

高 雄 榮 民 總 醫 院

食道癌診療原則

2017年05月09日第一版

食道癌醫療團隊共同擬定

注意事項：這個診療準則主要作為醫師和其他保健專家診療癌症病人參考之用。假如你是一個癌症病人，直接引用這個研究資訊及診療準則並不恰當。只有你的醫師才能決定給你最恰當的治療。

修訂指引

- 本共識依下列參考資料修改版本

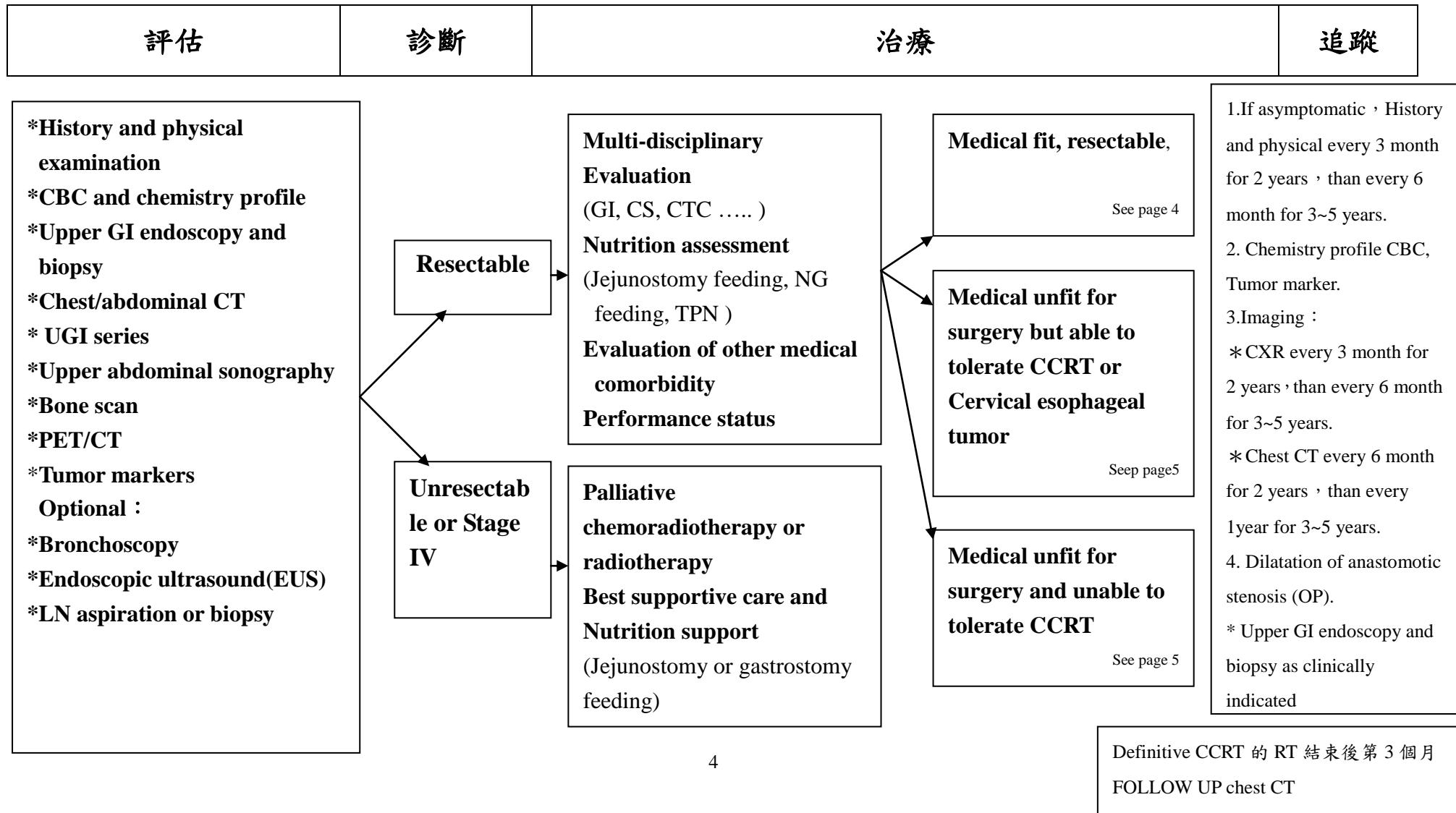
Reference: NCCN Clinical Practice Guidelines in
Oncology™, Esophageal cancer, V.1.2017

