

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

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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 to identify otherwise undetected distant metastases or in diagnosis of suspected recurrence [II, B].

In locally advanced (T3/T4) adenocarcinomas of the esophagogastric junction (EGJ) 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 EGJ [IV, C].

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

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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 have indicated 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 all types of esophageal cancer, though is stronger for adenocarcinoma. Patients with adenocarcinomas of the lower esophagus/EGJ may be managed with pre- and postoperative chemotherapy. [I, B].

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

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

Surgery is the treatment of choice in early cancer (Tis–T1aN0). Endoscopic mucosal resection is under investigation.

Surgery is regarded as standard treatment of localized SCC (T1–2N0–1), 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].

Preoperative chemotherapy is considered as a standard treatment option for localized adenocarcinoma.

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, with increasing 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 a definitive treatment for locally advanced disease (particularly in the upper third of the oesophagus), as supported by recent results of a French and a German trial (FFCD 9102 and Stahl 2005, respectively) [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.

In experienced hands tumor response can be predicted early by PET.

follow-up

Except for those patients that may be candidates for salvage surgery after definitive chemoradiation, there is no evidence that regular follow-up after initial therapy influences the outcome. Follow-up visits should be concentrated on symptoms, nutrition and psychosocial 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 clinical practice by the experts and the ESMO faculty.

literature

- Boyle P, Ferlay J. Cancer incidence and mortality in Europe, 2004. *Ann Oncol* 2005; 16: 481–488.
- Juweid ME, Cheson BD. Positron-emission tomography and assessment of cancer therapy. *N Engl J Med* 2006; 354: 496–507.
- 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: 1167–1174.
- Fiorca F, Di Bona D, Schepis F et al. Preoperative chemoradiotherapy for oesophageal cancer: a systematic review and meta-analysis. *Gut* 2004; 53: 925–930.
- Cunningham D, Allum WH, Stenning SP et al. Perioperative chemotherapy versus surgery alone for resectable gastroesophageal cancer. *N Engl J Med* 2006; 355: 11–20.
- Stahl M, Stuschke M, Lehmann N et al. Chemoradiation with and without surgery in patients with locally advanced squamous cell carcinoma of the esophagus. *J Clin Oncol* 2005; 23: 2310–2317.
- Sumpster K, Harper-Wynne C, Cunningham D et al. Report of two protocol planned interim analyses in a randomised multicentre phase III study comparing capecitabine with fluorouracil and oxaliplatin with cisplatin in patients with advanced oesophagogastric cancer receiving ECF. *Br J Cancer* 2005; 92: 1976–1983.
- Gebbski V, Burmeister B, Smithers BM et al. Survival benefits from neoadjuvant chemoradiotherapy or chemotherapy in esophageal carcinoma: a meta-analysis. *Lancet Oncol* 2007; 8: 226–234.
- Bedenne L, Michel P, Bouche O et al. Randomized phase III trial in locally advanced esophageal cancer: radiochemotherapy followed by surgery versus radiochemotherapy alone (FFCD 9102). *Proc Am Soc Clin Oncol* 2002; 21: 130a (Abstr 519).