Editorial Commentary

Type II and III adenocarcinoma of the esophago-gastric junction: esophageal extent ≥1.5 cm critical for mediastinal nodal disease

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In their seminal work on adenocarcinoma of the esophago-gastric junction, Mitchell *et al*. (1) rise the important question of mediastinal nodal involvement specifically in patients with Siewert II/III cancer following trimodality therapy. The standard surgical adenocarcinoma of the esophago-gastric junction. As for treatment strategies include esophagectomy for type I and gastrectomy for type III "true junctional cancers", i.e., type II, it remains debatable whether the extension of resection in the oral or aboral direction represents the most effective surgical therapy (2). From a clinical viewpoint nothing is more frustrating and devastating than the appearance of a mediastinal recurrence after chemoradiation and highly sophisticated surgical procedures. In our own series of 51 patients that were treated by aggressive neoadjuvant chemoradiation with inclusion of mediastinal nodes followed by the Ivor-Lewis procedure, only 4/51 (8%) of the patients experienced late locoregional recurrence (3).

Interestingly, Mitchell and coauthors (1) found increasing ypN+ rates for mediastinal nodes following CRT depending on the pretreatment tumor extent (above Z-line): <1 cm 0%, 1–2 cm 11%, 2–3 cm: 20%, >3 cm: 16%. For the composite endpoint "mediastinal involvement" (i.e., ypN+ and mediastinal recurrence within 2 years) the corresponding rates were: <1 cm: 4.3%, 1–2 cm: 13%, 2–3 cm: 20%, >3 cm: 22%. In addition, on multivariate analysis of patients with intrathoracic cN0-disase, esophageal extent of ≥1.5 cm was independently predictive of mediastinal involvement (OR 5.46, P=0.01).

Apart from the typical mechanistic view of a given problem with cancer, on the other hand it would seem interesting to have measures that will be able to a-priori identify those patients that clearly have no benefit from neoadjuvant CRT. Albeit knowledge about immunoregulation and cancer surveillance has risen enormously over the past decades, only few publications deal with esophageal adenocarcinoma and adenocarcinoma of the esophago-gastric junction. Data addressing the role of regulatory (FoxP3+) and cytotoxic (CD8+) T-cells (TIL) in these cancer types mainly focussed on their prognostic impact following a surgical approach only (4-6) or were obtained from post therapeutic specimen, respectively. Moreover, results considering the role of FoxP3+ and CD8+ TIL were conflicting, so the prognostic impact of TIL remains controversial. Addressing this dilemma, a crucial key could be to contemplate functional activity of TIL. Recently our study group presented comprehensive data for gastric, rectal and anal cancer, that cell-to-cell distances of FoxP3+ and CD8+ cells may reflect functional interactions of these cells and in this way to predict prognosis (7).

As of today, any adenocarcinoma of the esophago-gastric junction extending more than 1.5 cm above the Z-line irrespective of the given Siewert classification will need critical assessment and treatment of mediastinal lymph nodes. These findings seem equally important for delineation of the appropriate planning target volume of radiation as well as for

choosing the optimal surgical strategy.

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Footnote

Conflicts of Interest: The author has no conflicts of interest to declare.

Ethical Statement: The author is accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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