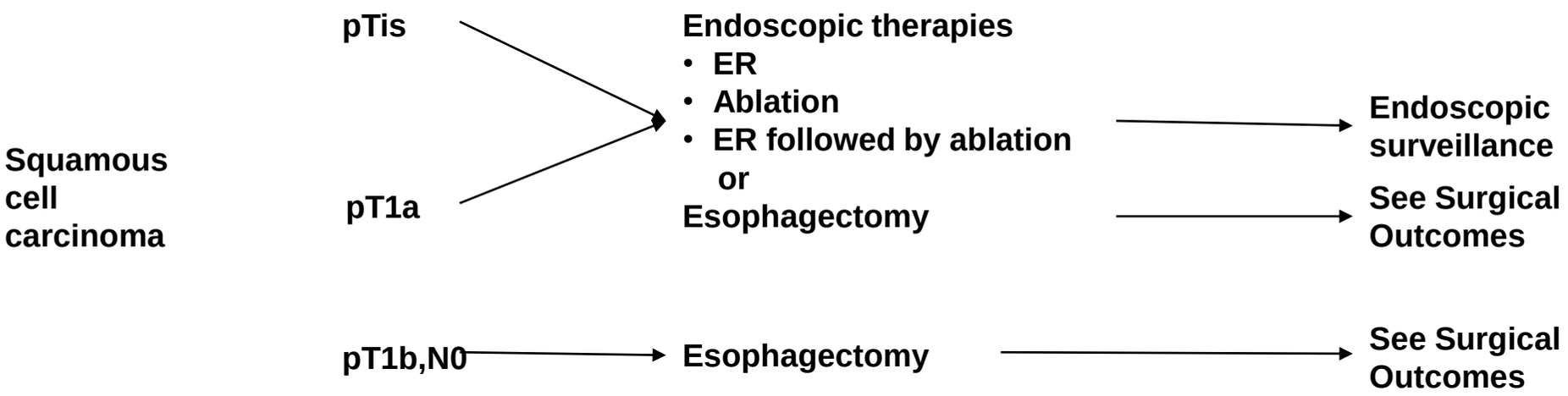
Oncology
Esophageal Cancer
Principles of Surgical Resection

Two Different Cell Types

- **SCC**
- **Adenocarcinoma**


Histology
Clinical stage
Clinically indicated
Squamous cell Carcinoma
Stage I-IVA (locoregional disease, except T4b or unresectable N3)
* Multidisciplinary evaluation
Consider enteric feeding tube for preoperative nutritional support
Medically fit for surgery
Non-surgical candidate

FOR SQUAMOUS CELL CARCINOMA



FOR SQUAMOUS CELL CARCINOMA

Squamous cell carcinoma

cT1b-cT2, N0 (low-risk lesions: <3cm, well differentiated) → **Esophagectomy (for non-cervical esophagus)** → **See Surgical Outcomes**

cT2, N0(high-risk lesions: LVI, ≥ 3cm, poorly differentiated)
cT1b-cT2, N+ or
cT3-cT4a, Any N →

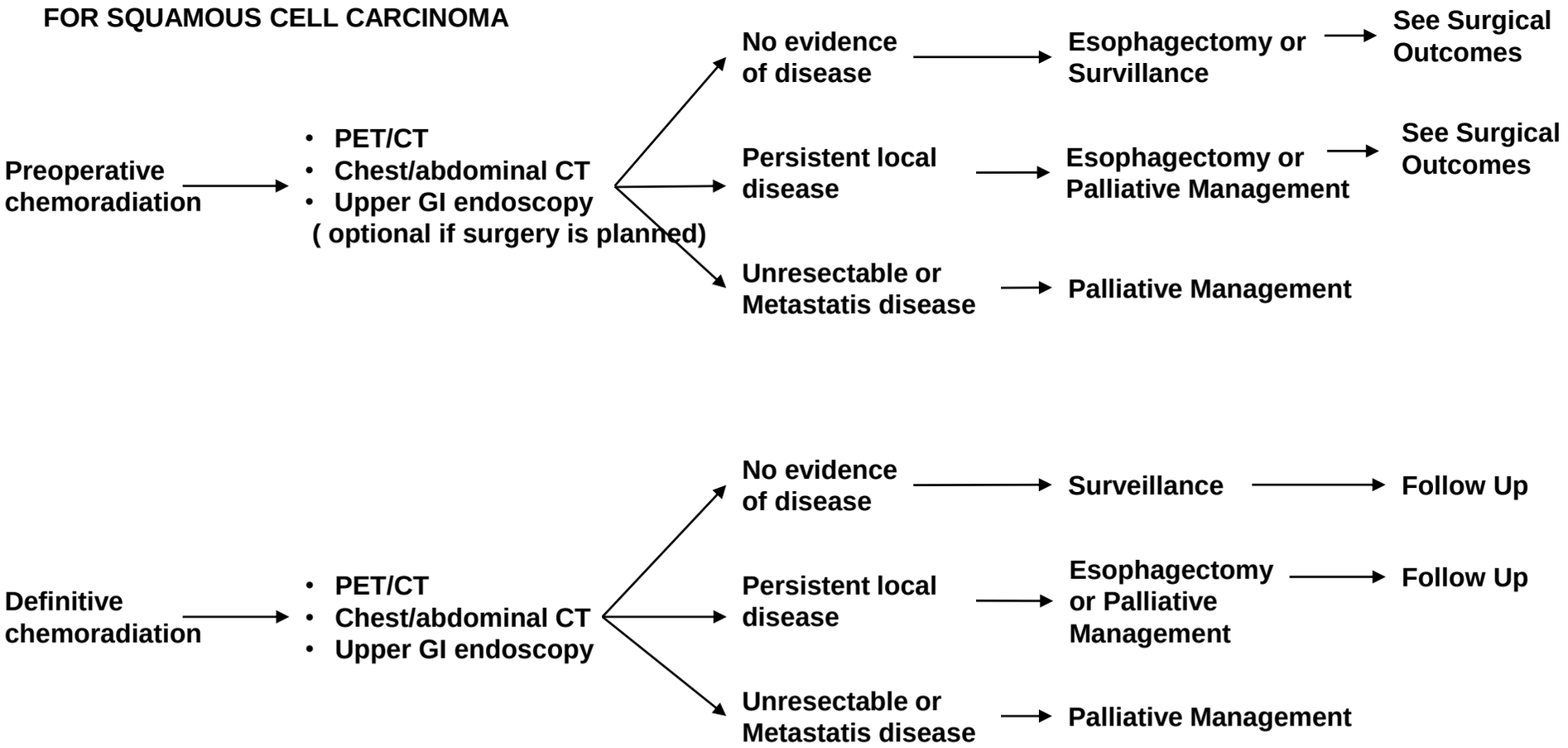
- **Preoperative chemoradiation** → **See Response Assessment**
  (RT, 41.4-50.4 Gy + concurrent chemotherapy)
  or
- **Definitive chemoradiation** → **Follow Up**
  (RT, 50.4-60 Gy + concurrent chemotherapy;
  59.4-66 Gy for cervical esophagus + concurrent chemotherapy)

