

高雄榮民總醫院

食道癌診療原則

2019年05月28日 第二版

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, Version 1.2019

會議討論

上次會議：2019/01/22

本共識與上一版的差異

上一版	新版
<p>1. 原化療處方有：Cisplatin/Carboplatin + 5-FU、Cisplatin/Carboplatin+Etoposide、Taxol+ Cisplatin/Carboplatin+ 5-FU、Cisplatin + Capecitabine、MCF(Mitomycin + CDDP + 5-FU)、MCF(mitomycin+cisplatin+UFUR)、Ramucirumab + Paclitaxel、Ramucirumab only、Ufur oral Tarceva、Afatinib、TS-1。</p> <p>2. 原有化學治療處方，無其他治療處方分類。</p>	<p>1. 新增治療處方： keytruda(Page 11) CCRT with cisplatin (Page 12)</p> <p>2. 分類出標靶治療處方、免疫治療處方及放射治療處方 (Page 11-12)</p>

食道癌(總表)

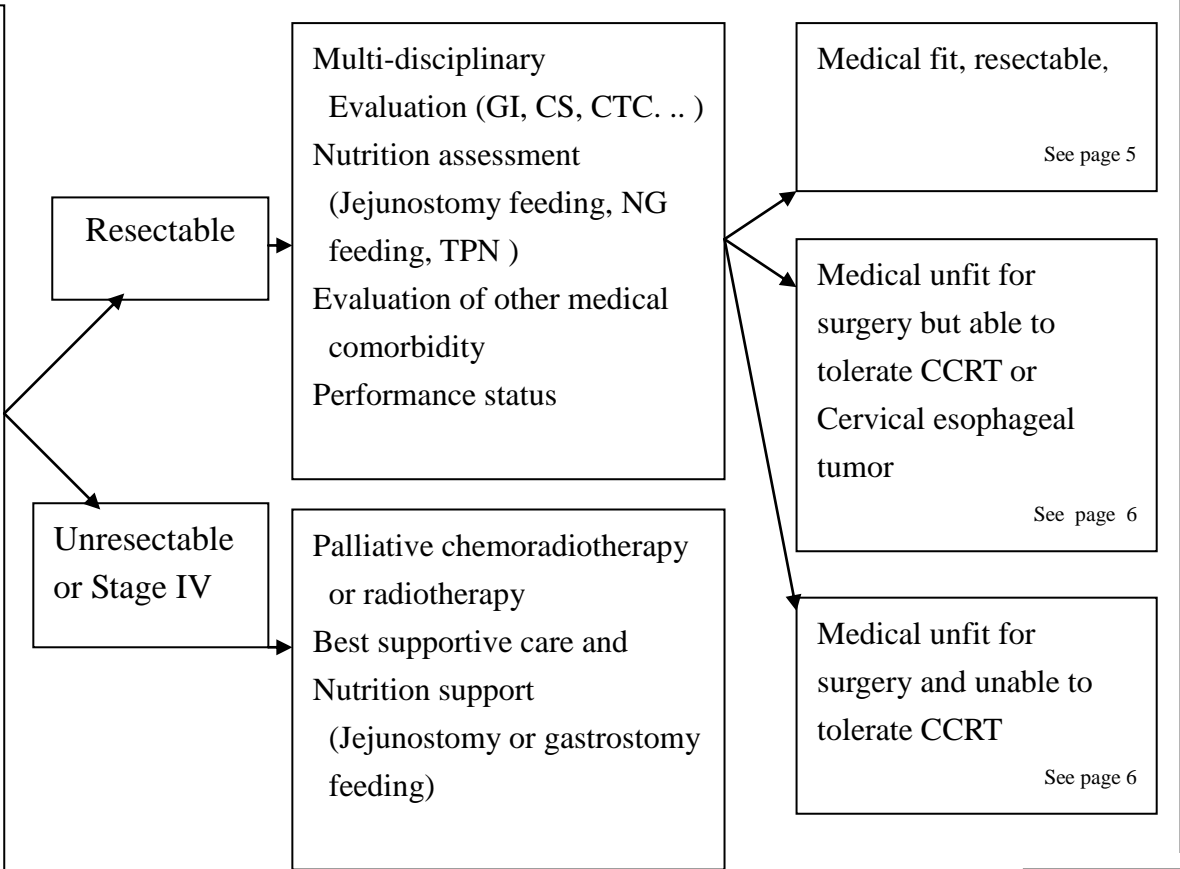
高雄榮民總醫院

臨床診療指引 2019.05 第二版

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
 Tumor markers
Optional :
 PET/CT
 Bronchoscopy
 Endoscopic ultrasound(EUS)
 LN aspiration or biopsy

與期別相關之主要檢查



- 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 1 year for 3~5 years.
4. Dilatation of anastomotic stenosis (OP).
5. Upper GI endoscopy and biopsy as clinically indicated

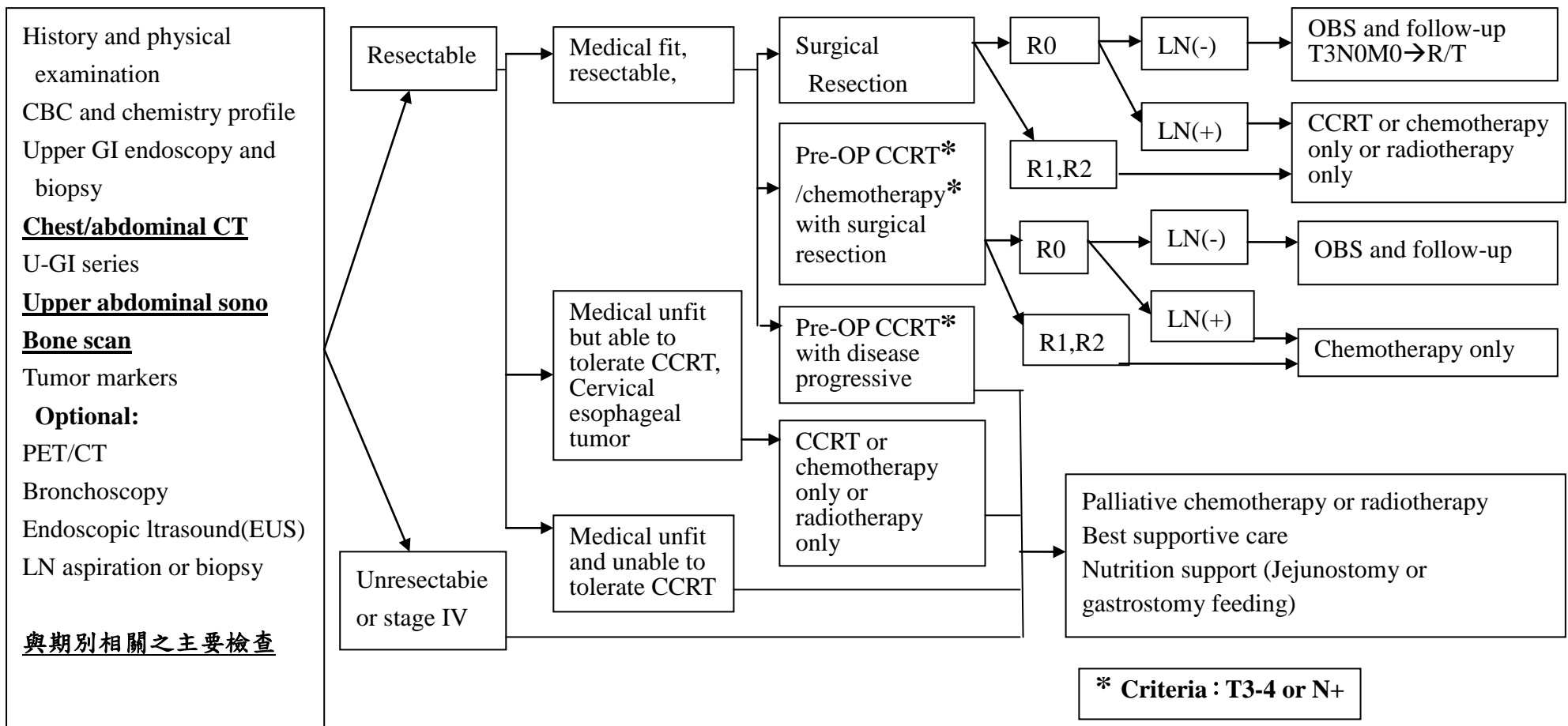
Definitive CCRT 的 RT 結束後第 3 個月
 FOLLOW UP chest CT

