**Optimizing Patient Selection for Total Laryngectomy Versus Larynx-Preserving Chemoradiotherapy for Locally Advanced Laryngeal Squamous Cell Carcinoma: An Analysis of the National Cancer Data Base**

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**Purpose/Objective(s):** The decline in survival of laryngeal cancer patients over the past few decades has been associated with a rise in non-surgical management of stage III/IV disease following results from the VA Larynx Trial and RTOG 91-11. To clarify potential driving factors for this decrement, this analysis assesses patterns of use and overall survival (OS) amongst the primary NCCN-recommended modalities of therapy stratified by T-stage and radiation (RT) dose.

**Materials/Methods:** The National Cancer Data Base was used to identify 10,228 patients with stage T2N1-3 or T3-4N0-3 glottic/supraglottic squamous cell carcinoma (SCC) treated between 2003 and 2011 with total laryngectomy (TL) or definitive chemoradiation (CRT). Treatment modality was divided into concurrent CRT, TL alone, and TL with adjuvant RT/CRT (TL+A). Kaplan-Meier method was used to estimate OS for each treatment group. Hazard ratios (HR) for OS with 95% confidence intervals (CI) were computed using Cox regression modeling, adjusting for date of treatment, treatment facility (community vs. academic), age, gender, race, insurance status, tumor grade, stage, and Charlson-Deyo comorbidity score.

**Results:** The median follow-up was 30.5 months for the entire population and 42.9 months for surviving patients. Among this cohort between 2003 and 2011, the use of CRT increased from 87.1% to 93.7% for T2 and 71.0% to 80.6% for T3, but remained steady for T4 tumors (47.9% to 46.7%). With 4,935 deaths reported, the estimated 3- and 5-year OS for CRT, TL, and TL+A was 60.6%/47.1%, 56.5%/46.4%, and 63.3%/50.8%, respectively (omnibus P = 0.002). Compared to CRT, the adjusted HR (95% CI) for OS for TL and TL+A was 1.01 (0.91-1.12, P = 0.87) and 0.82 (0.75-0.90, P<0.0001), respectively. When including only patients treated with an optimal RT dose (i.e. 70-74 Gy, 58.5-65.25 in 2.25 Gy/fx, or 79.2 Gy in 1.2 Gy/fx BID), the adjusted HR (95% CI) for TL and TL+A compared to optimal CRT was 1.08 (0.96-1.20, P = 0.19) and 0.88 (0.79- 0.97, P = 0.01), respectively. However, after excluding all patients with T4-tumors, the benefit of TL+A over CRT was lost, as the adjusted HR (95% CI) for TL and TL+A compared to any CRT regimen was 1.09 (0.95- 1.25, P = 0.22) and 1.04 (0.91-1.18, P = 0.58), respectively, and compared to an optimal CRT regimen only was 1.14 (0.99-1.31, P = 0.07) and 1.09 (0.95-1.24, P = 0.22), respectively.

**Conclusion:** In this population-based cohort, CRT and TL+A resulted in equivalent OS for T2N1-3 and T3N0-3 glottic/supraglottic SCC. However, when including T4 patients to this analysis, TL+A was associated with better OS compared to CRT, even after including only optimal RT regimens. Given a relatively steady use of CRT for T4 tumors over this time, these results suggest that the OS decline seen with laryngeal cancer may be driven by T4-tumors treated with larynx preservation.