cT4b →

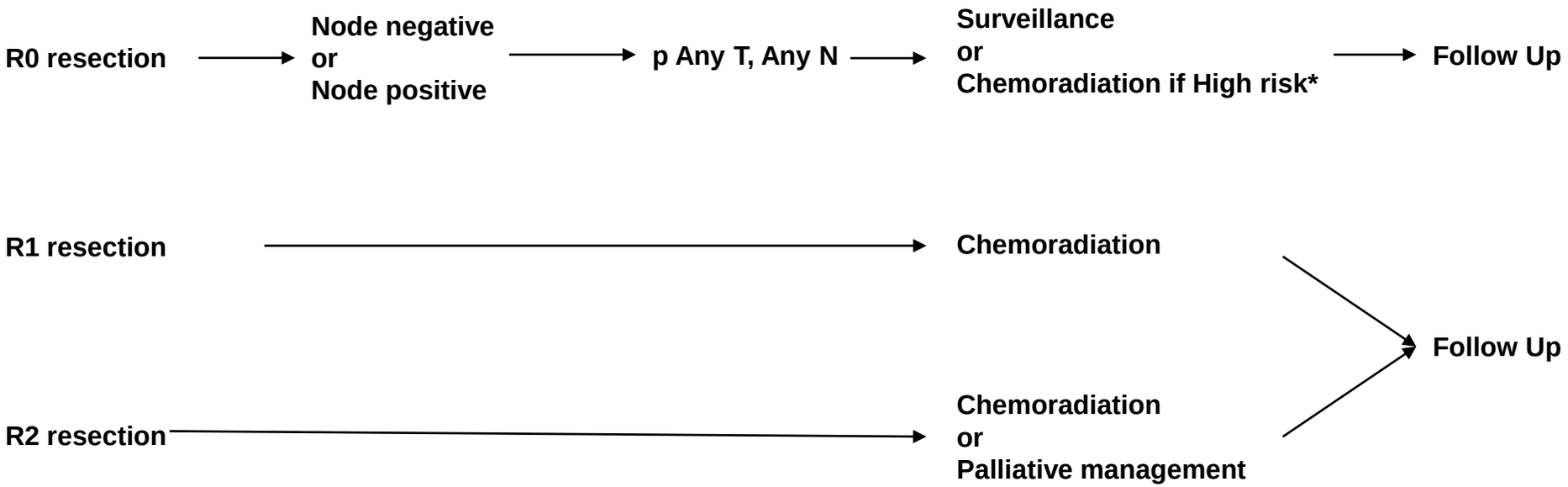
- **Definitive chemoradiation**
  (RT, 50.4-60 Gy + concurrent chemotherapy)
- **Neoadjuvant Chemotherapy follow by Definitive Chemoradiation**
  ****Consider chemotherapy alone in the setting of invasion of trachea, great vessels, or heart**

→ **See Response Assessment**

Esophageal Cancer

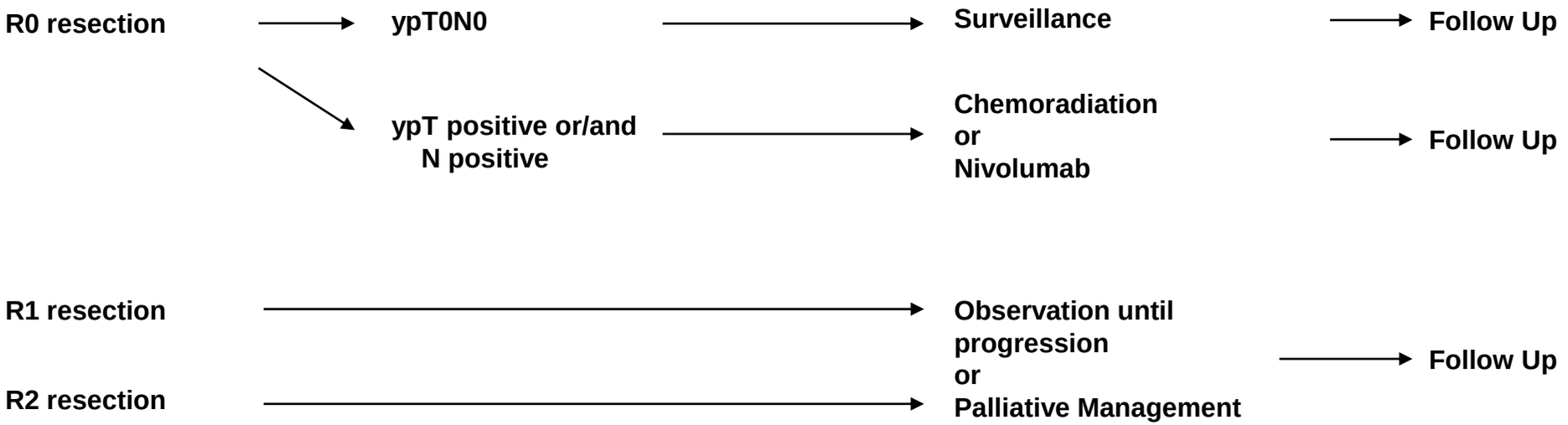


SURGICAL OUTCOMES
Squamous cell carcinoma
(Patients Have Not Reveived Preoperative Chemoradiation)

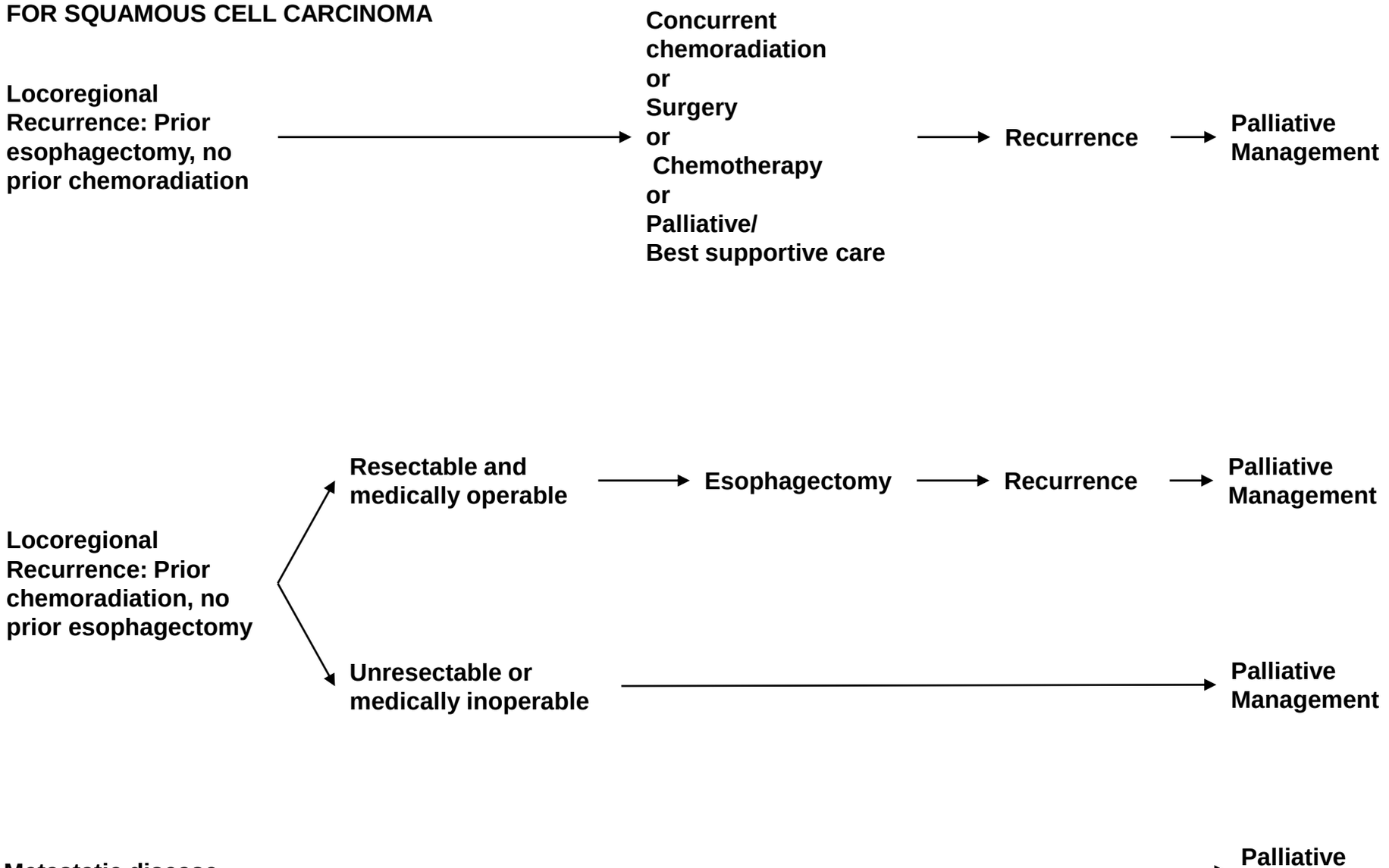


***High risk factors: advanced T/N stage, close circumferential margin, LVI, perineural invasion, extracapsular lymph node**

