

Esophageal cancer: ESMO Clinical Recommendations for diagnosis, treatment and follow-up

M. Stahl¹ & J. Oliveira²

On behalf of the ESMO Guidelines Working Group*

¹Department of Oncology and Centre of Palliative Care, Kliniken Essen-Mitte, Essen, Germany; ²Service of Medical Oncology, Portuguese Institute of Oncology, Lisbon, Portugal

incidence

The crude incidence of esophageal cancer in the European Union is ~4.5 cases/100 000/year (43 700 cases) and the mortality is ~3.5/100 000/year (39 500 cases).

diagnosis

The diagnosis should be made from an endoscopic biopsy with the histology to be given according to the WHO criteria. Small-cell carcinomas must be identified and separated from squamous cell carcinomas and adenocarcinomas and be treated accordingly.

staging

Staging should include clinical examination, blood counts, liver and renal function tests, endoscopy (including upper-aerodigestive tract endoscopy in case of squamous cell carcinoma), and a CT scan of chest and abdomen. In candidates for surgical resection, esophagogram and endoscopic ultrasound have to be added to evaluate the T (and N) stage of the tumor and to assist in the planning of the surgical procedure [II, B]. When available, positron emission tomography (PET) may be helpful in identifying otherwise undetected distant metastases or in diagnosis of suspected recurrence [II, B].

In locally advanced (T3/T4) adenocarcinomas of the esophago-gastric junction infiltrating the anatomic cardia, laparoscopy can rule out peritoneal metastases [II, B].

For selection of local treatments the tumors should be assigned to the cervical or intrathoracic esophagus or to the esophago-gastric junction [IV, C].

The stage is to be given according to the tumor–node–metastasis system with corresponding American Joint Committee on Cancer stage grouping (see table).

*Correspondence to: ESMO Guidelines Working Group, ESMO Head Office, Via L. Taddei 4, CH-6962 Viganello-Lugano, Switzerland

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treatment

Primary interdisciplinary planning of the treatment is mandatory. Surgery is regarded as standard treatment only in carefully selected operable patients with localized tumors. Transthoracic esophagectomy with two-field resection is recommended for intrathoracic squamous cell carcinoma [III, C]. No standard treatment can be defined for carcinomas of the cervical esophagus. The extent of surgery in adenocarcinomas is still a matter of debate.

Preoperative (with and without postoperative) radiation does not add any survival benefit to surgery alone [I, A]. This treatment is not recommended.

Although meta-analyses and one recent phase III trial suggested that preoperative chemoradiation confers a survival benefit, it is not clear which patients (stage, tumor location, histology) will most benefit from this preoperative treatment [I, B] and postoperative mortality appears to be increased.

Evidence for clinical benefit from preoperative chemotherapy exists for adenocarcinoma. Patients with adenocarcinomas of the lower esophagus/esophago-gastric junction may be managed with pre- and postoperative chemotherapy [I, B].

Data on adjuvant chemo(radio)therapy are limited, except for lower esophageal/ esophago-gastric junction adenocarcinomas after limited surgery.

treatment of limited disease (Tis–T2 N0–1 M0)

Surgery is the treatment of choice in early cancer (Tis–T1a N0). Endoscopic mucosal resection is under investigation.

Surgery is regarded as standard treatment of localized SCC (T1–2 N0–1), although long-term survival does not exceed 25% if regional lymph nodes are involved.

For patients unable or unwilling to undergo surgery, combined chemoradiation is superior to radiotherapy alone [I, A].

Pre-operative chemotherapy is considered as a standard treatment option for localised AC.

treatment of extensive disease (T3–T4 N0–1 M0 or T1–4 N0–1 M1)

Surgery alone is not a standard treatment in these stages since even in M0 cases a complete tumor resection is not possible in ~30% (pT3) and ~50% (pT4) of the tumors. Furthermore, even after complete tumor resection long-term survival rarely exceeds 20%.

squamous cell carcinoma

Patients with locally advanced disease may benefit from preoperative chemotherapy or, particularly, preoperative chemoradiation, while increasing the rates of complete tumor resection, improving local tumor control and thereby improving survival in phase III trials [II, B]. It is suggested, however, that preoperative chemoradiation may increase postoperative mortality. Owing to its high complete response rate, chemoradiation with close surveillance and salvage surgery for relapse may be considered as a definitive treatment for locally advanced disease (particularly in the upper third of the oesophagus), as supported by recent results of a French (FFCD 9102) and a German (Stahl 2005) trial [I, B].

adenocarcinoma

It is a matter of debate whether radiation adds to the survival benefit compared with preoperative chemotherapy alone and which patients may not benefit from surgery.

Nevertheless, cisplatin/5-FU combined with ~40 Gy followed by surgery can be regarded as an option in these tumors [II, B].

Patients with metastatic esophageal cancer can be considered for different options of palliative treatment depending on the clinical situation. Single-dose brachytherapy may be a preferred option, since it provides better long-term relief of dysphagia with fewer complications than metal stent placement [I, B].

Chemotherapy is indicated for palliative treatment in selected patients [III, B].

response evaluation

Response is routinely evaluated by symptomatic evolution, esophagogram, endoscopy (with biopsies) and CT scan.

follow-up

Except for those patients that may be candidates to salvage surgery after definitive chemoradiation, there is no evidence

Stage 0	Tis	N0	M0
Stage I	T1	N0	M0
Stage IIA	T2, T3	N0	M0
Stage IIB	T1, T2	N1	M0
Stage III	T3	N1	M0
	T4	Any N	M0
Stage IVA	Any T	Any N	M1a
Stage IVB	any T	Any N	M1b

M1a, cervical lymph node metastases for upper thoracic tumors, celiac lymph nodes for lower thoracic tumors, not applicable for mid-thoracic tumors; M1b, other lymph node or distant metastases.

that regular follow-up after initial therapy may influence the outcome. Follow-up visits should be concentrated on symptoms, nutrition and psycho-social problems [IV, D].

note

Levels of evidence [I–V] and grades of recommendation [A–D] as used by the American Society of Clinical Oncology are given in square brackets. Statements without grading were considered justified standard clinical practice by the experts and the ESMO faculty.

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