

# Saudi Oncology Society clinical management guideline series

## *Esophageal cancer 2014*

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A total of 123 cases of esophageal cancer have been diagnosed in Saudi Arabia in 2010 accounting for 1.25% of all cancers for that year.<sup>1</sup> The age standardized rate was 1.4/100,000 for males and 1/100,000 for females.<sup>1</sup>

A committee of experts in the medical and surgical treatment of esophageal cancer was established under the supervision of the SOS.

The evidence adopted in these guidelines is rated at 3 levels: 1) Evidence level-1 (EL-1) (highest level) evidence from phase III randomized trials or meta-analyses, 2) EL-2 (intermediate-level) evidence from good phase II trials or phase III trials with limitations, and 3) EL-3 (low-level) from retrospective or observational data and/or expert opinion. This easy-to-follow grading system is convenient for the reader and allows accurate assessment of the applicability of the guidelines in individual patients.<sup>2</sup>

All esophageal cancer cases are preferably seen or discussed in a multidisciplinary form.

### 1. Pre-treatment evaluation:

- 1.1. Clinical examination
  - 1.2. Blood count
  - 1.3. Barium swallow
  - 1.4. Upper gastrointestinal (GI) endoscopy and biopsy. Multiple biopsies are preferred.
  - 1.5. Computed tomography (CT) scan of the chest, abdomen, and pelvis
  - 1.6. Endoscopic ultrasound (EUS) ± biopsy
  - 1.7. Positron emission tomography (PET)/PET-CT in patients who lack evidence of distant metastasis on CT scan
  - 1.8. Bronchoscopy: preoperative bronchoscopy with biopsy and brush cytology for patients with locally advanced non-metastatic tumors that are located at or above the level of the carina
  - 1.9. Laparoscopy (optional): if no evidence of metastatic (M1) disease by radiological examination and tumor is at the gastroesophageal (GE) junction. Biopsy confirmation is mandatory
  - 1.10 Her-2 testing if metastatic adenocarcinoma is documented
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- 1.11 Nutritional assessment (in preoperative setting): consider naso-gastric tube (percutaneous endoscopic gastrostomy is not recommended)
2. **Surgical pathology report requirement. The following parameters should be mentioned in all surgical pathology reports of esophageal cancer;**<sup>5</sup>
  - 2.1 Specimen
  - 2.2 Tumor site (location)
  - 2.4 Relationship of tumor to esophagogastric junction
  - 2.5 Distance of tumor center from esophagogastric junction (specify, if applicable)
  - 2.6 Tumor size
  - 2.7 Histologic type
  - 2.8 Histologic grade
  - 2.9 Microscopic tumor extension
  - 2.10 Margins: proximal, distal, and circumferential or deep
  - 2.11 If all margins uninvolved by invasive carcinoma: distance of invasive carcinoma from closest margin in cm
  - 2.12 Treatment effect (applicable to carcinomas treated with neoadjuvant therapy)
  - 2.13 Lymphovascular invasion
  - 2.14 Perineural invasion
  - 2.15 Pathological tumor-node-metastasis: this should include number of lymph nodes examined, number of lymph nodes involved, and distant metastasis (pM)
  - 2.16 Additional pathologic findings
  - 2.17 Clinical history
3. **Staging:**

TNM - 2007 pathological staging system will be used<sup>6</sup>
4. **Treatment:**
  - 4.1 Clinically localized resectable disease: Treatment will depend on the clinical status of the patient and resectability of the tumor
    - 4.1.1 Medically fit and resectable disease
      - 4.1.1.1 Stage T<sub>is</sub> (in-situ), N0: Endoscopic mucosal resection (EMR) or ablation<sup>7</sup> (EL-3)
      - 4.1.1.2 Stage T1a, N0: Endoscopic mucosal resection<sup>8</sup> (EL-2) or esophagectomy<sup>9</sup> (EL-2)
      - 4.1.1.3 Stage T1b, N0: Esophagectomy (for non-cervical esophagus) (EL-1) and chemoradiation<sup>10,11</sup> (for cervical esophagus)
      - 4.1.1.4 For stage T2 or higher (except T4b): Any N or stage T1-4aN+: options are:
        - 4.1.1.4.1 Preoperative chemoradiotherapy with 41.4-50.4 Gy of external beam radiotherapy + concurrent chemotherapy (EL-1) (options of the regimen include 2 courses of cisplatin and 5-fluorouracil (5-FU) + 50.4 Gy of radiotherapy,<sup>12</sup> or low-dose weekly carboplatin plus paclitaxel regimen + 41.4 Gy)<sup>13</sup>
        - 4.1.1.4.2 Preoperative/perioperative chemotherapy for adenocarcinoma of distal esophagus or gastro-esophageal junction (GEJ, EL-1) (options include epirubicin, cisplatin, plus fluorouracil [ECF] chemotherapy or equivalent used in The Medical Research Council Adjuvant Gastric Infusional Chemotherapy trial,<sup>14</sup> or infusional 5-FU plus