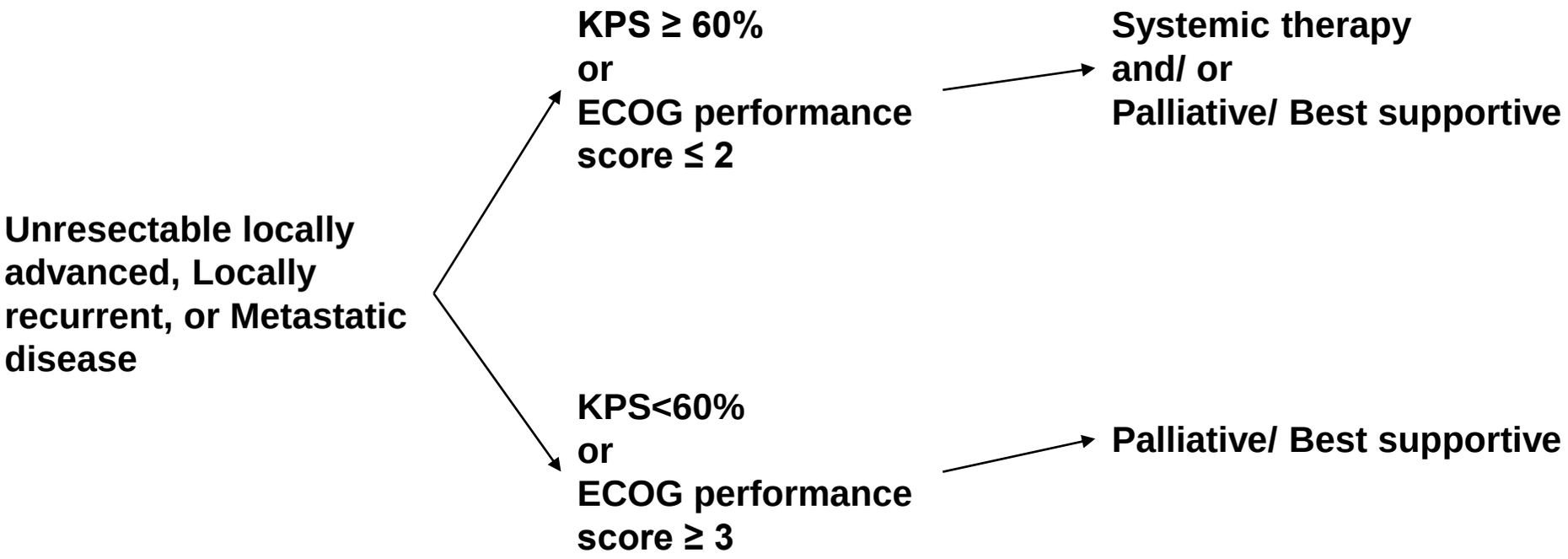
SURGICAL OUTCOMES
Squamous cell carcinoma
(Patients Have Reveived Preoperative Chemoradiation)



FOR SQUAMOUS CELL CARCINOMA



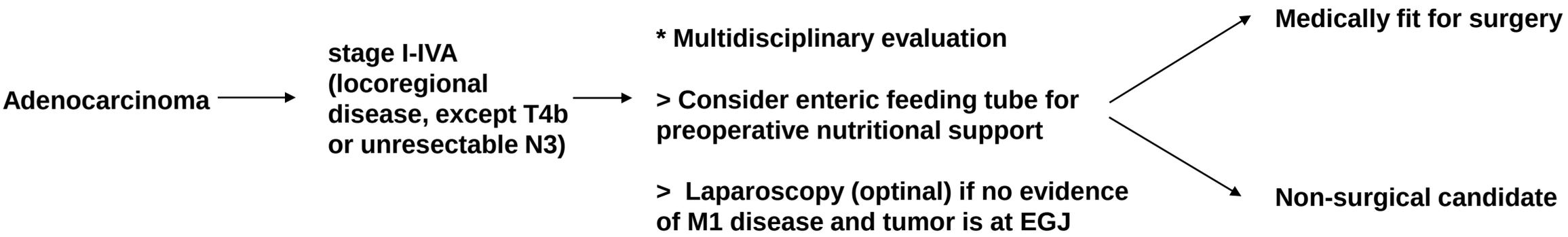
FOR SQUAMOUS CELL CARCINOMA



Two Different Cell Types

- **SCC**
- **Adenocarcinoma**

Esophageal Cancer



Esophageal Cancer

FOR ADENOCARCINOMA

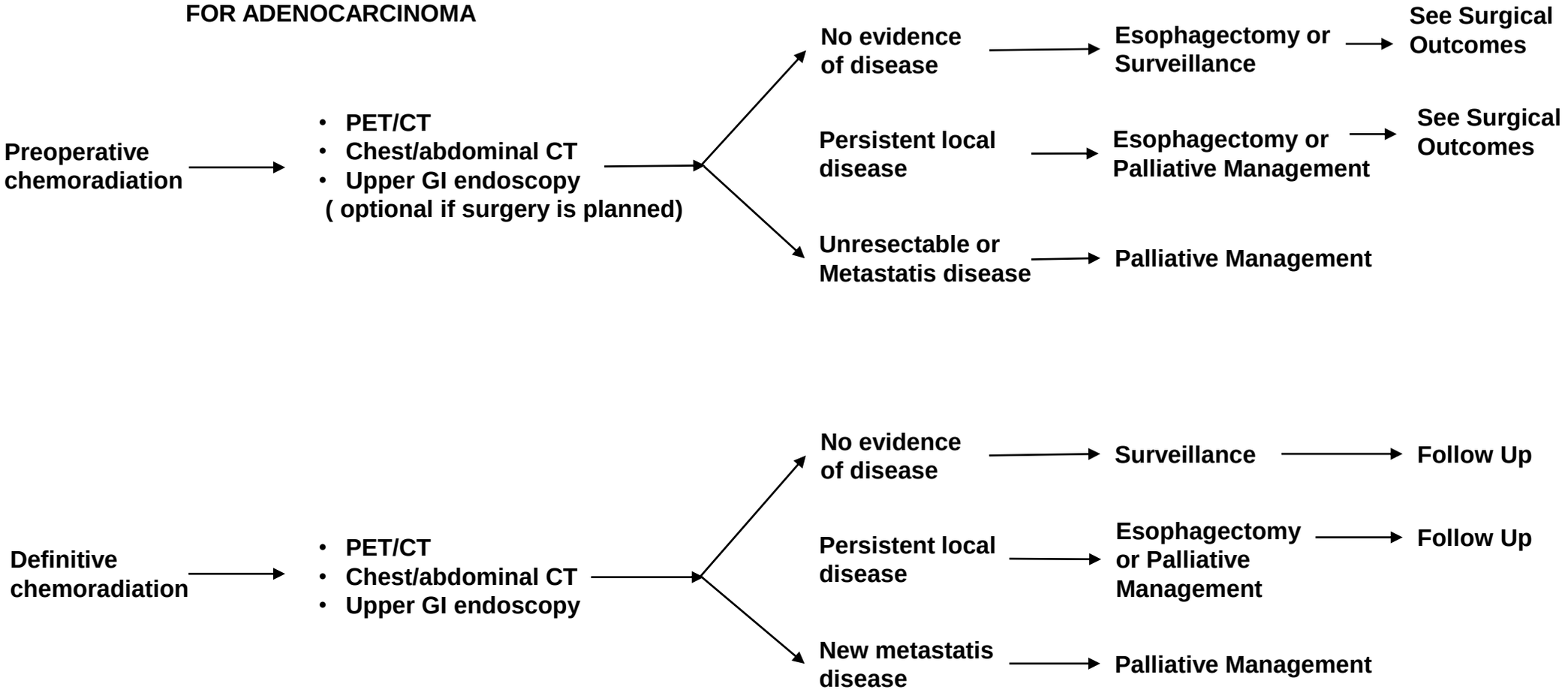
Adenocarcinoma

- **pTis** → **Endoscopic therapies (Preferred)**
  - **ER**
  - **Ablation**
  - **ER followed by ablation**