會議討論

上次會議：2016/03/22

本共識與上一版的差異

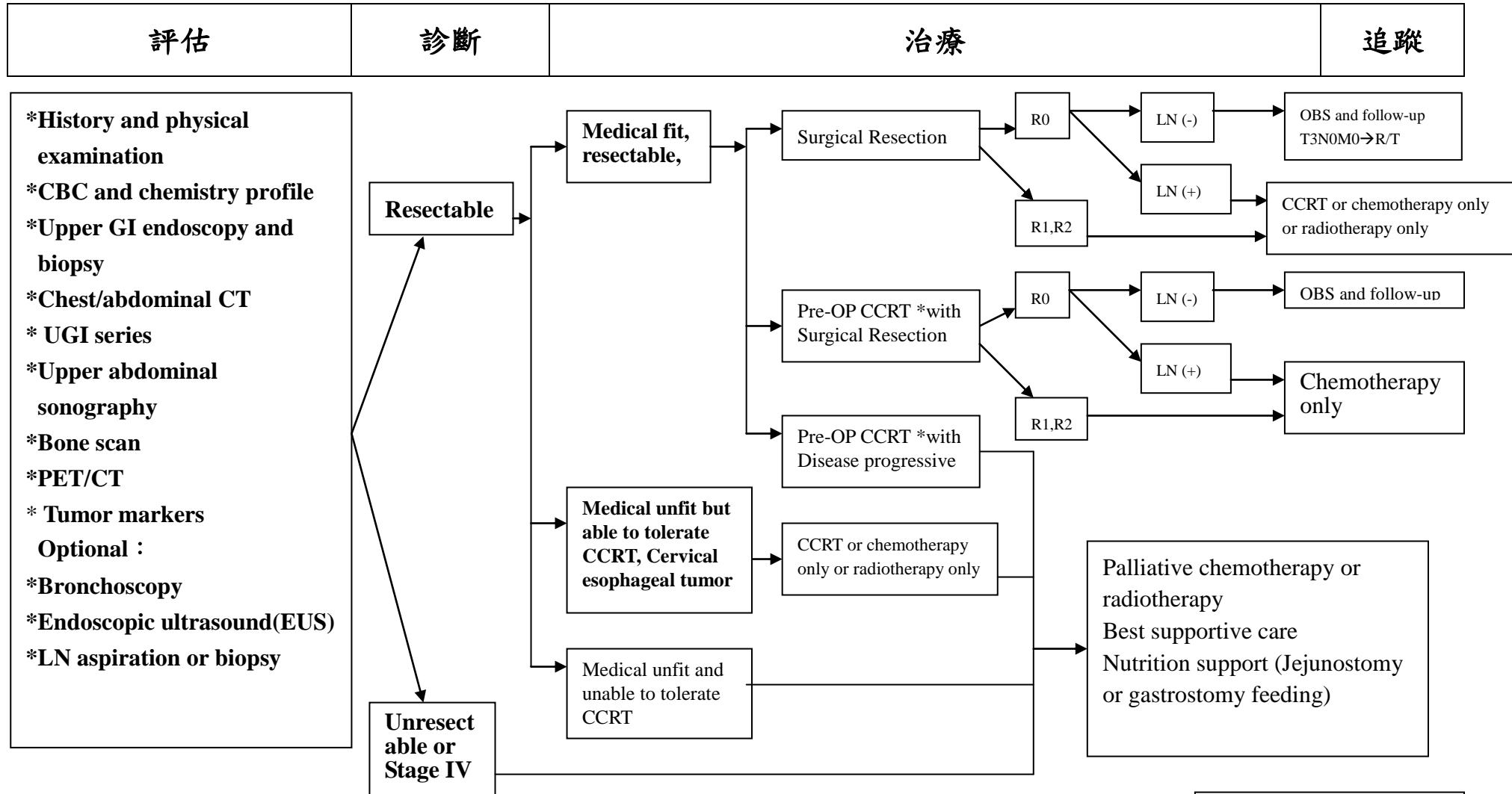
| 上一版 | 新版 |
|-----|-----------|
| | 經團隊審視無須修改 |