食道癌

高雄榮民總醫院

臨床診療指引 2019.05 第二版

評估	診斷	治療
----	----	----

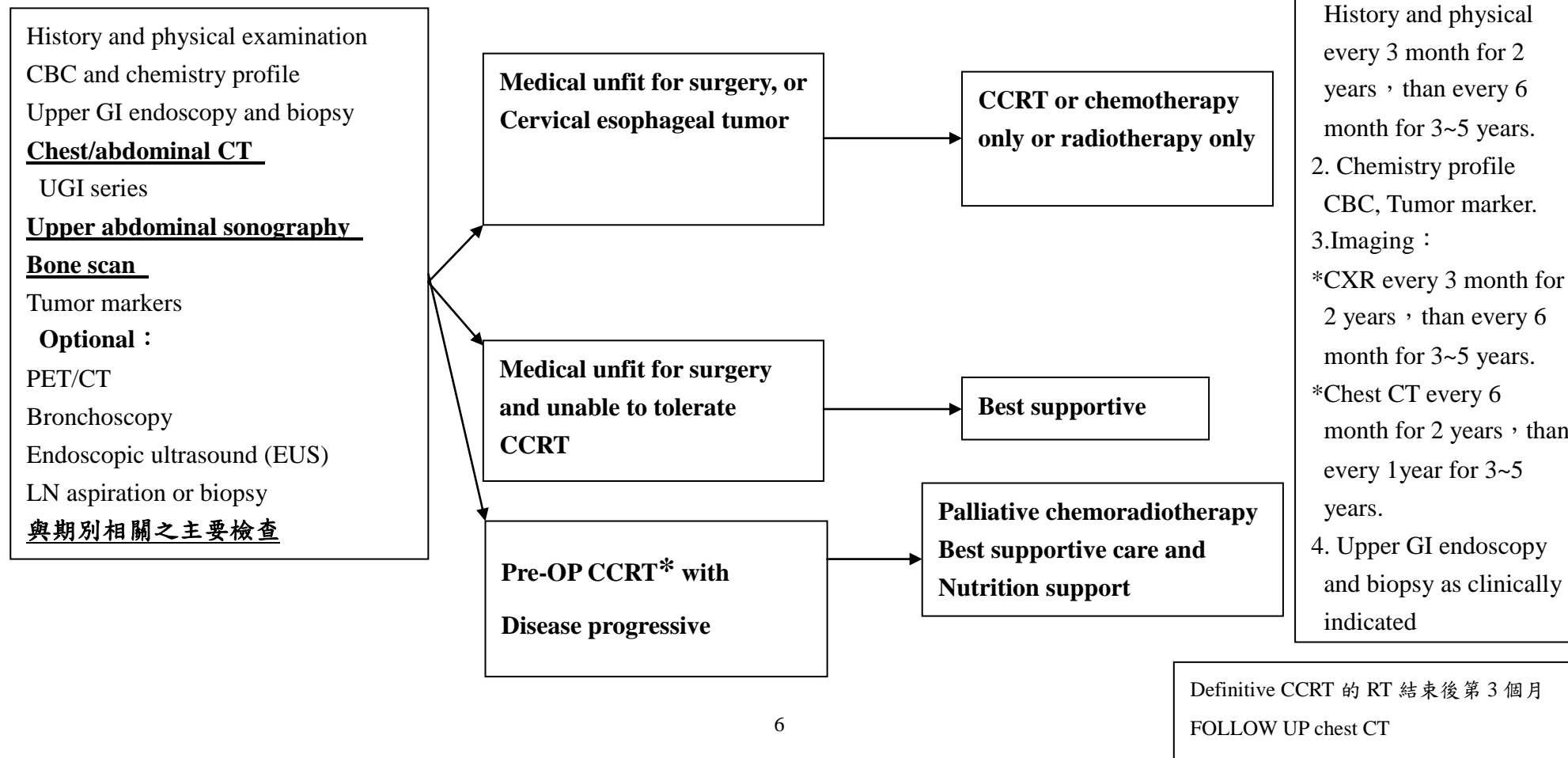


食道癌

高雄榮民總醫院

臨床診療指引 2019.05 第二版

評估	診斷	治療	追蹤
----	----	----	----

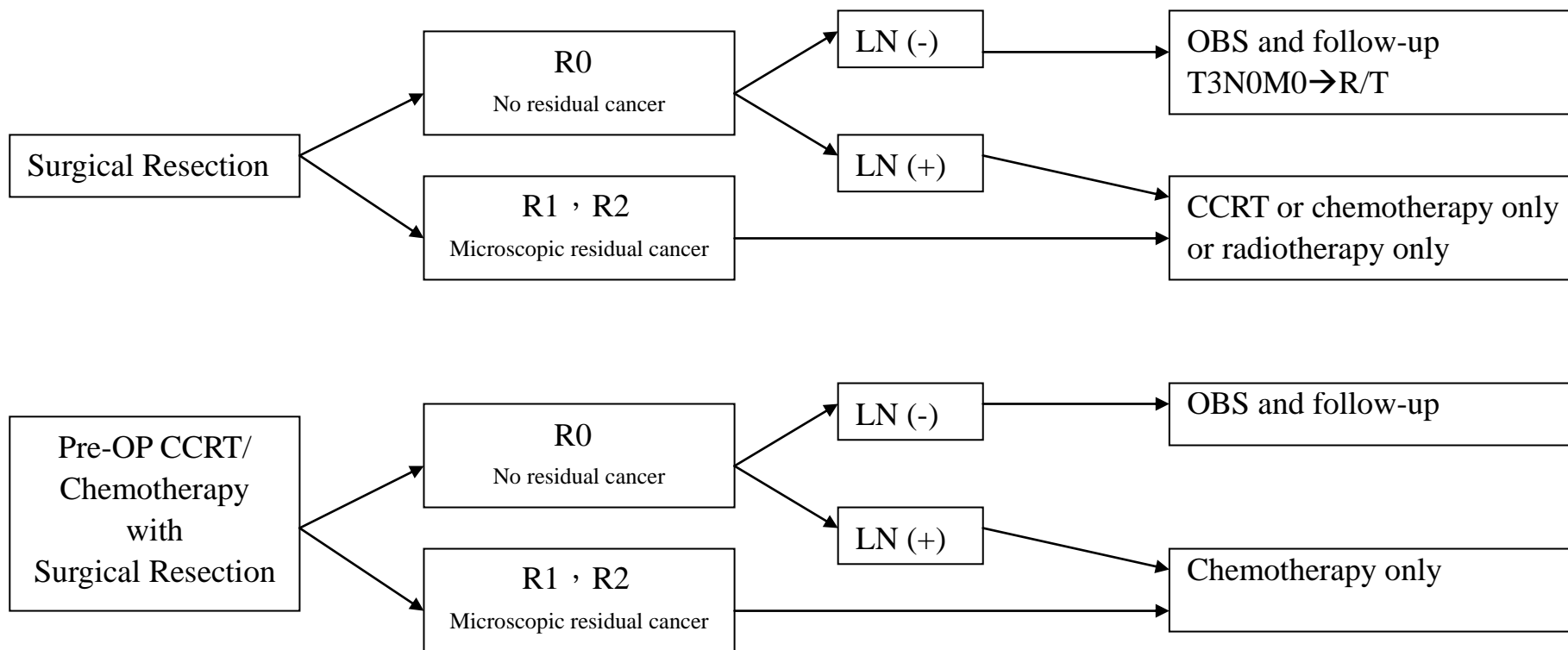


食道癌

高雄榮民總醫院

臨床診療指引 2019.05 第二版

Surgical outcomes after esophagectomy/ Clinical pathologic findings	Tumor classification	Postoperative treatment
------------------------------------------------------------------------	----------------------	-------------------------



