Supplemental Digital Content 1. Text that reviews the staging of esophageal cancer.

**Staging of Esophageal Cancer**

Management of esophageal cancer and patient survival depend on accurate staging. The 7th edition of The American Joint Committee on Cancer (AJCC) Staging Handbook for esophageal cancer includes the depth of local primary tumor invasion (T), the extent of regional lymph node involvement (N), the absence or presence of distant metastasis (M), and a stage grouping based on TNM.4,10,14,18 [**Table 1**] The T classification reflects the extent local tumor invasion into or through the esophageal wall. A higher T category (T3-4) is associated with a higher probability of nodal metastases.10,14,18 High-grade dysplasia represents tumor in situ (Tis). T1 tumors invade the mucosa (T1a) or submucosa (T1b). T2 cancer invades the muscular layer, while T3 cancer invades into adventitia. T4a cancer may invade adjacent structures such as pleura, pericardium, diaphragm or peritoneum and is potentially resectable. T4b cancer may invade other vital structures, such as trachea, aorta, or vertebral body and is not resectable.10,12,17,18

Regional lymph node (N) staging is the most important prognostic factor for esophageal cancer and is based on the number of involved nodes rather than location.4,10,14,18 The extensive submucosal network of esophageal lymphatics allows early longitudinal tumor spread to other parts of the esophagus and to para-esophageal regional lymph nodes, regardless of the primary tumor histology or location.4,18 For example, even patients with early esophageal cancer, such as T1a and T1b tumors, have a 7% and 27% risk of regional nodal metastases, respectively.16 Cervical and celiac lymph node metastases are now considered as regional nodal involvement, rather than metastases.14,18 Nonetheless, celiac nodal metastases portend a poor prognosis.12 No metastatic involvement of regional nodes is classified as N0. N1 depicts metastases to 1 to 2 regional lymph nodes. N2 reflects metastases to 3 to 6 regional lymph nodes, and N3 involves 7 or more regional nodes.4,18

Lymphadenectomy with histologic evaluation, at the time of esophagectomy, is the only accurate method to classify lymph nodes.14 The aim of optimum lymphadenectomy, with resection of up to 30 lymph nodes, is to improve N staging and is associated with improved survival in most patients.3,17,82,83

Metastases (M) are classified as M0 or M1 based on the absence or presence of distant metastasis, respectively.4,18 Liver, lungs, bone, and adrenal glands are the most commonly involved sites. Adenocarcinomas frequently metastasize to the abdomen, typically liver and peritoneum, while SCC manifests with locoregional thoracic metastases.10,13

The current 8th edition revision (2017) of the AJCC/Union for International Cancer Control (UICC) Staging of Cancers of the Esophagus and EGJ recognizes that patients with SCC do more poorly than those with adenocarcinoma and provides separate clinical and pathologic stage grouping based on cell type. Of interest, after induction therapy, ypTNM stage classifications are identical for SCC and adenocarcinoma.14,17