食道癌

高雄榮民總醫院

臨床診療指引 2017.05 第一版



* Criteria : T3-4 or N+

食道癌

高雄榮民總醫院

臨床診療指引 2017.05 第一版

評估

診斷

治療

追蹤

- *History and physical examination
- *CBC and chemistry profile
- *Upper GI endoscopy and biopsy
- *Chest/abdominal CT
- * UGI series
- *Upper abdominal sonography
- *Bone scan
- *PET/CT
- Tumor markers
Optional :
 - *Bronchoscopy
 - *Endoscopic ultrasound (EUS)
 - *LN aspiration or biopsy

Medical unfit for surgery, or
Cervical esophageal tumor

CCRT or chemotherapy
only or radiotherapy only

Medical unfit for surgery
and unable to tolerate
CCRT

Best supportive

Pre-OP CCRT * with
Disease progressive

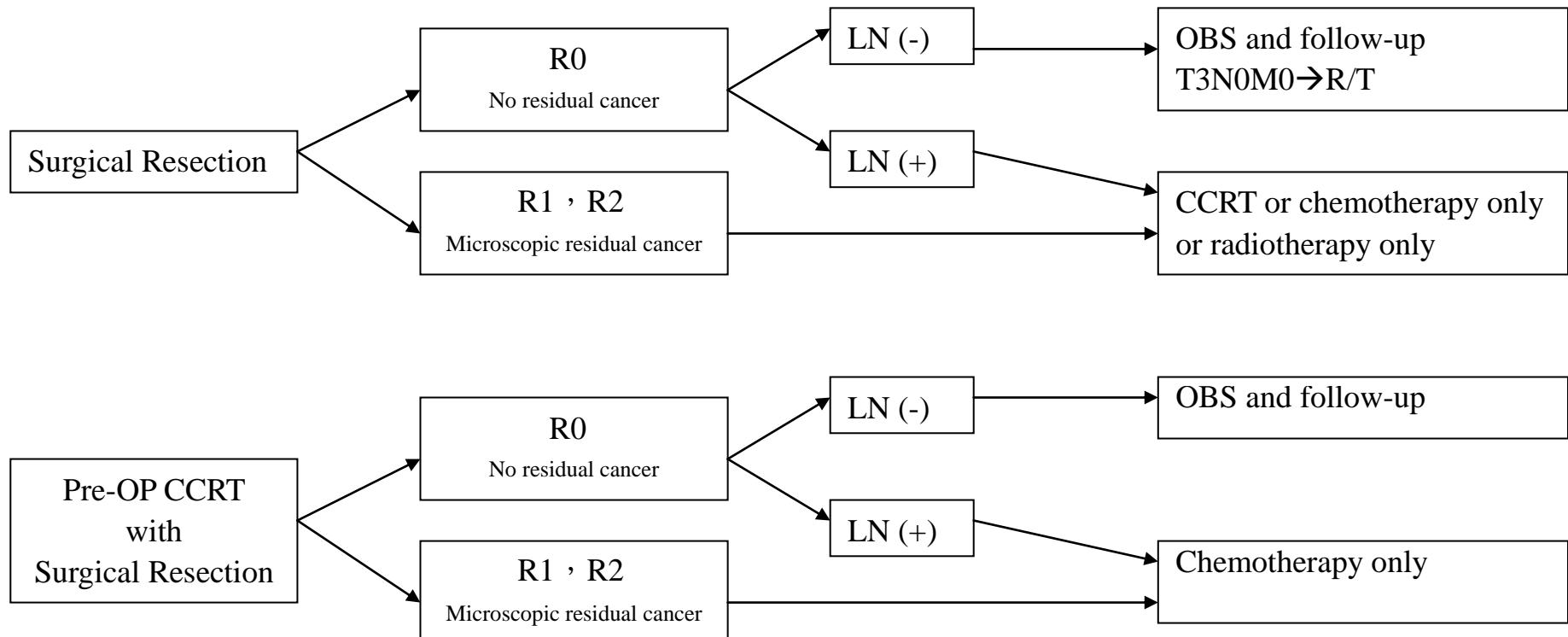
Palliative chemoradiotherapy
Best supportive care and
Nutrition support

- 1.If asymptomatic ,
History and physical
every 3 month for 2
years , than every 6
month for 3~5 years.
 2. Chemistry profile
CBC, Tumor marker.
 - 3.Imaging :
 - * CXR every 3 month
for 2 years , than every 6
month for 3~5 years.
 - * Chest CT every 6
month for 2 years , than
every 1year for 3~5
years.
- * Upper GI endoscopy
and biopsy as clinically
indicated

