

Margin Analysis Squamous Cell Carcinoma of the Oropharynx



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KEYWORDS

- Surgical margins • Oropharyngeal cancer • Squamous cell carcinoma • Prognosis • Local control
- Head and neck • HPV

KEY POINTS

- Oropharyngeal carcinoma should now be considered as a distinct subsite of head and neck carcinoma because of the distinct biological differences and response to treatment.
- There seems to be a consistently favorable outcome not only in survival but also locoregional control of human papilloma virus–positive oropharyngeal squamous cell carcinoma.
- Special optical imaging devices (eg, narrow band imaging) have been used for better delineation of surgical margins resulting in lower rates of positive margins.
- Molecular assessment of margins is still evolving and not yet clinically practical for everyday use of margin assessment; but in the era of immunotherapy, there is ongoing research to determine the markers that can be used to predict responders to nonresponders of immunotherapy.

INTRODUCTION

Surgical margins have been an ongoing topic of discussion in head and neck surgery. It is well accepted that close or positive margins are related to increased risk of locoregional recurrence. In their review of surgical margins in head and neck cancer, Alicandri-Ciufelli and colleagues¹ confirmed that inadequate surgical resection margins contribute to increased local recurrence and decreased survival rates.

The oropharynx includes the segment of the pharynx from the level of the hard palate down to the hyoid bone. Anatomically, it is composed of the base of the tongue, palatine tonsil, soft palate, and lateral and posterior pharyngeal wall. Worldwide, there are more than 400,000 new cases of

oropharyngeal carcinoma per year with nearly 46,000 new cases in the United States alone.² Most of these carcinomas are squamous cell carcinomas (SCCs). Historically and up to this day, because of the common shared risk factors of smoking and heavy alcohol consumption, literature involving oropharyngeal SCC (OPSCC) is often combined with oral SCC. However, since the introduction of a link between human papilloma virus (HPV) and OPSCC more than 15 years ago,^{3,4} HPV is now confirmed to be a major risk factor of OPSCC with its distinct epidemiology and favorable treatment outcome; there is a need to consider OPSCC separate from the other subsites of head and neck SCC. Two recent meta-analyses by Petrelli and colleagues⁵ and O'Rorke and colleagues⁶ both confirm a survival advantage

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for patients with HPV-positive head and neck carcinoma as compared with those with HPV-negative disease (hazard ratio [HR] 0.46; 95% confidence interval [CI], 0.37–0.57 and HR = 0.33; 95% CI, 0.27–0.40, respectively). Excess tobacco use is shown to have a negative influence, as patients with HPV-positive head and neck cancer and significant tobacco use histories have outcomes intermediate to those in HPV-positive nonsmokers or traditional HPV-negative (ie, tobacco and/or alcohol associated) head and neck cancers.^{7,8} The incidence of larynx, oral cavity, and hypopharynx SCC is declining, whereas the incidence of OPSCCs, particularly in the tonsillar and base of tongue region, have demonstrated a recent increase in incidence in the United States, Canada, Australia, Denmark, Japan, Slovakia, and the United Kingdom.⁹ Patients with HPV-positive OPSCC are usually nonsmokers, male, and younger with a median age of 58 years compared with the median age of 63 years for classic smoker- and drinker-related OPSCC.^{9,10}

Before the advent of sophisticated radiation techniques and transoral laser and robotic surgery, OPSCC was managed surgically via invasive lip split mandibulotomy to gain access to the base of the tongue and palatine tonsil with subsequent reconstruction of the defect with a vascularized free flap.^{11,12} Most of these patients still required adjuvant radiation therapy. In the effort to improve function and minimize morbidity of surgery, definitive radiotherapy was shown to be an effective method of treating stage I and II OPSCC with 5-year local control, regional control, locoregional control, and disease-free survival (DFS) rates of 85%, 93%, 81%, and 77%, respectively.¹³ An Eastern Cooperative Oncology Group (E2399) clinical trial examining the addition of induction and concurrent paclitaxel chemotherapy to the radiation regime showed reduction of the 2-year local failure rate of stage III and IV OPSCC to 16% with a 2-year overall survival rate of 83%.¹⁴ In 2002, a meta-analysis of patients with OPSCC found equivalent survival outcomes for patients treated with surgery and adjuvant radiotherapy versus definitive radiotherapy with salvage neck dissection. It also found that there was a significant difference in severe complications between the two cohorts favoring definitive radiotherapy.¹⁵ Despite this effectiveness, chemoradiation is still associated with significant long-term toxicity and functional impairment.^{16,17} Up until 2009, in most countries in the world, primary radiation with or without chemotherapy is still the main treatment option for OPSCC.

SURGICAL TREATMENT OF OROPHARYNGEAL SQUAMOUS CELL CARCINOMA

With the improved outcomes to radiotherapy of HPV-related OPSCC as elucidated earlier, and the never-ending quest of providing the most effective treatment with the least morbidity, there has been a recent paradigm shift of the management of early OPSCC toward minimally invasive transoral surgery. This review focuses on the analysis of margins obtained by these minimally invasive surgical treatments.

Transoral Laser Microsurgery

Transoral laser microsurgery (TLM) is not a novel concept and was introduced by Steiner and colleagues^{18,19} for the management of laryngeal and piriform sinus carcinomas over the last couple of decades. The same investigators described the use of TLM for OPSCC in 2003.²⁰ In this same period, TLM has gained popularity in centers in the United Kingdom and the United States as an alternative surgical option because of the reduced cost compared with transoral robotic surgery (TORS) and reported superior functional outcomes.^{21,22}

TLM is performed under suspended direct laryngoscopy and an operating microscope to expose and visualize the tumor. Resection is then carried out with a carbon dioxide (CO₂) laser. One key principle of TLM as described by Steiner and colleagues²⁰ that distinguishes it from other surgical treatment is that the tumor is transected at its most proximal portion with the CO₂ laser to estimate the depth of invasion. The primary tumor is then completely resected in multiple blocs to achieve tumor-free surgical margins. Large tumors are transected and cored out to reduce their size, allowing resection of the remaining shell of tumor using a series of transtumoral cuts.

Transoral Robotic Surgery

Weinstein and colleagues²³ reported the first case series using the da Vinci Surgical System (Intuitive Surgical, Inc, Sunnyvale, California) for radical tonsillectomy. After 4 phases of clinical trials confirming the safety, efficacy, and cost-effectiveness, in 2009, the US Food and Drug Administration approved the da Vinci Surgical System for TORS.

For a TORS case, patients are intubated orally with a reinforced endotracheal tube, which is sutured to the contralateral buccal mucosa. Patients are rotated 180° away from the anesthesiologist. The patients' eyes are protected using an adhesive plastic eye shield, and the maxillary teeth are often protected with a dental guard.

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