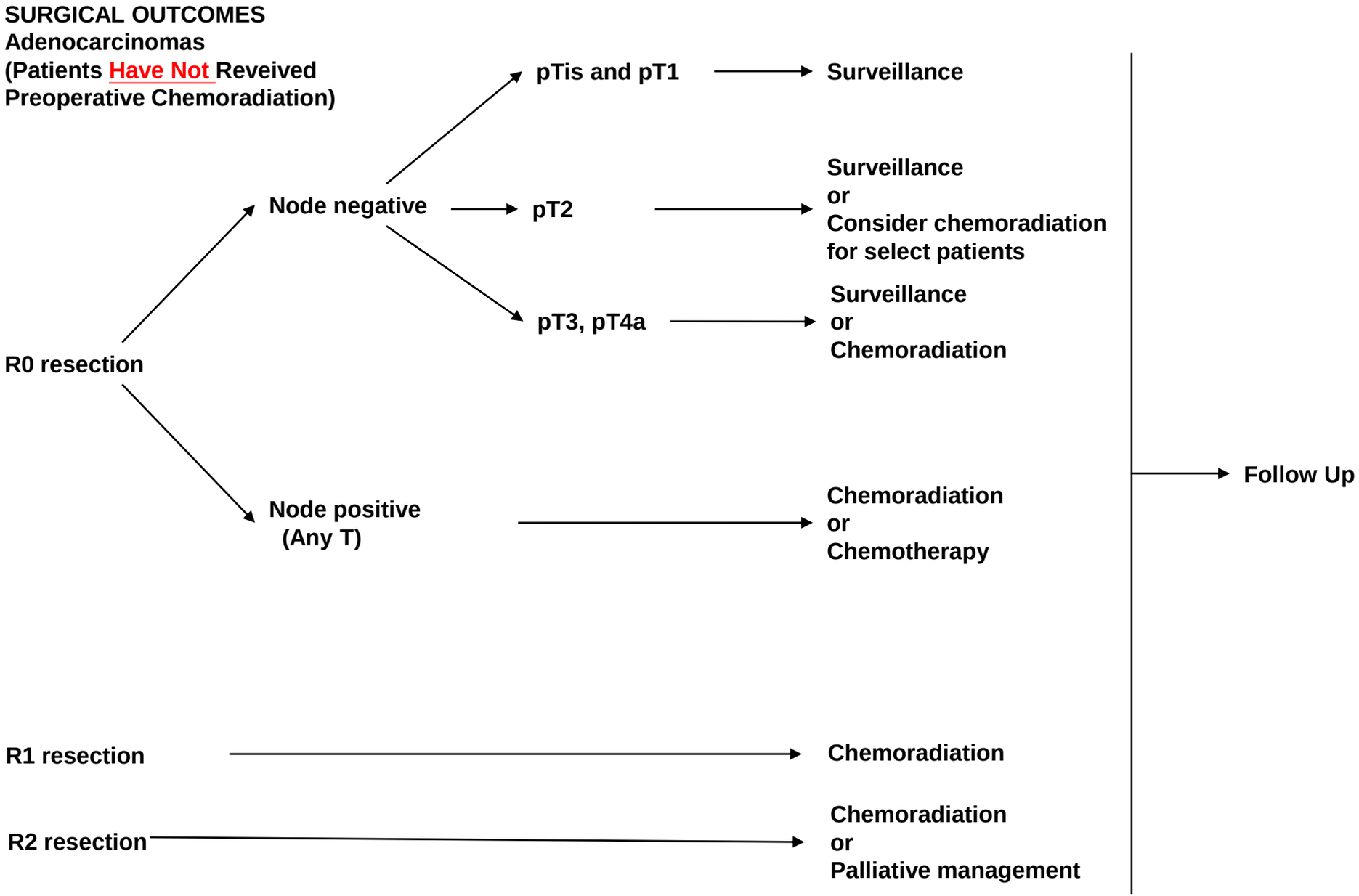
  → **Endoscopic surveillance**
- **pT1a** → **Endoscopic therapies (Preferred)** (ER / Ablation / ER followed by ablation)
  - **or Esophagectomy** → **See Surgical Outcomes**
- **Superficial pT1b,N0** → **ER followed by ablation**
  - → **Endoscopic surveillance**
  - **or Esophagectomy** → **See Surgical Outcomes**
- **pT1b,N0** → **Esophagectomy** → **See Surgical Outcomes**
- **cT1b-cT2, N0 (low-risk lesions: <3cm, well differentiated)** → **Preoperative chemoradiation (RT, 41.4-50.4 Gy + concurrent chemotherapy)** → **See Response Assessment**
  - **or Definitive chemoradiation (RT, 50.4-60 Gy + concurrent chemotherapy; 59.4-66 Gy for cervical esophagus + concurrent chemotherapy)** → **Follow Up**
  - **or Esophagectomy** → **See Surgical Outcomes**
- **cT2, N0(high-risk lesions: LVI, ≥3cm, poorly differentiated) cT1b-ct2, N+ or cT3-cT4a, Any N** → **Preoperative chemoradiation (RT, 41.4-50.4 Gy + concurrent chemotherapy)** → **See Response Assessment**
  - **or Definitive chemoradiation (RT, 50.4-60 Gy + concurrent chemotherapy; 59.4-66 Gy for cervical esophagus + concurrent chemotherapy)** → **Follow Up**
  - **or Esophagectomy** → **See Surgical Outcomes**
- **cT4b** → **Definitive chemoradiation (RT, 50.4-60 Gy + concurrent chemotherapy)** → **See Response Assessment**

Esophageal Cancer

FOR ADENOCARCINOMA



Esophageal Cancer



Esophageal Cancer

SURGICAL OUTCOMES
Adenocarcinoma
(Patients Have Reveived Preoperative Chemoradiation)

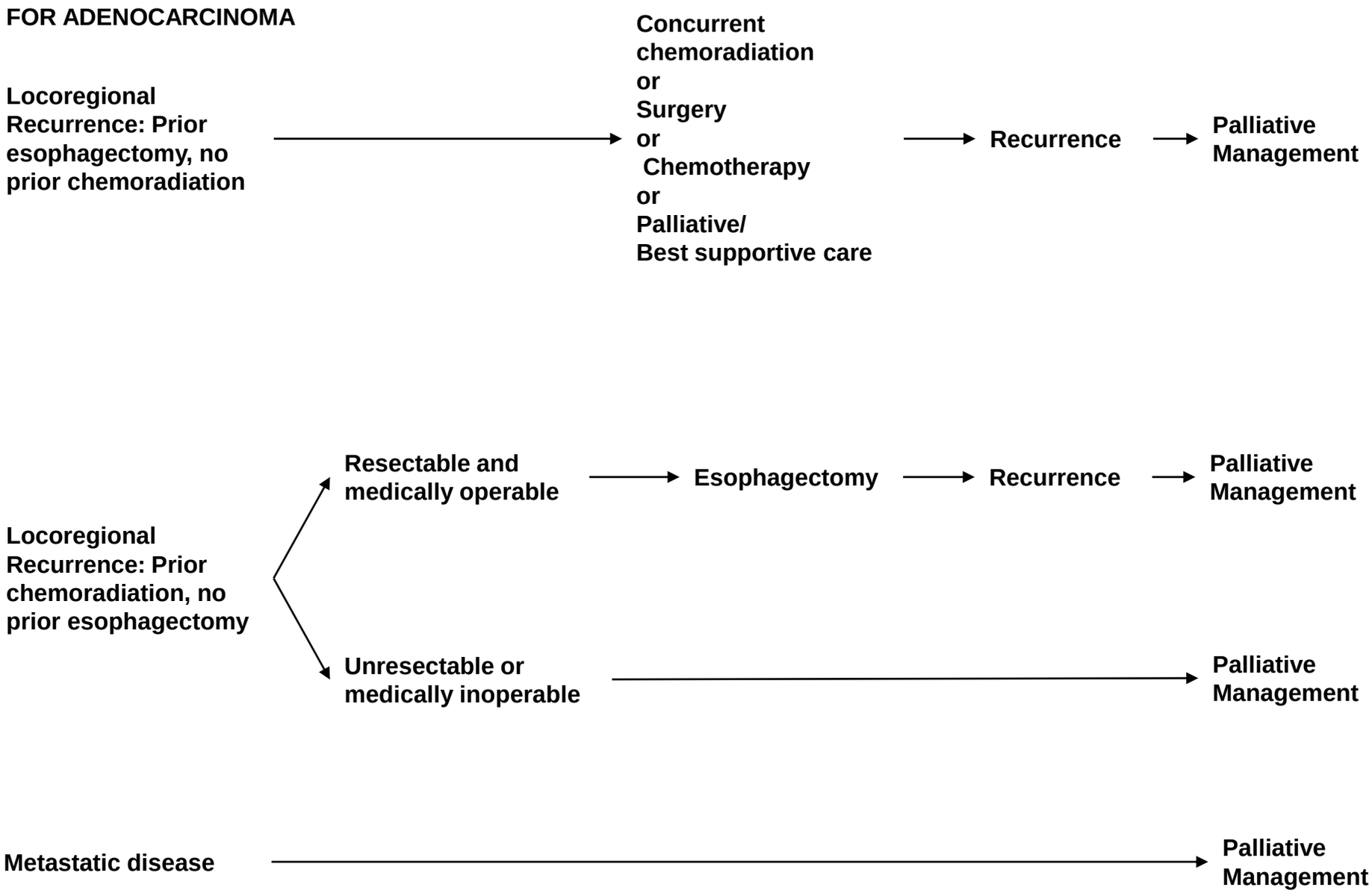
R0 resection

- **ypT0N0** → **Observation until progression or Chemotherapy If received perioperatively**
- **ypT positive or/and ypN positive** → **Observation until progression or Chemoradiation or Chemotherapy or Nivolumab If received perioperatively**