**Surgical outcomes after esophagectomy/
Clinical pathologic findings**

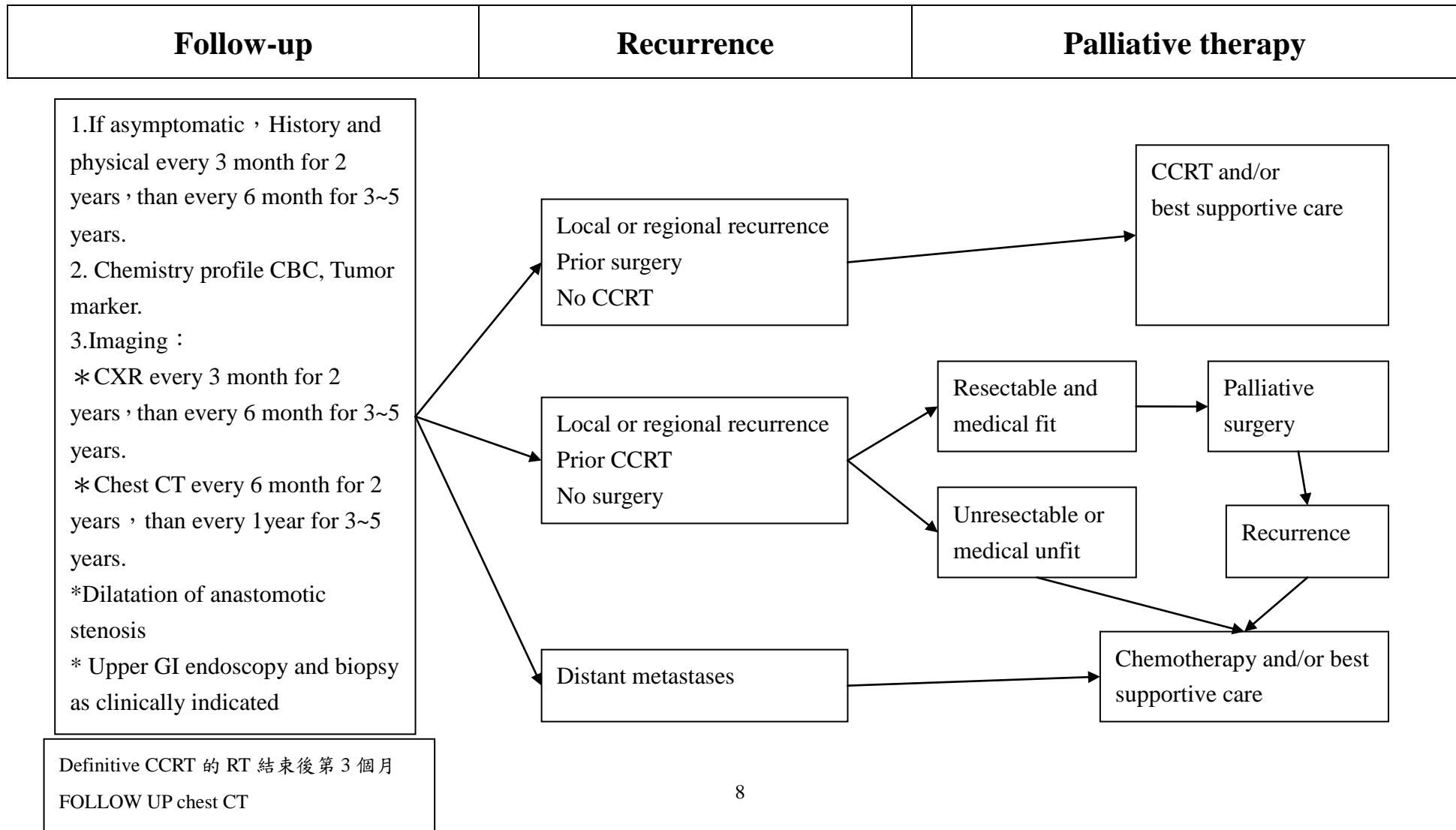
Tumor classification

Postoperative treatment



食道癌

高雄榮民總醫院
臨床診療指引 2017.05 第一版



食道癌

高雄榮民總醫院
臨床診療指引 2017.05 第一版

化學治療處方

| Published C/T regimens | Schedule | |
|---|--|---|
| Cisplatin 60-75mg/m ² , IV ,D1/ Carboplatin AUC 4-6 mg, IV ,D1 (Ccr <60) Fluorouracil, 600-1000 mg/m ² , IV ,D1-4 (Reference No.22) | Q28 D x 4-6 cycles | Performance status (ECOG)≤2 or Kamofsky Performance score≥60 |
| Cisplatin 60-75 mg/m ² , IV ,D1/ Carboplatin AUC 4-6 mg, IV ,D1 (Ccr <60) Etoposide 60-100 mg/m ² , IV ,D1-3 (Reference No.23) | Q21 D x 4-6 cycles | Performance status (ECOG)≤2 or Kamofsky Performance score≥60 |
| Taxol 140-175 mg/m ² , IV ,D1 Cisplatin 20 mg/m ² , IV ,D1-5/ Carboplatin AUC 1mg, IV ,D1-5 (Ccr <60) Fluorouracil,600-750 mg/m ² , IV ,D1-5 (Reference No.24) | Q14D x 4-6 cycles | Performance status (ECOG)≤2 or Kamofsky Performance score≥60 |
| Cisplatin 60 mg/m ² , IV ,D1/ Carboplatin AUC 4-6 mg, IV ,D1 (Ccr <60) Xeloda 2.5TAB/ m ² , PO,D1-14 (Reference No.27) | Q21 D x 4-6 cycles | Performance status (ECOG)≤2 or Kamofsky Performance score≥60 |
| Ufur 3CAP/m ² , PO,D1-14 | Q28D x6 cycles | Performance status (ECOG)≤2 or Kamofsky Performance score≥60 |
| Mitomycin 5- 7 mg/m ² , IV ,D1 Cisplatin 50-60 mg/m ² , IV ,D1/ Carboplatin AUC 4-6 mg, IV ,D1 (Ccr <60) Fluorouracil,480~600 mg/m ² , IV ,D1 (Reference No.28) | MitomycinQ42D Cisplatin Q21D 5-FU QD MCF x 4-6 cycles | Performance status (ECOG)≤2 or Kamofsky Performance score≥60 |

