Clinical practice guidelines have been developed after multi-disciplinary consensus based on best available literature. As the name suggests, these are to be used as a guide only. These guidelines do not replace Physician judgment which is based on multiple factors including, but not limited to, the clinical and social scenario, comorbidities, performance status, age, available resources and funding considerations.

Participating in clinical trials is encouraged when available.

A. ASSESSMENT & INVESTIGATIONS

- History and physical examination.
- CT scan of chest and abdomen
- Endoscopic examination (indicating the location of the tumor from the incisors, length of the tumor, nature of tumor ie polypoid, exophytic, ulcerated, extension into the stomach, percentage of circumference involved)
- Biopsy (Her2/neu overexpression in patients with adenocarcinoma of gastro-esophageal junction with distant metastasis.)

If there is a consideration for multimodality therapy further imaging studies may be required for T and N staging

- Endoscopic ultrasound examination (EUS)
- MRI for T staging and invasion of adjacent structures
- PET/CT scan
- Diagnostic laparoscopy for GE adenocarcinoma
- Bronchoscopy for lesions above the carina.
- Nutritional evaluation.

B. TREATMENT

B1. T1/2, N0, M0 (GOOD PERFORMANCE STATUS)

- Surgery alone is the treatment of choice.
- Definite chemoradiation therapy can be considered in medically unfit patients for surgery or if patient decline surgery or in patients with squamous cell carcinoma of cervical esophagus (Cisplatin /5FU ×2 cycles concurrent with radiation followed by 2 more cycles of chemotherapy. Radiation doses range from 45 -50.4 Gy /25-28 fractions). Higher radiation dose to be considered for squamous cell cancer of cervical esophagus.
• Radical radiation alone to a dose of 54-60Gy in 1.8 to 2Gy/# may be considered in selected patients refusing or medically unfit for surgery and chemotherapy.

B2. (Selected T2)/ T3/T4, N0/N+, M0 (GOOD PERFORMANCE STATUS)

Multimodality therapy is preferred in patients with ≥ stage 2 esophageal cancers.

• Preoperative chemoradiation can be considered in eligible patients (cisplatin/5FU and external RT doses of 45-50.4 Gy in 25–28 fractions followed by surgery in 4-6 weeks or weekly carboplatin/paclitaxel and RT (doses of 41.4 Gy in 23 fractions or 45 -50.4 Gy in 25 -28 fractions followed by surgery in 4-6 weeks).

• For adenocarcinoma of the gastro-esophageal junction and distal esophagus preoperative chemoradiation with ECF/ECX for 3 cycles followed by surgery followed by 3 cycles of chemotherapy can be considered if chemoradiation is not a consideration.

• In selected patients with esophageal cancer 2 cycles chemotherapy with Cisplatin/5FU followed by surgery in 4-6 weeks’ time can be considered.

• Definite chemoradiation therapy can be considered in medically unfit patients for surgery or if patient decline surgery or in patients with squamous cell carcinoma of cervical esophagus (Cisplatin /5FU ×2 cycles concurrent with radiation followed by 2 more cycles of chemotherapy. Radiation doses range from 45 -50.4 Gy /25-28 fractions). Higher radiation dose to be considered for Squamous cell Cancer of cervical esophagus.

• Radical radiation alone to a dose of 54-60Gy in 1.8 to 2Gy/# may be considered in selected patients refusing or medically unfit for surgery and chemotherapy

B3. T1-T4, N0/N+, M0 (POOR PERFORMANCE STATUS)

• Palliative radiotherapy (40Gy/ 16#, 36Gy/12 #, 30Gy/10#, 20Gy/5#, 8Gy/1#).

• Palliative chemotherapy.

• Best supportive care.

• Palliative stenting for relief of dysphagia.

• Intra-luminal brachytherapy may be considered in selected patients.

B4. ADJUVANT THERAPY AFTER SURGERY (PROXIMAL, MID AND DISTAL ESOPHAGUS)

• Currently no randomize clinical trial is available to answer the question if adjuvant therapy offers any benefit in this group of patients. In selected group of patients this option could be considered after discussion with the multidisciplinary tumor group.

B5. ADJUVANT THERAPY AFTER SURGERY (GASTRO-ESOPHAGEAL JUNCTION ADENOCARCINOMA)

• pT2-T3-T4, or node positive disease or R1 resection: Adjuvant chemoradiation in patients with good performance status.
B6. METASTATIC DISEASE (M+)

Palliative chemotherapy (Combination of chemotherapy can be considered in patients with good performance status).