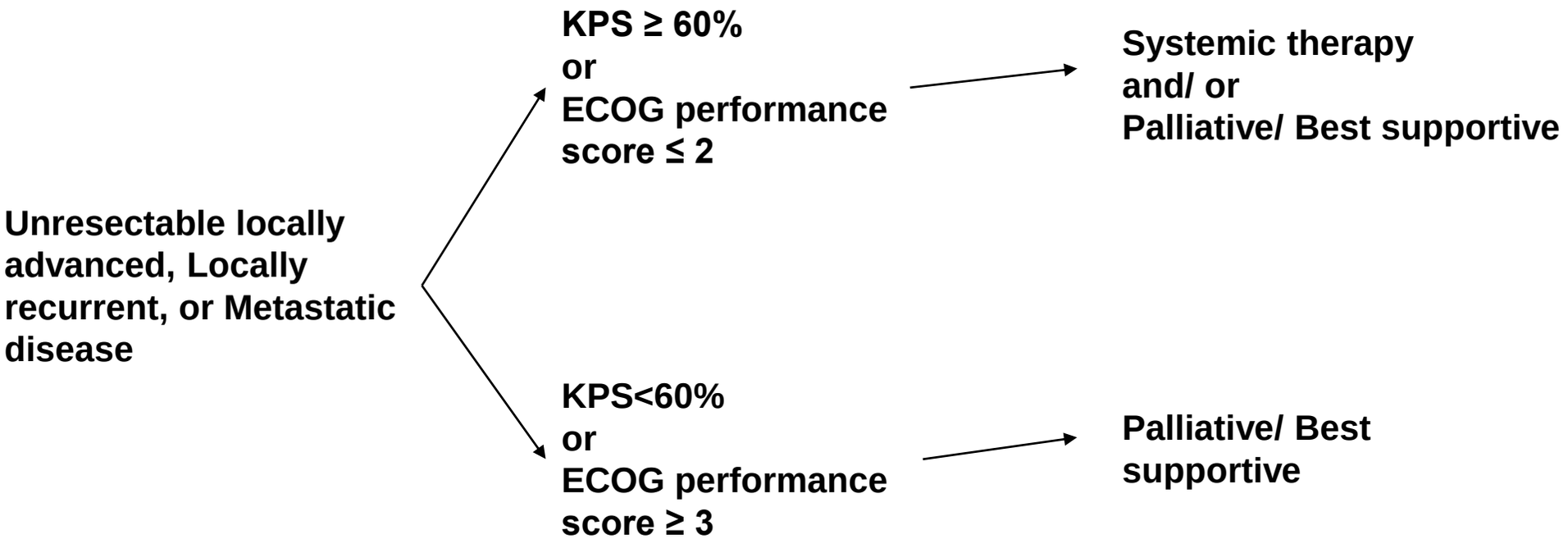
R1 resection → **Chemoradiation or Chemotherapy or Consider re-resection**

R2 resection → **Chemoradiation or Palliative Management**

All → **Follow Up**


FOR ADENOCARCINOMA
Locoregional Recurrence: Prior esophagectomy, no prior chemoradiation
Concurrent chemoradiation or Surgery or Chemotherapy or Palliative/ Best supportive care
Recurrence
Palliative Management
Locoregional Recurrence: Prior chemoradiation, no prior esophagectomy
Resectable and medically operable
Esophagectomy
Recurrence
Palliative Management
Unresectable or medically inoperable
Palliative Management
Metastatic disease
Palliative Management

FOR ADENOCARCINOMA



Reference of Surgical Resection

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3. Hsu PK, Huang CS, Wang BY, Wu YC, Hsu WH. Survival Benefits of Postoperative Chemoradiation in Lymph Node-Positive Esophageal Squamous Cell Carcinoma. Ann Thorac Surg 2014;97:1734-41.(SCI)
4. Hsu PK, Huang CS, Wu YC, Chou TY, Hsu WH. Open versus Thoracoscopic Esophagectomy in Patients with Esophageal Squamous Cell Carcinoma. World J Surg. 2014;38:402-9. (SCI)
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7. Wang BY, Liu CY, Lin CH, Hsu PK, Hsu WH, Wu YC, Cheng CY. Endoscopic Tumor Length Is an Independent Prognostic Factor in Esophageal Squamous Cell Carcinoma. Ann Surg Oncol. 2012;19:2149-58. (SCI)
8. Hsu PK, Wang BY, Huang CS, Wu YC, Hsu WH. Prognostic factors for post-recurrence survival in esophageal squamous cell carcinoma patients with recurrence after resection. J Gastrointest Surg. 2011;15:558-65. (SCI)
9. Hsu PK, Wang BY, Chou TY, Huang CS, Wu YC, Hsu WH. The total number of resected lymph node is not a prognostic factor for recurrence in esophageal squamous cell carcinoma patients undergone transthoracic esophagectomy. J Surg Oncol. 2011;103:416-20. (SCI)
10. Wang BY, Goan YG, Hsu PK, Hsu WH, Wu YC. Tumor length as a prognostic factor in esophageal squamous cell carcinoma. Ann Thorac Surg. 2011;91:887-93. (SCI)

AJCC Cancer Staging Manual, Eighth edition(2018-)

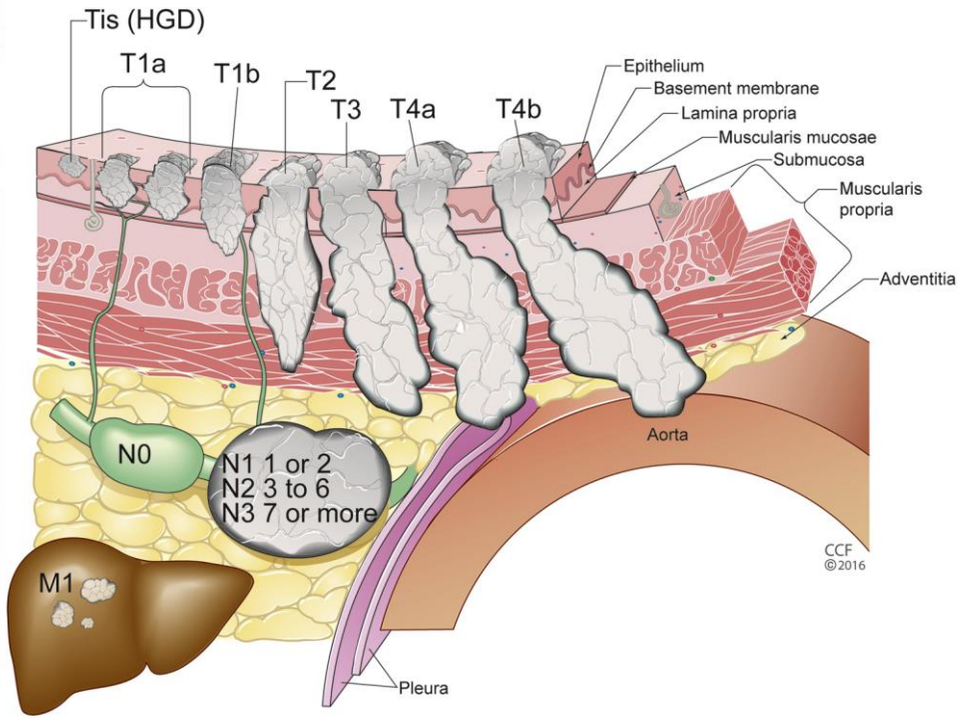
TNM STAGING

AJCC Cancer Staging Manual, Eighth edition

Definition of Primary Tumor (T)