| | | |
|---|--|---|
| Mitomycin 5- 7 mg/m ² , IV ,D1 Cisplatin 45-60 mg/m ² , IV ,D1/ Carboplatin AUC 4-6 mg, IV ,D1 (Ccr <60) Ufur 3CAP/m ² , PO,D1-14 (Reference No.28) | MitomycinQ42D Cisplatin Q21D Ufur QD MCU x 4-6 cycles | Performance status (ECOG)≤2 or Kamofsky Performance score≥60 |
| Tarceva 150mg 1TAB, PO (Reference No.29) | QD (to disease progression) | Performance status (ECOG)≤2 or Kamofsky Performance score≥60 |

備註 【1】依據影像學檢查發現疾病 progression disease 或 【2】依據達到 Grade 3 : Severe or advance Side effect，即先停藥，再視病患情況決定繼續治療或改變處方。

食道癌

高雄榮民總醫院
臨床診療指引 2017.05 第一版

Radiotherapy (Reference No.15-21)

Dose prescription

| | |
|--|---|
| Combination with operation (Pre-operative or post operative RT) | 1.8-2 Gy, total 45-50.4 Gy, 25-28 fraction |
| Concurrent CCRT without operation | 1.8-2 Gy, total 50.4-59.4 Gy, 28-33 fractions |
| RT alone | 1.8-2 Gy, total 54-64 Gy, 27-35 fractions |

When the radiation dosage reach 45 Gy , the stomach area should be blocked.

Field design

Preoperative RT or CCRT :

GTV = primary lesion and involved LN; CTV = GTV + subclinical disease (regional LN and submucosal), 4 cm proximal/distal and 1 cm radial;
PTV = CTV + 1 – 2 cm.

Tumors above the carina: treat SCV and mediastinal LN.

Tumors at or below the carina: treat mediastinal LN, and include celiac LN for lower 1/3 and gastroesophageal junction tumors.

Postoperative RT : depended by operative findings and pathological report.

