

Patterns of Nodal Metastasis and Prognosis in Human Papilloma Virus Positive Oropharyngeal Squamous Cell Carcinoma

Objective: Patients with oropharyngeal squamous cell carcinoma (OPSCC) that are HPV positive have an excellent prognosis. The current AJCC nodal staging system is based on the size, number and laterality of lymph nodes involved with cancer and may not accurately reflect survival in these patients. The purpose of this study is to develop a nodal staging system in HPV positive patients with OPSCC that more precisely predicts survival.

Methods: CT scans from 78 previously untreated patients who underwent weekly carboplatin and paclitaxel with concomitant intensity modulated radiation therapy for advanced stage (III, IV) OPSCC were reviewed regarding nodal characteristics. The largest two dimensions, distribution (level I-V), and radiologic evidence of extracapsular spread of each imaged lymph node was recorded. HPV status was determined by immunohistochemistry on a tissue microarray and 78% (61/78) of patients were HPV positive.

We modeled patterns of nodal metastasis in HPV positive patients that were associated with different survival rates. We previously found that matted cervical lymph nodes, defined as three nodes abutting one another with loss of intervening fat plane that is replaced with radiologic evidence of extracapsular spread predict a poor prognosis independent of age, T stage, HPV, EGFR and smoking status. Matted nodes were not a surrogate marker for extracapsular spread and were seen in AJCC stage N2b, N2c and N3 patients; within the same nodal group, matted nodes were associated with a poorer survival compared to patients without matted nodes. Therefore, we defined $_{\text{HPV}^+}\text{N1}$ (low risk) as patients who had a single node $<6\text{cm}$, unilaterally or bilaterally (AJCC N1, N2a or N2c with a single node bilaterally). $_{\text{HPV}^+}\text{N2}$ (moderate risk) was defined as patients who had a single node $\geq 6\text{cm}$ or ≥ 3 nodes unilaterally or bilaterally (AJCC N2b, N2c with ≥ 3 nodes, or N3, without matted nodes). $_{\text{HPV}^+}\text{N3}$ (high risk) was defined as patients with matted nodes.

Results: The 3-year DSS and OS for the entire cohort was 89% and 86%, respectively, with a median follow-up of 47 months. There was no significant difference in DSS ($p=0.36$) or OS ($p=0.43$) by the AJCC staging system. However, in patients grouped by $_{\text{HPV}^+}\text{N1}$, $_{\text{HPV}^+}\text{N2}$, and $_{\text{HPV}^+}\text{N3}$ nodal staging, significant differences in the 3-year DSS (100%, 92%, 60%, respectively, $p=0.001$) and OS (100%, 85%, 60%, respectively, $p=0.013$) were observed.

Conclusion: A nodal staging system based on reclassification of size, laterality and matted nodes more accurately reflects survival differences in this cohort of HPV positive patients with OPSCC. A larger review of the nodal classification in the AJCC staging system with these criteria should be considered for patients with HPV positive cancer.