Squamous Cell Carcinoma and Adenocarcinoma

T Category	T Criteria
TX	Tumor cannot be assessed
T0	No evidence of primary tumor
Tis	High-grade dysplasia, defined as malignant cells confined to the epithelium by the basement membrane
T1	Tumor invades the lamina propria, muscularis mucosae, or submucosa
T1a	Tumor invades the lamina propria or muscularis mucosae
T1b	Tumor invades the submucosa
T2	Tumor invades the muscularis propria
T3	Tumor invades adventitia
T4	Tumor invades adjacent structures
T4a	Tumor invades the pleura, pericardium, azygos vein, diaphragm, or peritoneum
T4b	Tumor invades other adjacent structures, such as the aorta, vertebral body, or airway



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Definition of Regional Lymph Nodes (N)

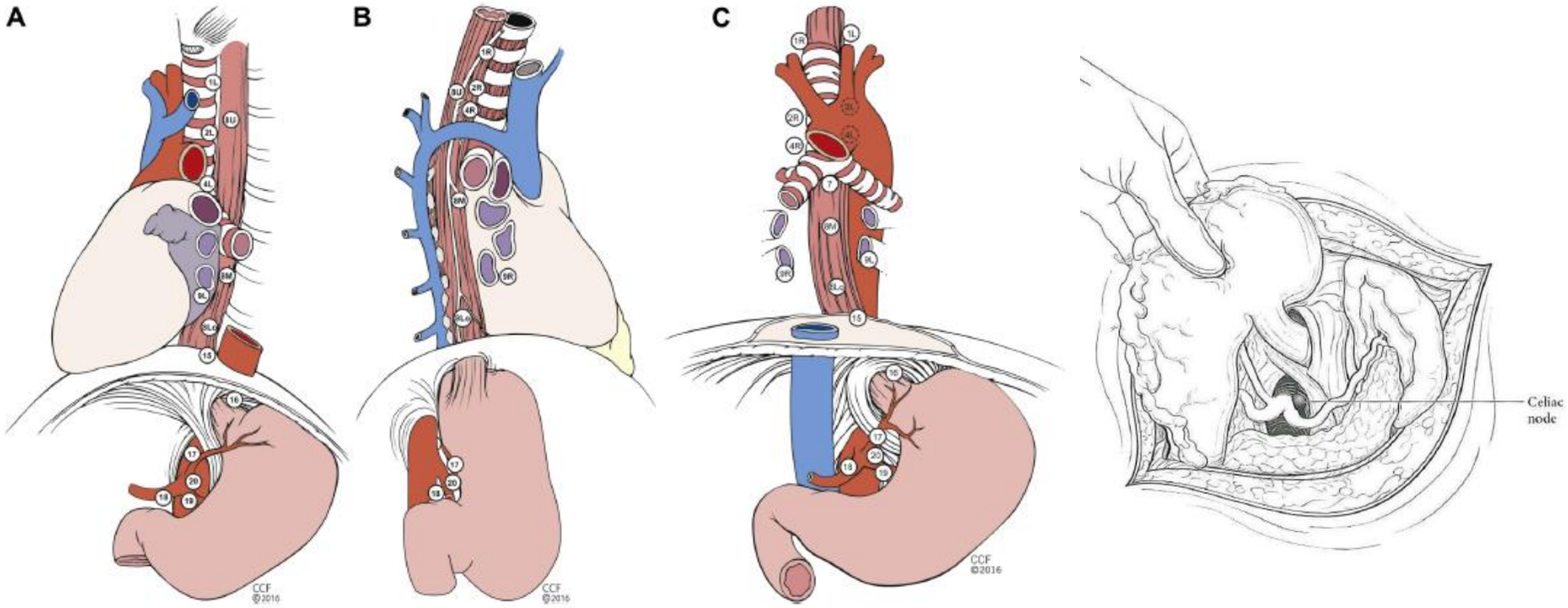
Squamous Cell Carcinoma and Adenocarcinoma

N Category	N Criteria
NX	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1	Metastasis in one or two regional lymph nodes
N2	Metastasis in three to six regional lymph nodes
N3	Metastasis in seven or more regional lymph nodes

Definition of Distant Metastasis (M)

Squamous Cell Carcinoma and Adenocarcinoma

M Category	M Criteria
M0	No distant metastasis
M1	Distant metastasis



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Definition of Histologic Grade (G)

Squamous Cell Carcinoma and Adenocarcinoma

G	G Definition
GX	Grade cannot be assessed
G1	Well differentiated
G2	Moderately differentiated
G3	Poorly differentiated, undifferentiated

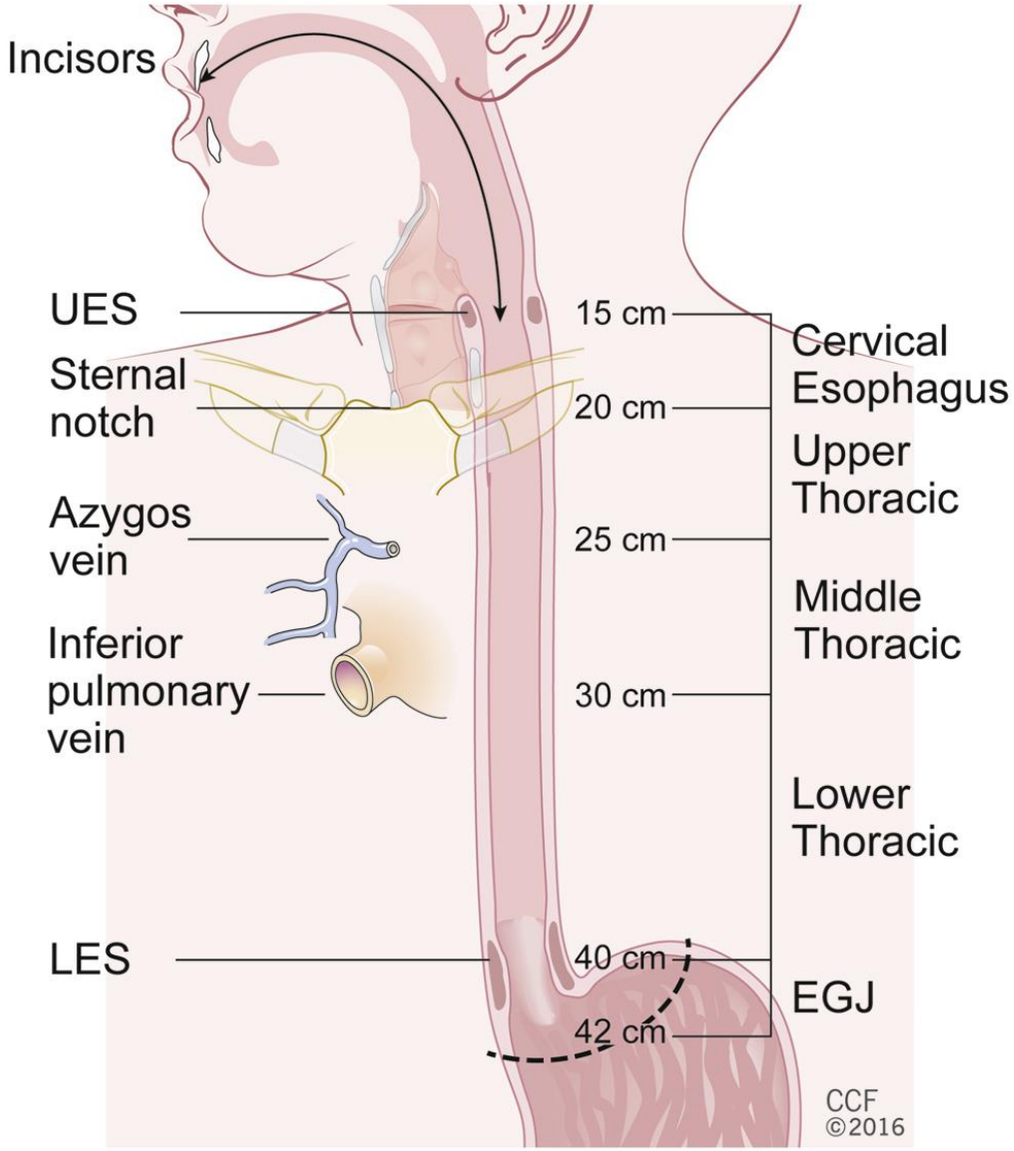
Definition of Location (L)

Squamous Cell Carcinoma

Location plays a role in the stage grouping of esophageal squamous cancers.