Dose limitation :

Spinal cord : Dmax \leq 46 Gy at 1.8-2 Gy/fraction

Lung : V20 (volume receiving \geq 20 Gy) < 35% 。

Heart : V40 < 50% 。

Reference :

1. NCCN Clinical Practice Guidelines in OncologyTM ,Esophageal cancer , V.1.2017.
2. Steyerberg EW, Neville BA, Kopper LB, Lemmens VE, et al. Surgical mortality in patients with esophageal cancer: development and validation of a simple risk score. *J Clin Oncol* 2006;24 (26):4277-4284.
3. Fujita H, Sueyoshi S, Yamana H, Shinozaki K et al., Optimum treatment strategy for superficial esophageal cancer: Endoscopic mucosal resection versus radical esophagectomy. *World Journal of Surgery*; 2001; 25: 424-431.
4. Ell C, May A, Gossner L, Pech O, et al., Endoscopic mucosal resection of early cancer and high-grade dysplasia in Barrett's esophagus. *Gastroenterology* 2000; 118: 670-677.
5. Conio M, Repici A, Cestari R, Blanchi S, et al., Endoscopic mucosal resection for high-grade dysplasia and intramucosal carcinoma in Barrett's esophagus: An Italian experience. *World Journal of Gastroenterology* 2005; 11(42): 6650-6655.
6. Larghi A, Lightdale CJ, Ross AS, Fedi P, et al., Long-term follow-up of complete Barrett's eradication endoscopic mucosal resection (CBE-EMR) for the treatment of high-grade dysplasia and intramucosal carcinoma. *Endoscopy* 2007;39: 1086-1091.
7. Lopes CV, Hela M, Pesenti C, Bories E, et al., Circumferential endoscopic resection of Barrett's esophagus with high-grade dysplasia or early adenocarcinoma. *Surgical Endoscopy* 2007; 21: 820-824.
8. Overholt BF, Wang KK, Burdick S, Lightdale CJ, et al., Five-year efficacy and safety of photodynamic therapy with Photofrin in Barrett's high-grade dysplasia. *Gastrointestinal Endoscopy* 2007; 66(3): 460-468.
9. de Hoyos A, Little VR, and Luketich JD. Minimally invasive esophagectomy. *Surg Clin North Am* 2005;85 (3): 631-647.
10. Hofstetter 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.
11. Swisher SG, Wynn P, Putnam JB, Mosheim MB, et al. Salvage esophagectomy for recurrent tumors after definitive chemotherapy and radiotherapy. *J Thorac Cardiovasc Surg* 2002;123:175-183.
12. Birkmeyer JD, Siewers AE, Finlayson EVA, Stukel TA, et al. Hospital volume and surgical mortality in the United States. *N Engl J Med* 2002;346(15):1128-1137.
13. Hulscher JBF, van Sandick JW, de Boer AG, et al. Extended transthoracic resection compared with limited transhiatal resection for adenocarcinoma of the esophagus. *N Engl J Med*, 2002;347(21):1662-1669
14. AJCC 7th edition

Reference for Radiotherapy :

15. Herskovic A; Martz K; al-Sarraf M et al.: Combined chemotherapy and radiotherapy compared with radiotherapy alone in patients with cancer of the esophagus. *N Engl J Med* 1992;326(24):1593-8.
16. Al-Sarraf M; Martz K; Herskovic A et al.: Progress report of combined chemoradiotherapy versus radiotherapy alone in patients with esophageal cancer: an intergroup study. *J Clin Oncol* 1997;15(1):277-84.
17. Cooper JS; Guo MD; Herskovic A et al.: Chemoradiotherapy of locally advanced esophageal cancer: long-term follow-up of a prospective randomized trial (RTOG 85-01). *Radiation Therapy Oncology Group. JAMA* 1999;281(17):1623-7.
18. Minsky BD; Pajak TF; Ginsberg RJ et al.: INT 0123 (Radiation Therapy Oncology Group 94-05) phase III trial of combined-modality therapy for esophageal cancer: high-dose versus standard-dose radiation therapy. *J Clin Oncol* 2002;20(5):1167-74.
19. Shioyama Y; Nakamura K; Sasaki T et al.: Clinical results of radiation therapy for stage I esophageal cancer: a single institutional experience. *Am J Clin Oncol* 2005;28(1):75-80.
20. Chen J; Zhu J; Pan J et al: Postoperative radiotherapy improved survival of poor prognostic squamous cell carcinoma esophagus. *Ann thorac surg* 2010;90(2):435-42
21. Chen J; Pan J; Zheng X et al: Number and location of positive nodes, postoperative radiotherapy and survival after esophagectomy with three field lymph node dissection for thoracic esophageal squamous cell carcinoma. *Int. J. Radiation Oncology Biol. Phys.* 2012; 82 (1):475–82

Reference for Chemotherapy :