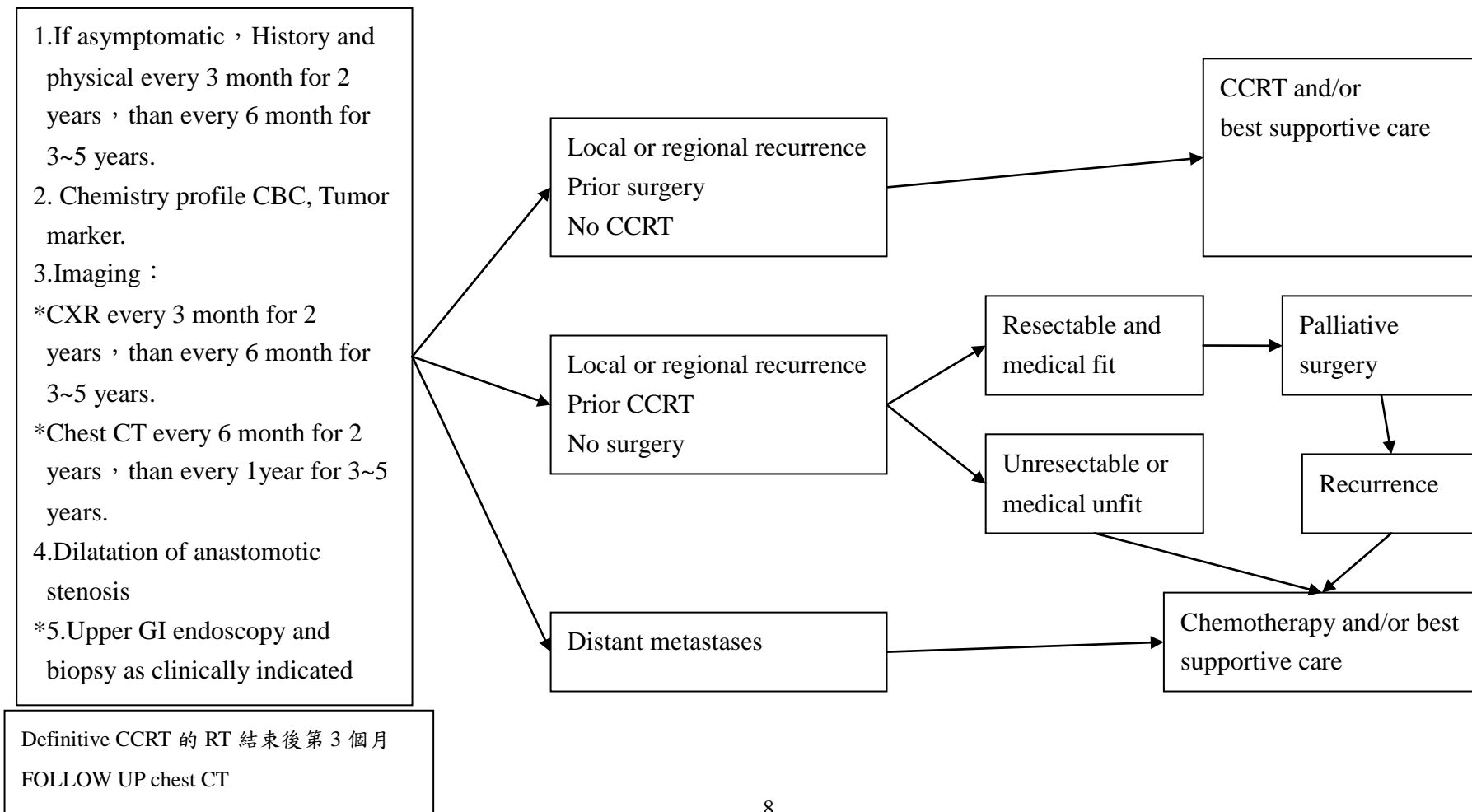
* Criteria : T3-4 or N+

食道癌

高雄榮民總醫院

臨床診療指引 2019.05 第二版

Follow-up	Recurrence	Palliative therapy
-----------	------------	--------------------



