Current standard and trends in oesophageal cancer

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Background

Oesophageal adenocarcinoma and oesophago-gastric junction (EGJ) cancer have shown an increasing incidence over the past three decades. In addition, they are among the most common cancers in Europe and in other parts of the world. If diagnosed at early stage I, which is rarely the case, they have a very good prognosis. Endoscopic resection can be recommended in selected cases where the infiltration does not go beyond the mucosal layer. Alternatively, surgical resection leads to cure in the vast majority of early-stage cases. In contrast, at stages II and III the prognosis is more critical. Local relapses and distant metastases occur frequently in the post-surgical follow-up. The 5-year survival rate used to be as poor as 20–30% [1]. Using the increasing opportunities of multimodal treatment and the experience at specialised centres, the outcome of oesophageal cancer can be significantly improved [2].

Article

Randomised studies have shown that neoadjuvant and perioperative chemotherapy leads to an improved outcome for patients with adenocarcinoma of the oesophagus and EGJ. On the basis of current meta-analyses, patients are now treated with pre- and perioperative chemotherapy. In some centres, neoadjuvant simultaneous chemoradiation is the preferred approach [3]. Combined chemoradiation has not shown a superior outcome when compared directly with neoadjuvant chemotherapy alone, but it may lead to enhanced morbidity and also to increased perioperative mortality. This is why the majority of European centres regard perioperative chemotherapy without radiation as their standard approach. In the recently published European guidelines, perioperative chemotherapy is recommended in cases of T3/T4 oesophageal and EGJ cancer. Neoadjuvant chemoradiation is regarded as an alternative approach [4].

In locally advanced squamous cell cancer of the oesophagus, preoperative chemoradiation has shown a proven benefit [3]. It is a matter of debate as to when oesophageal resection should be performed and in which subgroups of patients definitive chemoradiation leads to satisfying long-term results. Comparative studies have shown comparable outcomes [5]. Functional imaging and molecular prognostic markers may support decision-finding in the future. Currently, it is recommended that patients presenting with resectable tumours and without limiting cardio-respiratory, hepatic and other comorbidities should be offered surgical resection. Neoadjuvant concurrent chemoradiation can be recommended in tumour categories $\geqslant$T3 [3,4].

Despite the improved outcome due to multimodal treatment, a proportion of the patients do not respond to preoperative chemotherapy or radiation therapy and therefore obtain no benefit, but encounter time delay and potential toxicity. Positron emission tomography with [18F]fluorodeoxyglucose (FDG-PET) offers the chance to monitor response early in the course of preoperative treatment. Early changes in tumour glucose uptake can also serve as a prognostic marker. In patients who do not respond to treatment at an early time point, we have shown that treatment can be modified and alternative concepts can be offered [6]. Such innovative strategies are currently validated in clinical trials, but should still be regarded as investigational [7].

In addition to conventional chemotherapy, the role of biologically targeted drugs has been studied in resectable oesophageal cancer. The most interesting results from studies carried out in metastatic oesophago-gastric cancer appear to be the inhibition of Her-1 and Her-2, two members of the epidermal growth factor receptor (EGFR) family, by cetuximab (anti Her-1) [8,9] or trastuzumab (anti Her-2) [10]. These targeted drugs are currently being investigated in the perioperative setting.

Conclusions

The prognosis of patients with localised oesophageal cancer can be improved by optimal surgery and

perioperative care provided in specialised referral centres. In addition, the consequent use of the multimodal treatment options offers enhanced chances for cure. Further progress can be expected from a more sophisticated guidance of treatment by functional response imaging and by the integration of molecularly targeted drugs into perioperative treatment.

Conflict of interest statement

There are no conflicts of interest associated with this article.

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