22. Phase III Trial of Trimodality Therapy With Cisplatin, Fluorouracil, Radiotherapy, and Surgery Compared With Surgery Alone for Esophageal Cancer: CALGB 9781. *J Clin Oncol* 26:1086-1092.
23. Chemotherapy with cisplatin or carboplatin in combination with etoposide for small-cell esophageal cancer: a systemic analysis of case series. *Diseases of the Esophagus* 9 OCT 2013, DOI: 10.1111/dote.12149.
24. Phase II trial of paclitaxel, fluorouracil, and cisplatin in patients with advanced carcinoma of the esophagus. *JCO* 1998, 16(5),p 1826-1834.
25. Phase III Study of Docetaxel and Cisplatin Plus Fluorouracil Compared With Cisplatin and Fluorouracil As First-Line Therapy for Advanced Gastric Cancer: A Report of the V325 Study Group. *J Clin Oncol* 24:4991-4997.
26. Perioperative Chemotherapy versus Surgery Alone for Resectable Gastroesophageal Cancer. *N Engl J Med* 2006; 355:11-20.
27. Definitive Chemoradiotherapy with Capecitabine and Cisplatin in Patients with Esophageal Cancer: A Pilot Study. *J Korean Med Sci* 2009; 24:

120-5.

28. Prospective Randomized Trial Comparing Mitomycin, Cisplatin, and Protracted Venous-Infusion Fluorouracil (PVI 5-FU) With Epirubicin, Cisplatin, and PVI 5-FU in Advanced Esophagogastric Cancer. *J Clin Oncol* 20:1996-2004.
29. A Phase 2 Trial of Erlotinib in Patients With Previously Treated Squamous Cell and Adenocarcinoma of the Esophagus. *Cancer* 2011;117:1409-14.
30. Common Terminology Criteria for Adverse Events (CTCAE) Version 4.0 Published: May 28, 2009 (v4.03: June 14, 2010) U.S.DEPARTMENT OF HEALTH AND HUMAN SERVICES. National Institutes of Health National Cancer Institute.

附件：

| DEFINITIONS OF TNM | |
|---------------------------------|---|
| Primary Tumor (T) | |
| TX | Primary tumor cannot be assessed |
| T0 | No evidence of primary tumor |
| Tis | High-grade dysplasia |
| T1 | Tumor invades lamina propria, muscularis mucosae, or submucosa |
| T1a | Tumor invades lamina propria or muscularis mucosae |
| T1b | Tumor invades submucosa |
| T2 | Tumor invades muscularis propria |
| T3 | Tumor invades adventitia |
| T4 | Tumor invades adjacent structures |
| T4a | Resectable tumor invading pleura, pericardium, or diaphragm |
| T4b | Unresectable tumor invading other adjacent structures, such as aorta, vertebral body, trachea, etc. |
| Regional Lymph Nodes (N) | |
| NX | Regional lymph nodes cannot be assessed |
| N0 | No regional lymph node metastasis |
| N1 | Metastasis in 1-2 regional lymph nodes |
| N2 | Metastasis in 3-6 regional lymph nodes |
| N3 | Metastasis in seven or more regional lymph nodes |
| Distant Metastasis (M) | |
| M0 | No distant metastasis |
| M1 | Distant metastasis |

| ANATOMIC STAGE/PROGNOSTIC GROUPS | | | | | |
|--|-------------------|-------------------|----------------|-------------------|---------------------------|
| Squamous Cell Carcinoma (Figure 10.6) | | | | | |
| Stage | T | N | M | Grade | Tumor Location |
| 0 | Tis (HGD) | N0 | M0 | 1, X | Any |
| IA | T1 | N0 | M0 | 1, X | Any |
| IB | T1 T2-3 | N0 N0 | M0 M0 | 2-3 1, X | Any Lower, X |
| IIA | T2-3 T2-3 | N0 N0 | M0 M0 | 1, X 2-3 | Upper, middle Lower, X |
| IIB | T2-3 T1-2 | N0 N1 | M0 M0 | 2-3 Any | Upper, middle Any |
| IIIA | T1-2 T3 T4a | N2 N1 N0 | M0 M0 M0 | Any Any Any | Any Any Any |
| IIIB | T3 | N2 | M0 | Any | Any |
| IIIC | T4a T4b Any | N1-2 Any N3 | M0 M0 M0 | Any Any Any | Any Any Any |
| IV | Any | Any | M1 | Any | Any |

Or mixed histology including a squamous component or NOS.