食道癌

高雄榮民總醫院

臨床診療指引 2019.05 第二版

化學治療處方

Neoadjuvant/Adjuvant/CCRT/Metastasis	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)	Q28D 4-6 cycles	Performance status (ECOG) ≤ 2 or Kamofsky Performance score ≥ 60
Taxol 160-200 mg/m ² , IV ,D1 Cisplatin 60-80 mg/m ² , IV ,D1 / Carboplatin AUC 4-6mg, IV ,D (Ccr <60) (Reference No.38)	Q21D 4-6 cycles	Performance status (ECOG) ≤ 2 or Kamofsky Performance score ≥ 60
Docetaxel 60-85mg/m ² , IV ,D1 Cisplatin 60-85mg/m ² , IV ,D1 / Carboplatin AUC4-6 mg, IV ,D1 (Ccr <60) (Reference No.31)	Q21D x 4-6 cycles	Performance status (ECOG) ≤ 2 or Kamofsky Performance score ≥ 60

Docetaxel 60-75mg/m ² , IV ,D1 Cisplatin 60-75mg/m ² , IV ,D1 / Carboplatin AUC4-6 mg, IV ,D1 (Ccr <60) Fluorouracil ,600-750 mg/m ² , IV ,D1-5 / Fluorouracil,800-1200 mg/m ² , IV ,D1-3 (Reference No.26,33)	Q21D x 4-6 cycles	Performance status (ECOG) ≤ 2 or Kamofsky Performance score ≥ 60
Gemzar 1000mg/m ² , IV ,D1.8 (Reference No.32)	Q21~28D 4-6 cycles	Performance status (ECOG) ≤ 2 or Kamofsky Performance score ≥ 60
Gemzar 800-1000mg/m ² , IV ,D1.8 Cisplatin 60-80mg/m ² , IV ,D1 / Carboplatin AUC4-6 mg, IV ,D1 (Ccr <60) (Reference No.32)	Q21~28D 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
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 /d, IV (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
Ufur 3CAP/m ² , PO,D1-14 (Reference No.39)	QD x1year	Performance status (ECOG) ≤ 2 or Kamofsky Performance score ≥ 60
TS-1 (BSA >1.5) 120mg/day, PO BID, D1-28 TS-1 (BSA 1.25-1.5) 100mg/day, PO BID, D1-28 (吃四週休二週或吃二週休一週) (Reference No.37)	Q42D x1year	Performance status (ECOG) ≤ 2 or Kamofsky Performance score ≥ 60

食道癌

高雄榮民總醫院
臨床診療指引 2019.05 第二版

標靶治療處方

Ramucirumab 8 mg/kg, IV, D1 (Reference No.34)	Q14D	Performance status (ECOG) \leq 2 or Kamofsky Performance score \geq 60
Ramucirumab (8 mg/kg, IV, D1, D15) Paclitaxel (50~80 mg/m ² , IV, D1, D8, D15) (Reference No.35)	Q28D	Performance status (ECOG) \leq 2 or Kamofsky Performance score \geq 60
Tarceva 150mg 1TAB, PO, QD (Reference No.29)	QD until disease progression	Performance status (ECOG) \leq 2 or Kamofsky Performance score \geq 60
Afatinib 40mg/day, PO, QD (Reference No.36)	QD until disease progression	Performance status (ECOG) \leq 2 or Kamofsky Performance score \geq 60

免疫治療處方

Keytruda 2mg/kg ,IV, D1 (Reference No.39)	Q21D until disease progression	Performance status (ECOG) \leq 2 or Kamofsky Performance score \geq 60
-----------------------------------------------------	-----------------------------------	-------------------------------------------------------------------------------