- **1**\(^{\text{st}}\) Line combination therapy – Cisplatin/5FU, ECF, ECX, EOX, or DCF
  - Cisplatin /5FU/Herceptin in adenocarcinoma of GE junction.
- **2**\(^{\text{nd}}\) line – There is no standard chemo regimen. Taxanes (docetaxel or paclitaxel) or irinotecan alone or in combination with 5FU (FOLFIRI) can be considered in patients with good performance status.

- Palliative radiotherapy (40Gy/16#, 36Gy/12#, 30Gy/10#, 20Gy/5#, 8Gy/1#).
- Best supportive care.
- Palliative stenting for relief of dysphagia.
- Intra-luminal brachytherapy may be considered in selected patients.

C. FOLLOW-UP

- In patients treated with curative intent history and physical examination every 3–6 months for the first 3 years then every 6–12 months for the next 2 years and annually thereafter.
- Imaging studies, endoscopic examination, and laboratory testing as clinically indicated.

D. APPENDIX (CHEMOTHERAPY REGIMENS)

D1. Preop Chemotherapy alone (Esophagus)

1. Cisplatin 80mg/m\(^2\) Day1, 5FU 1000 mg/m\(^2\) Day1-4 continuous infusion (q 21 Days x 2 cycles).

D2. Preop Chemotherapy alone (Lower Esophageal/GE junction adenocarcinoma)

1. Epirubicin 50mg/m\(^2\), Cisplatin 60mg/m\(^2\), 5FU 200 mg/m\(^2\) CVI (q 21 Days x 3 cycles Pre/Post op).
2. Epirubicin 50mg/m\(^2\), Cisplatin 60mg/m\(^2\), Capecitabine 625mg/m\(^2\) continuous (q 21 Days x 3 cycles Pre/Post op).

D3. Preop Chemo Radiation

1. Cisplatin 75mg/m\(^2\) D1 or 25mg/m\(^2\) D1-3, 5FU 1000 mg/m\(^2\) D1-4 (2 cycles Week 1+5 with RT)
2. Carboplatin AUC2, Taxol 50mg/m\(^2\) (weekly for 5 weeks with RT)

D4. Definitive Chemoradiotherapy (Esophagus)

1. Cisplatin 75mg/m\(^2\) D1 or 25mg/m\(^2\) D1-3, 5FU 1000 mg/m\(^2\) D1-4 (2 cycles Week 1+5 with RT, 2 more cycles 3 weekly to start 3 weeks after radiation). Capecitabine can be substituted for 5FU.
D5. Adjuvant ChemoRT for GE junction Adenocarcinoma
Chemotherapy, 5FU 425mg/m² IV Day 1-5, Folinic Acid 20mg/m² IV Day 1-5 →
RT to start on Day1 of week 5. (RT dose is 45GY in 25 Fractions)

*Week 1 of ChemoRT:* 5FU 400mg/m² IV Day 1-4, Folinic Acid 20mg/m² IV Day 1-4.

*Week 5 of ChemoRT:* 5FU 400mg/m² IV Day 1-3, Folinic Acid 20mg/m² IV Day 1-3

*4 weeks following RT:* Further 2 cycles of every 28 days
5FU 425mg/m² IV Day 1-5, Folinic Acid 20mg/m² IV Day 1-5.

Alternatively continuous infusion 5FU 200 to 250mg/m²/day during the whole duration of radiation therapy can be considered.

D6. Palliative chemotherapy
1. Epirubicin 50mg/m², Cisplatin 60mg/m², 5FU 200 mg/m² CVI (q21 Days, up to 6 cycles).
2. Epirubicin 50mg/m², Cisplatin 60mg/m², Capecitabine 625mg/m² continuous (q21 Days, up to 6 cycles).
3. Cisplatin 75mg/m² D1 or 25mg/m² D1-3, 5FU 1000 mg/m² D1-4 (q21 Days, up to 6 cycles)
4. Cisplatin 80 mg/m² D1, 5FU 800mg/m² D1-5 CVI, Herceptin 8mg/kg LD after 6 cycles if no progression, Herceptin 6mg/kg MD (q21 Days, up to 6 cycles. Herceptin can be continued after 6 cycles if no progression).
Capecitabine can be substituted for 5FU. If poor PFS or reduced Creatinine clearance, consider Carboplatin instead of Cisplatin.

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E. REFERENCES


Additional resources

www.nccn.org

www.cancer.gov

http://www.bccancer.bc.ca

http://www.cancercare.on.ca