Esophageal Carcinoma

Most esophageal malignancies are diagnosed between 50 and 60 years of age, with males predominating in a 4:1 ratio. The physiologic constrictions of the esophagus are sites of predilection for esophageal carcinoma. Approximately 50% of cases present clinically in the middle third of the esophagus (constricted by the aortic arch and left main bronchus at the T4 level), while 35% present in the distal third (at the esophageal aperture of the diaphragm).

Two histologic types of esophageal carcinoma are distinguished:

- Squamous cell carcinoma (≥95% of cases, Fig. 2.31), which occurs predominantly in the middle and upper thirds of the esophagus.
- Adenocarcinoma (approx. 4% of cases, Fig. 2.32), which occurs in the distal esophagus and at the gastroesophageal junction. This tumor is associated with Barrett syndrome (columnar epithelium lining the lower esophagus).

Accurate tumor staging and the determination of histologic tumor type are essential in treatment planning for esophageal carcinoma.

Staging

The extent of esophageal carcinoma is described with the TNM classification, where T indicates the depth of tumor invasion, N describes lymph node status, and M denotes the presence or absence of distant metastasis.

Routes of metastasis. Because the esophagus lacks a serosal covering, esophageal cancer often undergoes early submucous spread to the cervical and thoracic levels. Even early stages show clinical evidence of lymphogenous spread to paraesophageal, mediastinal, cervical, and perigastric regional lymph nodes (stage N1).
Imaging studies. Diagnostic imaging during preoperative staging provides a basis for deciding among several treatment options: radical excision with curative intent, neoadjuvant therapy, or a palliative approach. The gold standard for initial diagnosis is endoscopic examination and biopsy. Endoscopy permits a reliable evaluation of the mucosa, but the depth of tumor invasion into the esophageal wall cannot be accurately assessed. This has led to greater reliance on the combined use of esophagogastroduodenoscopy (EGD) and endosonography, although this method has limited application in patients with strictures and stenoses.

CT. The goal of primary staging is to ascertain the preoperative extent of disease as an aid to planning neoadjuvant therapy or defining the radiotherapy field. Multislice spiral CT is used for this purpose. This procedure can evaluate possible tumor invasion of adjacent organs (stage T4)—especially the tracheal wall, bronchi, pericardium, and aorta—as well as lymphogenous and hematogenous metastasis. The following CT signs are considered definitive for the invasion of adjacent organs:

- Obliteration of the paraesophageal fat plane
- More than 90° encasement of the aortic circumference
- Airway displacement or compression with intraluminal convexity
- Tracheoesophageal or bronchoesophageal fistula
- Cortical erosion of vertebral bodies

Fig. 2.31 a–d  Squamous cell carcinoma of the middle third of the esophagus in a 63-year-old man (stage: uT3, N-positive). Follow-up study. CT (a, c) and FDG PET-CT (b, d) before treatment and after completion of the first cycle of neoadjuvant chemotherapy (cisplatin/5-FU). The SUV was reduced from 22.5 (b) to 4.8 (d). Final stage after esophageal resection: ypT0N0.
Fig. 2.32 a–h  Adenocarcinoma of the gastroesophageal junction in a 50-year-old man (stage: uT3, N-positive). Follow-up study. CT and FDG PET-CT before treatment (a, b, e, f) and after completion of the first cycle of neoadjuvant chemotherapy (cisplatin/5-FU; c, d, g, h). The SUV was reduced from 17.3 to 3.5. Final stage after esophageal resection: ypT0N0.

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Enlargement of paraesophageal or infradiaphragmatic lymph nodes to more than 8 mm is considered evidence of lymphogenous metastasis.

**T staging with PET.** In several studies, FDG PET has shown a high sensitivity (95%) and specificity (>90%) in the initial evaluation of squamous cell carcinoma and adenocarcinoma of the esophagus (Luketich et al. 1997; Block et al. 1997; Kole et al. 1998; McAteer et al. 1999; Kim et al. 2001; Kato et al. 2002). Most false-negative findings in these studies resulted from very small lesions that were below the 3- to 5-mm spatial resolution limit of PET imaging. No correlation has been found between the intensity of FDG uptake and the depth of tumor invasion in the esophageal wall (Fukunaga et al. 1998; Flamen et al. 2000).

FDG PET and CT have comparable sensitivity in the staging of esophageal cancer (Block et al. 1997; Kim et al. 2001). Due to difficulties in the anatomic correlation of PET findings, however, PET cannot add to the information supplied by endosonography in the assessment of wall invasion.

**N staging with PET.** The detection of locoregional lymph node metastases (N staging) has considerable prognostic importance. Contrast-enhanced CT is sensitive for this indication but has limited specificity. PET has 100% specificity for the N staging of esophageal carcinoma, but its sensitivity is only 45% (Luketich et al. 1997). The spatial resolution of conventional PET scanners is insufficient to positively distinguish locoregional lymph node metastasis from primary tumor involvement. Peripheral lymph nodes can be more accurately identified, however.

In recent studies, [18F]FDG PET has been combined with [11C]choline PET to permit the more accurate evaluation of mediastinal lymph nodes. To date, however, this combination has not yielded a diagnostic gain: the sensitivity of [18F]FDG PET was 100% compared with 73% for [11C]choline PET (Jager et al. 2001). This question has not yet been investigated by prospective studies in large groups of patients.

**M staging with PET.** The detection of distant metastases from esophageal carcinoma (M staging) is a critical factor in determining whether or not surgery is indicated. Patients with nodal or organ metastases have a poor prognosis that would contraindicate a radical excision with its attendant risks and morbidity. In patients with no evidence of distant metastases, the locoregional lymph node status determines the prognosis (Figs. 2.33 and 2.34).

FDG PET has a sensitivity of 69% and a specificity of 93% in the identification of distant metastases (Luketich et al. 1999), compared with only 46% and 74%, respectively, for CT. Even when compared with CT plus endosonography, FDG PET showed a higher sensitivity of 78% (vs. 46%) and a specificity of 90% vs. 69% (Lerut et al. 2000). The additional information supplied by FDG PET over morphologic imaging can influence treatment planning (Chatterton et al. 2009). This prompted the Third German Interdisciplinary Consensus Conference, titled “Onc-Pet III,” to give FDG PET a class 1a indication (es-