Location Category	Location Criteria
X	Location unknown
Upper	Cervical esophagus to lower border of azygos vein
Middle	Lower border of azygos vein to lower border of inferior pulmonary vein
Lower	Lower border of inferior pulmonary vein to stomach, including gastroesophageal junction

Note: Location is defined by the position of the epicenter of the tumor in the esophagus.



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- **Squamous cell carcinoma**

Clinical (cTNM) (Fig. 16.6)

When cT is…	And cN is…	And M is…	Then the stage group is…
Tis	N0	M0	0
T1	N0–1	M0	I
T2	N0–1	M0	II
T3	N0	M0	II
T3	N1	M0	III
T1–3	N2	M0	III
T4	N0–2	M0	IVA
Any T	N3	M0	IVA
Any T	Any N	M1	IVB

Postneoadjuvant Therapy (ypTNM) (Fig. 16.8)

When yp T is…	And yp N is…	And M is…	Then the stage group is…
T0–2	N0	M0	I
T3	N0	M0	II
T0–2	N1	M0	IIIA
T3	N1	M0	IIIB
T0–3	N2	M0	IIIB
T4a	N0	M0	IIIB
T4a	N1–2	M0	IVA
T4a	NX	M0	IVA
T4b	N0–2	M0	IVA
Any T	N3	M0	IVA
Any T	Any N	M1	IVB

Pathological (pTNM) (Fig. 16.7)

When pT is…	And pN is…	And M is	And G is…	And location is…	Then the stage group is…
Tis	N0	M0	N/A	Any	0
T1a	N0	M0	G1	Any	IA
T1a	N0	M0	G2–3	Any	IB
T1a	N0	M0	GX	Any	IA
T1b	N0	M0	G1–3	Any	IB
T1b	N0	M0	GX	Any	IB
T2	N0	M0	G1	Any	IB
T2	N0	M0	G2–3	Any	IIA
T2	N0	M0	GX	Any	IIA
T3	N0	M0	Any	Lower	IIA
T3	N0	M0	G1	Upper/middle	IIA
T3	N0	M0	G2–3	Upper/middle	IIB
T3	N0	M0	GX	Any	IIB
T3	N0	M0	Any	Location X	IIB
T1	N1	M0	Any	Any	IIB
T1	N2	M0	Any	Any	IIIA
T2	N1	M0	Any	Any	IIIA
T2	N2	M0	Any	Any	IIIB
T3	N1–2	M0	Any	Any	IIIB
T4a	N0–1	M0	Any	Any	IIIB
T4a	N2	M0	Any	Any	IVA
T4b	N0–2	M0	Any	Any	IVA
Any T	N3	M0	Any	Any	IVA
Any T	Any N	M1	Any	Any	IVB

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- **Adenocarcinoma**

Clinical (cTNM) (Fig. 16.9)

When cT is…	And cN is…	And M is…	Then the stage group is…
Tis	N0	M0	0
T1	N0	M0	I
T1	N1	M0	IIA
T2	N0	M0	IIB
T2	N1	M0	III
T3	N0–1	M0	III
T4a	N0–1	M0	III
T1–4a	N2	M0	IVA
T4b	N0–2	M0	IVA
Any T	N3	M0	IVA
Any T	Any N	M1	IVB

Postneoadjuvant Therapy (ypTNM) (Fig. 16.11)

When yp T is…	And yp N is…	And M is…	Then the stage group is…
T0–2	N0	M0	I
T3	N0	M0	II
T0–2	N1	M0	IIIA
T3	N1	M0	IIIB
T0–3	N2	M0	IIIB
T4a	N0	M0	IIIB
T4a	N1–2	M0	IVA
T4a	NX	M0	IVA
T4b	N0–2	M0	IVA
Any T	N3	M0	IVA
Any T	Any N	M1	IVB

Pathological (pTNM) (Fig. 16.10)

When pT is…	And pN is…	And M is…	And G is…	Then the stage group is…
Tis	N0	M0	N/A	0
T1a	N0	M0	G1	IA
T1a	N0	M0	GX	IA
T1a	N0	M0	G2	IB
T1b	N0	M0	G1–2	IB
T1b	N0	M0	GX	IB
T1	N0	M0	G3	IC
T2	N0	M0	G1–2	IC
T2	N0	M0	G3	IIA
T2	N0	M0	GX	IIA
T1	N1	M0	Any	IIB
T3	N0	M0	Any	IIB
T1	N2	M0	Any	IIIA
T2	N1	N0	Any	IIIA
T2	N2	M0	Any	IIIB
T3	N1–2	M0	Any	IIIB
T4a	N0–1	M0	Any	IIIB
T4a	N2	M0	Any	IVA
T4b	N0–2	M0	Any	IVA
Any T	N3	M0	Any	IVA
Any T	Any N	M1	Any	IVB

Taipei Veterans General Hospital Practices Guidelines Oncology

Esophageal Cancer

Principles of Chemotherapy

Principle of Chemotherapy

- For localized esophageal carcinoma, the listed regimens mainly in the context of phase II trials.
- For metastatic esophageal carcinoma, phase III trials have not been performed for many years.Some regimens listed below are derived from the gastric adenocarcinoma phase III trials that have included patients with lower esophageal cancer and/or gastroesophageal junction cancer.
- Please refer to the original reports for toxicity, doses, schedule, and dose modifications.
- Prior to recommending chemotherapy, the requirements for adequacy of organ function and performance status should be met.
- The schedule, toxicity, and potential benefits should be thoroughly discussed with the patient and caregivers.
- Patients should be observed closely and treated for any complications during chemotherapy. Appropriate blood work should be monitored.
- Upon completion of chemotherapy, patients should be assessed for response and monitored for any long-term complications.

Recommended regimens of concurrent chemo-radio-therapy

Prefer regimen: Cisplatin plus fluoropyrimidine

5-FU + Cisplatin+RT*

Regimen 1[1]: 4-day PFL (Q3-4W) of Week 1, 5, 8, 11

- Cisplatin (CDDP) 80 mg/m2 infusion for 3 hours on Day 1
- 5-FU 400mg/m2/day per 24 hours as a 96 hours continuous infusion on Day 1-4
- Leucovorin 90 mg/m2/day per 24 hours as a 96 hours continuous infusion on Day 1-4

Regimen 2[2]: Paclitaxel and Carboplatin (QW)

- Paclitaxel 50 mg/m2 infusion for 1 hour
- Carboplatin AUC 2 mg/mL infusion for 1 hour

Regimen 3: CFHx (Q3W) x 2 cycles

- Hydroxyurea 500 mg po stat and bid x 11 doses
- Cisplatin 20mg/m2 infusion for 4 hours
- 5-FU 600 mg/m2 per 24 hours as a 96-hour continuous infusion

Regimen 4: Weekly Cisplatin (QW) x 5 cycles

- Cisplatin 35-40mg/m2 infusion for 1 hours

Regimen 5: 4-day FL (Q3-4W) of Week 1, 5, 8, 11

- 5-FU 400mg/m2/day per 24 hours as a 96 hours continuous infusion on Day 1-4
- Leucovorin 90 mg/m2/day per 24 hours as a 96 hours continuous infusion on Day 1-4

***RT: please see radiotherapy recommendation part**

Recommended regimens of adjuvant chemotherapy

Prefer regimen: Cisplatin plus fluoropyrimidine

Regimen 1[1]: 4-day PFL (Q3-4W) of Week 1, 5, 8, 11

- Cisplatin (CDDP) 80 mg/m2 infusion for 3 hours on Day 1
- 5-FU 400mg/m2/day per 24 hours as a 96 hours continuous infusion on Day 1-4
- Leucovorin 90 mg/m2/day per 24 hours as a 96 hours continuous infusion on Day 1-4

Regimen 2: 4-day FL (Q3-4W) of Week 1, 5, 8, 11

- 5-FU 400mg/m2/day per 24 hours as a 96 hours continuous infusion on Day 1-4
- Leucovorin 90 mg/m2/day per 24 hours as a 96 hours continuous infusion on Day 1-4

Recommended regimens of palliative chemotherapy

Prefer regimen: Cisplatin plus fluoropyrimidine

Regimen 1[1]: 4-day PFL (Q3-4W) of Week 1, 5, 8, 11

- Cisplatin (CDDP) 80 mg/m2 infusion for 3 hours on Day 1
- 5-FU 400mg/m2/day per 24 hours as a 96 hours continuous infusion on Day 1-4
- Leucovorin 90 mg/m2/day per 24 hours as a 96 hours continuous infusion on Day 1-4

