



## **Laryngeal Malignancy (Squamous Cell Carcinoma)**

### **Introduction**

The genetic and molecular alterations that lead to the development of laryngeal cancer are similar to other human papillomavirus-negative cancers of the upper aerodigestive tract. Advanced laryngeal cancer is dissimilar to other cancers in the impact of its treatment. Through control of voice, swallow and breathing, the larynx is responsible for many of the essential functions that define our humanity. Although any major cancer resection and associated reconstruction can be disfiguring, treatment of laryngeal cancer with surgical or “organ preservation” techniques can be functionally devastating and lead to social isolation and impaired quality-of-life in many cases<sup>1,2</sup>. One of our many tasks as laryngeal cancer surgical oncologists is to be cognizant of these issues, and advocate for our patients with treatment guidance that takes into consideration both oncologic and functional goals<sup>3</sup>.

### **Pathophysiology**

Malignant disease of the larynx can take many forms, but the overwhelming majority are squamous cell carcinomas (SCC) that arise from the laryngeal epithelium. Rare malignancies include hematologic cancers such as lymphomas, and mesenchymal cancers such as sarcomas. This review will focus on SCC.

Laryngeal SCCs arise from underlying genomic alterations in one or a few cells acquired most commonly through carcinogen exposure (tobacco). The mutations that most commonly drive laryngeal SCC include *TP53* loss of function mutations, *CDKN2A* (p16) inactivation, and copy number alterations on chromosomes 3 and 11 that lead to overexpression of several driver, oncogenic proteins<sup>4</sup>. High-risk human papillomaviruses may infect laryngeal cancers like they can infect any epithelial surface<sup>5</sup>, but virus-positive laryngeal SCCs harbor similar genomic alterations compared to virus-negative<sup>4</sup>, and virus-positive laryngeal SCCs demonstrate similar responses to treatment and survival compared to virus-negative<sup>6</sup>. Thus, high-risk human papillomaviruses do not induce a biologically distinct malignancy in the larynx like they do in the tonsils of the oropharynx. This is why virus testing is not indicated in laryngeal SCCs<sup>7</sup>.

Once a laryngeal SCC develops, it undergoes rapid expansion and develops multiple heterogeneous cell populations due to genomic instability. Due to differences in underlying mutations and ability to be detected by the immune system, tumor cells that have the ability to



survive and grow in low nutrient and hypoxic conditions and evade immune elimination are selected for and expand to form a clinically relevant tumor<sup>8</sup>. One subpopulation of tumor cells may be susceptible to a specific type of treatment, and others may not. This is a fundamental problem in cancer biology and is the single strongest argument for surgical resection of malignant lesions.

### **Diagnosis and Staging**

The need to properly evaluate and diagnose both the origin and extent of laryngeal carcinoma is critical to treatment outcomes. The supraglottis, glottis and subglottis arise from distinct embryologic origins that can be used to predict the pattern of SCC spread based upon the anatomic compartments and lymphatics<sup>9</sup>. Once manifestation of these anatomic principles is the high degree of likelihood that supraglottic cancers will metastasize to bilateral level II and III cervical lymph nodes given the rich lymphatic supply in the supraglottis.

The indicated workup for a suspected laryngeal cancer includes a thorough history and physical with a focus on subjective symptoms of laryngeal dysfunction and examination of the aerodigestive tract and neck. Endoscopic evaluation to identify potential lesions and to visualize both the anatomy and function of the larynx is mandatory as the American Joint Committee on Cancer (AJCC) staging system for laryngeal SCC incorporates both anatomic (tumor size and extent) and functional (TVF motion) data. AJCC laryngeal SCC staging can be found here:

<https://www.cancer.org/cancer/laryngeal-and-hypopharyngeal-cancer/detection-diagnosis-staging/staging.html>

Once a suspicious lesion is identified, tissue is needed from the primary tumor or from a metastatic neck node to confirm the diagnosis. The remaining workup is driven by the suspected stage of the tumor. Some advocate endoscopy and mapping biopsies in all cases of newly diagnosed laryngeal SCC, but in practice this is not always done. Radiographic workup of a suspected malignancy must include neck and chest imaging for a patient to be properly staged. MRI may be a useful adjunct to CT imaging when cartilage invasion is a concern<sup>10</sup>, but the routine use of PET scans in the initial diagnosis of laryngeal malignancy is controversial<sup>11</sup>.

### **References**



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