

14 Applications in Esophageal and Gastric Cancer

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14.1 Esophageal Cancer

14.1.1 Introduction

Esophageal cancer has been regarded traditionally as an aggressive malignancy with an increasing incidence of squamous cell cancer in developing countries due to increasing consumption of alcohol and tobacco during the last decades (odds ratio of 23.1 when both risk factors are present) (LAGERGREN

et al. 2000), and an even more pronounced rise of adenocarcinoma of the esophagogastric junction in the western world mainly caused by reflux disease. For both entities, there is a poor outcome in all advanced stages. While surgical resection or definitive radio- or radiochemotherapy (RCT) may be curative with better long-term outcome in early stage cancer, most patients with symptomatic esophageal cancer die within 3 years after diagnosis, in spite of complex treatment concepts. Therefore, continued clinical research is justified, including the evaluation of more aggressive neoadjuvant and adjuvant treatments as well as an improvement of combined RCT.

14.1.2 Epidemiology and Staging

Squamous cell cancer is the predominant histology in esophageal malignancies, with a heterogeneous worldwide pattern: regions with a very high incidence of up to 200 new cases per 100,000 inhabitants are in Iran, southern Russian republics, South Africa and central areas of China. In Europe and America, the incidence is approximately 6.6 per 100,000 residents, with male persons being affected five times more frequently than females, and a mortality of 6.1/100,000 (ESMO GUIDELINES 2005). Most patients are older than 30 years, with a median age of 65 years (BAREISS et al. 2002). Unfortunately, esophageal cancer is usually detected in advanced stages, with 70 % of all new cases being stage III or IV. Therefore, the 5-year survival rate of all patients is not higher than 5% (BAREISS et al. 2002).

Adenocarcinoma of the pericardial area (adenocarcinoma of the esophagogastric junction, AEG) is the second most common cancer of the esophagus, and the most common one below the tracheal carina. It is subdivided into three groups, dependent on the relation to the cardia: AEG I from 5 cm to 1 cm cranial of the cardia, with a behavior similar to squamous cell cancer of the distal esophagus – and

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therefore integrated into the sections on esophageal cancer – and AEG II and III, located in the cardia and from 2 cm to 5 cm distal of the cardia, respectively, mentioned in sections on gastric cancer.

14.1.3

Anatomy and Tumor Spread

The classification of esophageal cancer into subgroups depends on the location of the cancer and the resulting therapeutic procedure: cancer of the cervical part, intrathoracic cancer with close relation to the tracheobronchial tree, or infrabifurcal cancer, with the latter usually being resectable even in locally advanced stages. The former should be offered a multidisciplinary concept, in principle, with neoadjuvant chemo- or radiochemotherapy dependent on the histology and local growth, or definitive combined RCT.

The second, more historical classification into two subgroups – cervical and intrathoracic cancer – was based on the surgical approach and the distribution of the lymph node involvement, but does not reflect the problems of R0 resection in all tumors close to the tracheobronchial tree, and the resulting multidisciplinary aspect.

The most important prognostic factor is the tumor stage (DALY et al. 1996), or local tumor spread – infiltration of the mediastinum, tracheobronchial tree, and pericardium – and the infiltration of locoregional lymph nodes, with the latter being present in 5% of mucosal carcinoma, in 30% of submucosal cancer, and in even more than 80% of tumors extending beyond the esophagus (HOSCH et al. 2001), causing about 40% of all local tumor recurrences.

Cancer of the upper third of the esophagus usually infiltrates the cervical and mediastinal lymph nodes, whilst tumors of the middle third mainly spread to the mediastinal and upper perigastric lymph nodes, and carcinoma of the lower third to the lower mediastinal and abdominal lymph nodes. The distribution of lymph node infiltration has major implications on the target volume of both definitive and preoperative radiotherapy, and should be taken into account when customizing the radiation portals. Intraesophageal spread of tumor cells in submucosal lymphatics influences the target volume, too. Its likelihood increases from 4% in pT1 tumors to 30% in pT4 tumors. It should be noted that a metachronous or even synchronous secondary cancer of the upper aerodiges-

tive tract can occur in up to 10% of patients, which will have a major impact on treatment decision. The classification of esophageal cancer follows guidelines by the UICC, recently actualised in 2002 (UICC 2002) (Table 14.1) and influences the treatment decision as well the prognosis: in an analysis of 4329 patients with esophageal cancer 5-year survival rates were 42% in stage I, 29% in stage II, 15% in stage III, and only 3% in stage IV (DALY et al. 1996). Besides tumor stage, the oral and aboral resection status (R classification) has a prognostic value, too, with a R0 resection being the primary goal of the surgeon (HERMANECK 1999). In recent years, a lot of different molecular markers have been evaluated regarding their prognostic impact, but none of them is established in clinical routine (gene aberration, transcription factors, apoptotic mechanisms, etc.).

An optimal and individual treatment decision is based on precise staging of the tumor: the depth of infiltration is evaluated by endoscopic ultrasound and the infiltration of adjacent organs by computed tomography (CT) and bronchoscopy. Further staging procedures depend on clinical symptoms and are not recommended on a routine basis. Magnetic resonance imaging (MRI) of the mediastinum has failed to show a higher accuracy than CT to detect mediastinal infiltration, and is therefore not recommended (KORST and ALTORKI 2004).

14.1.4

Therapy

14.1.4.1

Principles and Strategies

Esophageal cancer is a curable disease and the treatment decision is based on tumor extension, comorbidities and individual decision of the informed patient. Whilst esophagectomy is usually offered in early stages (uT1–2), both radical resection and combined RCT are standard procedures in locally advanced cancer (uT3). For tumors with close contact to the tracheobronchial tree preoperative RCT is used by a number of centers. To define the best individual concept, exact knowledge about the functional operability, organ function (liver, kidney, heart, lung) and expected tolerance to radio- and/or chemotherapy is essential. Continued alcohol consumption, reduced general condition (Karnofsky performance status < 70), excessive weight loss, and altered renal, hepatic, and/or