Regimen 2: 4-day FL (Q3-4W) of Week 1, 5, 8, 11

- 5-FU 400mg/m2/day per 24 hours as a 96 hours continuous infusion on Day 1-4
- Leucovorin 90 mg/m2/day per 24 hours as a 96 hours continuous infusion on Day 1-4

Regimen 3:TPF (Q3-4W)

- Docetaxel 60 mg/m2 infusion for 3 hours
- Cisplatin 75 mg/m2 infusion for 3 hours
- 5-FU: 850 mg/m2 per 24 hours as a 96-hour continuous infusion

Regimen 4: Cisplatin + DeGramount (Q2W)

- Cisplatin 50 mg/m2 infusion for 1 hour
- Leucovorin 200 mg/m2 infusion for 2 hours per day for 2 days
- 5-FU 400 mg/m2 infusion for 30 minutes per day for 2 days
- 5-FU 600 mg/m2 per 24 hours as a 48-hour continuous infusion

Regimen 5:Cisplatin and Etoposide

- Cisplatin 75 mg/m2 infusion for 3 hours
- Etoposide 75 mg/m2 infusion for 2 hours per day for 2 days

Recommended regimens of palliative immunetherapy

Prefer regimen:

Regimen 1[12]: Nivolumab

- Nivolumab 3 mg/kg every 2 weeks.

Regimen 2: Pembrolizumab

- Pembrolizumab 2 mg/kg every 3 weeks.

Reference of Chemotherapy

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Taipei Veterans General Hospital
Practices Guidelines Oncology
Esophageal Cancer
Principles of Radiotherapy

General Radiation Information

General Radiation Information

- Treatment recommendations should be made after joint consultation and/or discussion by a multidisciplinary team including surgical, radiation, medical oncologists, radiologists, gastroenterologists, and pathologists.
- CT scans, barium swallow, endoscopic ultrasound (EUS), endoscopy reports and PET or PET/CT scans, when available, should be reviewed by the multidisciplinary team. This will allow an informed determination of treatment volume and field borders prior to simulation.

Simulation and Treatment Planning

- CT simulation and 3D treatment planning. Intensity-modulated radiation therapy (IMRT) may be used in clinical settings where reduction in dose to organs at risk (e.g. heart, lungs) is required that cannot be achieved by 3-D techniques.
- When clinically appropriate, use IV contrast for CT simulation to aid in target localization.
- The slice thickness of CT simulation should be no more than 5 mm.
- Immobilization device is strongly recommended for reproducibility of daily set-up when supraclavicular fossa or neck need to be irradiated.
- When 4D CT planning or other motion management techniques are used, margins may be modified to account for observed motion and may also be reduced if justified. The 4D CT data may also be used to create an internal target volume (ITV) from which subsequent clinical target volume (CTV) and planning target volume (PTV) expansions can be made.

Principle of Target Volume Delineation

- **Gross Target Volume (GTV) delineation**
  - Target volume delineation based on CT simulation images. Diagnostic CT, barium, endoscopic ultrasound (EUS), endoscopic reports, and PET/CT scans should be reviewed, when available, for precise delineation of GTV
  - GTV should include the primary tumor and involved regional lymph nodes as identified on the planning scan and other pre-treatment diagnostic studies.
  - Esophageal wall thickness > 5mm, irregularity or asymmetric should be considered gross tumor
- **Clinical Target Volume (CTV) delineation**
  - The clinical target volume should include the areas at risk for microscopic disease
  - CTV_H: GTV of primary tumor and lymphadenopathy.
  - CTV_M: at least 3-4 cm superiorly and inferiorly expansion beyond the GTV; the nodal CTV should be 0.5-1.5 cm expansion from the nodal GTV.
  - CTV_M should also include coverage of elective nodal regions, depending on the location of the origin of primary tumor.
  - Recommended elective treatment of nodal regions:

Cervical esophagus	SCF lymph nodes, and consider higher echelon cervical nodes especially for N1 or greater
Upper third of esophagus	Para-esophageal and SCF lymph nodes
Middle third of esophagus	Para-esophageal lymph nodes
Lower third of esophagus and GE junction	Para-esophageal lymph nodes, lesser curvature lymph nodes and celiac axis

Principle of Target Volume Delineation

- **Planning Target Volume (PTV) and Internal target vdelineation**
  - The margins of PTV should consider *respiratory motion* and *setup errors*
  - Two-phase (end-inspiration and end-expiration) CT simulation, if applicable, to measure the organ motion to get the internal target volume (ITV)
  - 4DCT data may also be used to create an ITV
  - For single-phase CT simulation, PTV expansion should be 0.5 to 1 cm. The uncertainties arising from respiratory motion should also be taken into consideration .
  - PTV is defined as the ITV plus a 3-D margin of 5 mm
- **Radiation dose**
  - Preoperative radiotherapy: 41.4 – 50.4 Gy [a].
  - Definitive radiotherapy: 50.4 – 60 Gy. A higher dose is suggested for tumors of cervical esophagus [b].
  - Postoperative radiotherapy: 45 – 50.4 Gy
- **Radiation technique:** 3D-CRT, IMRT or VMAT, IGRT

[a] Patients who are at risk for not having surgery should receive radiation dose of 50 –50.4 Gy.
[b] Published studies have reported radiation dose from 60-66 Gy (no randomized evidence).

Principles of Radiation Therapy

- **Preoperative CCRT**
  - Candidate for preoperative CCRT
    - Resectable T1bN+, T2-T4aN0~N+
  - Radiation volume
    - The delineation of target volume follows the "***Principle of Target Volume Delineation"***
    - To spare the volume ＜ 5 cm from cricopharyngeus is strongly suggested
  - Radiation dose: 41.4 – 50.4 Gy at 1.8-2 Gy per fraction for primary tumors and prophylactic mediastinal LN region
  - Evaluation: the possibility of surgical resection should be evaluated at 4th -5th weeks after CCRT
    - Resectable: surgery should be done at the 6th weeks after preoperative CCRT
    - Unresectable (optional): boost to the gross tumor up to 59.4-66 Gy in total

Principles of Radiation Therapy

- **Definitive chemoradiotherapy**
  - Candidate for definitive CCRT
    - Resectable disease but medically unfit for surgery, or patients refuse surgery
    - Unresectable disease: T4b
    - Cervical esophageal cancer (tumor < 5 cm from cricopharyngeus)
  - Radiation volume
    - The delineation of target volume follows the "***Principle of Target volume delineation"***
  - Radiation dose:
    - 50.4-60 Gy at 1.8-2 Gy per fraction for all primary esophageal tumors and positive lymphadenopathy except tumors in cervical region.
    - 59.4-66 Gy at 1.8-2 Gy per fraction for tumors of the cervical esophagus.

[Note]

1. The radiation dose of 50-50.4 Gy as applied in the control arm in RTOG 9403 trial represents the "**evidence-based**' dose recommendation.
2. Most local failures after definitive chemoradiation for unresectable esophageal cancer occur in the GTV (Welsh *et al.* Cancer 2012;118:2632-40)
3. In recent clinical trials design, dose escalation successfully scheduled sum dose > 50 Gy without excess morbidity (Bedenne et al. *J Clin Oncol* 2007;25:1160-1168).
4. For T4b disease, consider endoluminal stenting when appropriate. Chemotherapy alone may be considered in the setting of invasion of trachea, great vessels, or heart

Principles of Radiation Therapy

- **Postoperative chemoradiotherapy**
  - Candidate for postoperative CCRT
    - Positive or close margins
    - Adenocarcinoma with positive lymph nodes
    - Optional for squamous cell carcinoma with T3 or T4 and positive lymph nodes
  - Radiation volume
    - The delineation of target volume follows the "***Principle of Target volume delineation"***
    - The radiation volume is determined based on preoperative image findings
    - The anastomosis should be included in the radiation volume
  - Radiation dose: 45-50.4 Gy at 1.8-2 Gy per fraction

Principles of Radiation Therapy

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Principles of Radiation Therapy

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Follow Up

- **History and Physical examination**
  - Every 3 to 6 months for 1 to 2 years.
  - Every 6 to 12 months for 3 to 5 years, then annually.

- **Clinical examination**

  Optional as clinically indicated
  - Chemistry profile and CBC, as clinically indicated.
  - Imaging as clinically indicated.
  - Upper GI endoscopy and biopsy as clinically indicated.
  - Dilatation for anastomotic stenosis.
  - Nutritional assessment and counseling.