Location of the primary cancer site is defined by the position of the upper (proximal) edge of the tumor in the esophagus.

Adenocarcinoma (Figure 10.7)

| Stage | T | N | M | Grade |
|--------------|-----------|----------|----------|--------------|
| 0 | Tis (HGD) | N0 | M0 | 1,X |
| IA | T1 | N0 | M0 | 1-2, X |
| IB | T1 | N0 | M0 | 3 |
| | T2 | N0 | M0 | 1-2, X |
| IIA | T2 | N0 | M0 | 3 |
| IIB | T3 | N0 | M0 | Any |
| | T1-2 | N1 | M0 | Any |
| IIIA | T1-2 | N2 | M0 | Any |
| | T3 | N1 | M0 | Any |
| | T4a | N0 | M0 | Any |
| IIB | T3 | N2 | M0 | Any |
| IIIC | T4a | N1-2 | M0 | Any |
| | T4b | Any | M0 | Any |
| | Any | N3 | M0 | Any |
| IV | Any | Any | M1 | Any |

| | |
|---------------------------|--|
| T | Tis high-grade dysplasia T1 lamina propria, muscularis mucosae, or submucosa T1a lamina propria or muscularis mucosae T1b submucosa T2 muscularis propria T3 adeventitia T4 adjacent structures T4a resectable tumor invading pleura, pericardium, or diaphragm T4b unresectable tumor invading other adjacent structures, such as aorta, vertebral body, trachea, etc. |
| N | N0 0 No regional lymph node metastasis N1 1-2 positive regional lymph nodes N2 3-6 positive regional lymph nodes N3 \geq 7 positive regional lymph nodes |
| M | M0 no distant metastasis M1 distant metastasis |
| Cell type | Squamous cell carcinoma ; Adenocarcinoma |
| Grade of histology | G1 well differentiated G2 moderately differentiated G3 poorly differentiated G4 Undifferentiated |
| Location of cancer | Proximal tumor margin (for squamous cell carcinoma only) Upper thoracic 15~24 cm Middle thoracic 24~32 cm Lower thoracic 32~40 cm Esophago-gastric junction : epicenter in esophagus, e-g junction, or within proximal 5 cm of the stomach |

Staging of esophageal carcinoma(AJCC 7th)

Stage grouping: Squamous cell carcinoma(AJCC 7th)

| Stage | T | N | M | G | Location |
|--------------|----------|----------|----------|----------|-----------------|
| 0 | is | 0 | 0 | 1 | Any |
| IA | 1 | 0 | 0 | 1 | Any |
| IB | 1 | 0 | 0 | 2-3 | Any |
| | 2-3 | 0 | 0 | 1 | Lower |
| IIA | 2-3 | 0 | 0 | 1 | U / M |
| | 2-3 | 0 | 0 | 2-3 | Lower |
| IIB | 2-3 | 0 | 0 | 2-3 | U / M |
| | 1-2 | 1 | 0 | Any | Any |
| IIIA | 1-2 | 2 | 0 | Any | Any |
| | 3 | 1 | 0 | Any | Any |
| | 4a | 0 | 0 | Any | Any |
| IIIB | 3 | 2 | 0 | Any | Any |
| IIIC | 4a | 1-2 | 0 | Any | Any |
| | 4b | Any | 0 | Any | Any |
| | Any | 3 | 0 | Any | Any |
| IV | Any | any | 1 | Any | Any |

Stage of grouping: Adenocarcinoma(AJCC 7th)

| Stage | T | N | M | G |
|--------------|----------|----------|----------|----------|
| 0 | is | 0 | 0 | 1 |
| IA | 1 | 0 | 0 | 1-2 |
| IB | 1 | 0 | 0 | 3 |
| | 2 | 0 | 0 | 1-2 |
| IIA | 2 | 0 | 0 | 3 |
| IIB | 3 | 0 | 0 | Any |
| | 1-2 | 1 | 0 | Any |
| IIIA | 1-2 | 2 | 0 | Any |
| | 3 | 1 | 0 | Any |
| | 4a | 0 | 0 | Any |
| IIIB | 3 | 2 | 0 | Any |
| IIIC | 4a | 1-2 | 0 | Any |
| | 4b | Any | 0 | Any |
| | Any | 3 | 0 | Any |
| IV | Any | Any | 1 | Any |