食道癌

高雄榮民總醫院
臨床診療指引 2019.05 第二版

放射治療處方

CCRT with weekly cisplatin 30mg/M2,IV,D1 (old age, Cr >1.5) (Reference No.40)	QW x4-6 cycles	Performance status (ECOG) ≤ 2 or Kamofsky Performance score ≥ 60
CCRT with weekly cisplatin 40mg/M2,IV,D1 (Reference No.40)	QW x4-6 cycles	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 2019.05 第二版

Radiotherapy (Reference No.15-21)

Dose prescription

Combination with operation (Pre-operative or post operative RT)	1.8-2 Gy, total 40-54 Gy
Concurrent CCRT without operation	1.8-2 Gy, total 50-66 Gy
RT alone	1.8-2 Gy, total 54-66 Gy

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

Field design

Preoperative RT or CCRT :

GTV = primary and involved regional nodes; CTV for primary = GTV + 3-4 cm proximal/distal and 1 cm radial, CTV for involved nodes includes 0.5-1.5 cm margin, CTV for elective nodes depends on location of primary; PTV = CTV + 0.5-1 cm.

Postoperative RT : depended by operative findings and pathological report.

Dose limitation :

Spinal cord : $D_{max} \leq 46$ Gy at 1.8-2 Gy/fraction

Lung : $V_{20} \leq 25\%$, $V5 \leq 50\%$ 。

Heart : $V_{40} \leq 33-50\%$, $Mean \leq 32\%$ 。

Reference :

1. NCCN Clinical Practice Guidelines in Oncology™, Esophageal cancer , V.1.2019.
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, Litle 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.
31. Jin YK, Young RD, Keon UP, et al. A multi-center phase II study of docetaxel plus cisplatin as first-line therapy in patients with metastatic squamous cell esophageal cancer: *Cancer Chemotherapy and Pharmacology*. May 2010, Volume 66, Issue 1, pp31–36.
32. Wang M, Gu J, Wang HX, Wu MH, Li YM, Wang YJ. Retrospective study of gemcitabine based chemotherapy for unresectable or recurrent esophagus squamous cell carcinoma refractory to first line chemotherapy. *Asian Pac J Cancer Prev*. 2012;13(8):4153-6.
33. NCCN Guidelines Esophageal and Esophagogastric Junction Cancers. Version 3.2015
34. Charles S Fuchs et al. Ramucirumab monotherapy for previously treated advanced gastric or gastro-oesophageal junction adenocarcinoma (REGARD): an international, randomised, multicentre, placebo-controlled, phase 3 trial. *The Lancet*. 2014;383(9911):1-98
35. Hansjochen Wilke et al. Ramucirumab plus paclitaxel versus placebo plus paclitaxel in patients with previously treated advanced gastric or gastro-oesophageal junction adenocarcinoma (RAINBOW): a double-blind, randomised phase 3 trial. *Lancet Oncol* 2014;15(11):1224–35.
36. Wong CH, Ma BBY, Hui CWC, Tao Q, Chan ATC. Preclinical evaluation of afatinib (BIBW2992) in esophageal squamous cell carcinoma (ESCC). *Am J Cancer Res*. 2015 Nov 15;5(12):3588-99.
37. Masashi Tamaoki¹, Yasumasa Ezoe¹, Ikuo Aoyama¹ et al. S-1 Salvage Chemotherapy for Esophageal Squamous Cell Carcinoma Refractory to the Standard Chemotherapy. *J Cancer Sci Ther* 2017,9:3.
38. Zhang X, Shen L, Li J, Li Y, Li J, Jin M. A phase II trial of paclitaxel and cisplatin in patients with advanced squamous-cell carcinoma of the esophagus. *Am J Clin Oncol*. 2008 Feb;31(1):29-33
39. Tsukuda M, Miyake H. Maintenance chemotherapy with UFT for head and neck carcinoma. *Oncology* 2000;14(Suppl 9):93–5
40. Bhandari V1. Role of concurrent chemoradiation in inoperable carcinoma esophagus: a prospective study. *J Cancer Res Ther*. 2014 Jan-Mar; 10(1): 11-4.