- cisplatin or equivalent as was used in the Federation Nationale des Centres de Lutte contre le Cancer/Federation Francophone de Cancerologie Digestive trial)<sup>15</sup>
- 4.1.1.4.3 Esophagectomy with postoperative adjuvant chemoradiotherapy for those with adenocarcinoma, node-positive disease or a T2 or higher primary tumor stage<sup>16</sup> (EL-3). Can use adjuvant chemotherapy alone if radiotherapy is contraindicated<sup>17</sup>
- 4.1.1.4.4 Definitive chemoradiation (for cervical cancer).<sup>18</sup> If there is still persistent local disease, perform a salvage esophagectomy if possible
- 4.1.2 Medically unfit for surgery or unresectable T4 (T4b) disease: options include
- 4.1.2.1. Definitive concurrent chemoradiotherapy.<sup>18</sup> Radiation dose is 45-50.4 Gy, the latter is preferred
- 4.1.2.2. Palliative chemotherapy (see metastatic disease)
- 4.1.2.3. Palliative radiotherapy if cannot tolerate chemotherapy
- 4.1.2.4. Best supportive care if cannot tolerate chemotherapy or radiotherapy
- 4.1.3 Radiation technique: 3D conformal/intensity-modulated radiation therapy (IMRT)/rapid arc techniques should be used for modern treatment planning to minimize toxicities to adjacent vital organs (namely, heart, lung, spinal cord, or liver)<sup>19</sup>
- 4.1.4 Surgical approach
- 4.1.4.2 The surgical approach should be based upon anatomic tumor location
- 4.1.4.3 Patients with Siewert type I tumors are not appropriate candidates for a purely transabdominal approach to surgical resection. The standard surgical approach is a transthoracic en bloc esophagectomy and partial gastrectomy with 2-field lymphadenectomy<sup>20</sup>
- 4.1.4.4 For the majority of Siewert type II and III tumors, total gastrectomy with a transabdominal/transhiatal resection of the distal esophagus with lymphadenectomy of the lower mediastinum and the abdominal D2 nodal compartment is adequate<sup>21</sup>
- 4.1.4.5 The surgical therapy does not differ in patients who have or have not undergone induction therapy. For most thoracic esophageal cancer resections, it is suggested that a total thoracic esophagectomy with cervical esophagogastrectomy, radical 2-field lymph node dissection, and jejunostomy feeding tube placement<sup>22</sup> (EL-2)
- 4.1.4.6 Tri-incisional approach is preferred, it consists of initial right posterolateral thoracotomy (or a thoracoscopic approach for mobilization of the intrathoracic portion of the esophagus and node dissection, in centers with expertise in these techniques) followed by laparotomy to obtain complete esophageal dissection and mobilize the gastric conduit, en bloc resection of both mediastinal and upper abdominal lymph nodes, and a left neck incision and cervical anastomosis<sup>23</sup>
- 4.1.4.7 Totally minimally invasive esophagectomy is considered as a second option if expertise is available and the tumor is small and adequate oncological resection is possible<sup>24</sup> (EL-2)
- 4.2 Advanced unresectable or metastatic disease: Treatment will consist of palliative chemotherapy, options are as follows:
- 4.2.1 docetaxel, cisplatin,<sup>25</sup> infusional 5-FU (DCF)<sup>26</sup> or epirubicin, oxaliplatin and capecitabine (EOX)<sup>27</sup> combinations are standard regimens for first-line treatment (EL-1). Alternative regimens are:
- 4.2.2 Cisplatin/Capecitabine<sup>28</sup> or cisplatin / 5FU<sup>29</sup>
- 4.2.3 Leucovorin, and oxaliplatin (FOLFOX) regimen and 5-FU<sup>30</sup>

- 4.2.4 Trastuzumab, to be added to any of the above regimens (except ECF/EOX) in adenocarcinoma of GEJ with positive Her-2 test (defined by 3+ immunohistochemical staining or florescent *in-situ* hybridization positivity)<sup>31</sup> (EL-1)
- 4.2.5 For elderly, or patients with performance status 3 (ECOG scale), options include single agent capecitabine, leucovorin modulated fluorouracil or best supportive care<sup>32</sup> (EL-3)
- 4.2.6 Second line chemotherapy: There is no standard approach for second-line therapy after failure of the first-line regimen. For patients who retain an adequate performance status, utilization of other active agents not used in the first-line regimen is reasonable, either in combination or as serial single agents. Quality of life and minimization of side effects are key considerations when choosing the therapeutic approach. Options include single agent irinotecan, or taxanes<sup>33</sup>
- 4.3 Follow up post esophagectomy or definitive chemoradiotherapy: For asymptomatic patients, follow-up should include a complete history and physical examination every 3-6 months for 1-2 years, then every 6-12 months for 3-5 years, and annually thereafter. Complete blood count, multichannel serum chemistry evaluation, upper GI endoscopy with biopsy and imaging studies should be obtained as clinically indicated (EL-3). Patients with Tis or T1a tumors who undergo EMR should undergo endoscopic surveillance every 3 months for one year, and then annually for 5 years (EL-3)

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