Changing Paradigms for Oropharynx Cancer: Swinging of Pendulum Back Towards Surgery

Abstract:

The oropharynx, extending from the soft palate to the level of the epiglottis, and containing the palatine tonsils and base of tongue (BOT), is a common site for Head and Neck cancer. Squamous cell carcinoma (SCC) comprises the overwhelming majority of cases. Traditional aetiological factors for oropharynx SCC (OPSCC) are smoking and alcohol consumption. In recent years, human papilloma virus (HPV) type 16 has emerged as the major cause of an ever increasing number of cases[1]. Over the last two decades, there has been a dramatic surge in the incidence of OPSCC. Figures obtained by the Irish National Cancer Registry show an increase from 50 cases per year in 1994 to over 100 cases per year in 2012. This recent rise in OPSCC incidence is almost exclusively related to an increase in HPV related cancers. In the United States, between 1988 and 2004, HPV related OPSCC showed a 225% increase, while HPV-negative OP SCC showed a 50% decline, attributed to decreased prevalence of smoking[1].

The last two decades have also been notable for major shifts in treatment approaches for OPSCC. Traditional surgical treatment with open resection usually required lip split and mandibulotomy, and had a high incidence of major complications including wound breakdown, pharyngocutaneous fistula, and non-union or malunion of the mandible, with little apparent oncological benefit over primary radiotherapy (RT)[2]. This set the stage for a major shift towards non-surgical management from 2000 onwards, which was largely driven by the publication of several landmark trials demonstrating superiority of concurrent chemoradiotherapy (CRT) over RT alone for OPSCC[3,4]. However, CRT is associated with a significantly higher incidence of major toxicity than RT alone[3], including higher incidence of long term swallowing problems, and a high incidence of gastrostomy tube dependence. Thus, enthusiasm for chemoradiotherapy has been tempered of late by concerns regarding increased toxicity and poor functional outcomes.

More recently, our understanding of OPSCC has progressed further with the realization that HPV-related OPSCC has a more favourable biology than HPV-negative OPSCC, and carries a significantly better prognosis[5]. Thus, given the recent marked increase in incidence of HPV-positive OPSCC cases, simultaneous with the increased use of CRT as primary treatment modality, it would appear that much of the excellent reported results for CRT are accounted for to a large extent by a high proportion of HPV-positive cancers. This realization has raised concerns that current CRT protocols with attendant high toxicity may represent overtreatment. However, even though CRT has not been compared with RT alone specifically for HPV-related cancer, the documented superiority of CRT in older trials has led to understandable reluctance by clinicians to withhold chemotherapy from fit patients with advanced stage OPSCC undergoing non-surgical treatment. The present decade has witnessed the development and refinement of new surgical techniques for removal of selected OPSCCs by a completely transoral approach using either laser or robotic assistance, which has offered an alternative approach to OPSCC[6,7]. Transoral laser surgery (TOLS) or transoral robotic surgery (TORS) avoids most of the morbidity of traditional open surgical resection, with much faster recovery of swallow function. These techniques would also appear to have advantages over primary CRT, including reduced toxicity and avoidance of need for routine gastrostomy tubes.

TOLS or TORS is generally performed under high magnification using an operating microscope or endoscope. In the case of TOLS, resection is effected using carbon dioxide (CO2) laser delivered by a fibreoptic cable. This allows complete transoral resection of tumours which would not be feasible using traditional instruments due to anatomical constraints, e.g. due to location of tumour â around the cornerâ from the surgeon, which is a particular issue for tumours involving the BOT. Concomitant or delayed neck dissection is generally required to deal with metastatic neck disease, or to exclude occult metastases in the case of patients with radiologically negative necks. For many patients, postoperative RT will still be required due to advanced stage neck disease (N2+), positive margins, or other adverse pathological features, however, this is generally a lower dose than given for primary CRT, and in most cases, chemotherapy can be withheld. For patients without adverse features, RT can be withheld altogether, and excellent oncological and functional outcomes anticipated. The oncological outcomes of TOLS/TORS would appear to be at least as good as the best reported results for CRT. Typically reported local control rates range from 91-98%[6,7], with overall survival reports of 86% at 3 years, and 85% at 5 years[8].

Where TOLS/TORS may offer significant advantages over CRT is with respect to functional outcomes. Even in cases where postoperative RT is recommended, the dose can usually be reduced compared to that given with primary CRT, and chemotherapy completely withheld, with reduced RT dose to constrictor muscles and avoidance of chemotherapy-related toxicity leading to better swallowing outcomes. This supposition would appear to be supported by the excellent reported functional outcomes of OPSCC patients treated by TOR, with normal swallowing achieved by most patients within 3 weeks, and rates of long-term gastrostomy dependence of 0-9%[6,7], which compares favourably to long-term gastrostomy dependence rates of 26-29% after CRT[3]. Furthermore, although prospective data comparing TOLS/TORS to CRT are lacking, there appears to be growing retrospective data suggesting a benefit for TOLS/TORS in swallowing outcomes and quality of life measures[10].

In the future, it is possible that further improvements in functional outcomes may emerge if the dose of postoperative RT can be further de-escalated in patients without adverse histological parameters. This is the subject of a currently ongoing randomized controlled trial (ECOG 3311). In conclusion, TOLS or TORS for treatment of suitable OPSCCs would appear to offer excellent oncological outcomes with superior functional outcomes compared to primary CRT, and thus should be considered as primary treatment option in appropriate cases.

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