#### **Editorial**

# The Role of Open Partial Laryngeal Surgery in the Era of Organ Preservation Protocols for Laryngeal Cancer

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# **Keywords**

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#### **Introduction**

We would like to take the opportunity to comment our point of view on the current role of open partial laryngeal surgery in the treatment of Laryngeal Squamous Cell Carcinoma (LSSC) in the era of "organ preservation" protocols.

The concept of "larynx preservation" (LP) protocols was developed with the purpose to heal locally-advanced (T3-T4) LSSC preserving a normal laryngeal anatomy and function.

Such treatments have increased in popularity during the last decades thanks to the development of new chemotherapeutic drugs (taxans and biological therapies) and to the improvement of radiotherapy technologies, (i.e. Intensity-modulated radiotherapy, IMRT). However, in the last years, new surgical options and techniques have been developed as well. In particular, the introduction of supratracheal laryngectomies (tracheohyoidopexy and tracheohyoidoepiglottopexy) have extended the potentialities of "Conservative" Laryngeal Surgery (CLS) in the treatment of locally advanced LSSC [1]. Moreover, the classification of such techniques into the Open Partial Horizontal Laryngectomies (OPHLs) system has allowed a standardization of CLS techniques and indications [1]. When the Department of Veterans Affair Laryngeal Cancer Group published in 1991 the landmark study that shifted the trend of laryngeal cancer treatment toward non-surgical management [2], the OPHLs system and surgical techniques had not been developed yet. Nowadays, the availability and the oncologic/functional results of partial laryngectomies [3-5], should be considered when selecting "organ preservation" treatments for locally-advanced (T3-T4) LSCC.

# Clarifying the Concept of "Organ Preservation"

Basing on the American Committee on Cancer (AJCC) system, T3-T4 LSSC categories include a variety of neoplasms with different extension: a) T3 may include LSCC with vocal cord fixation and/or invasion of paraglottic spaces, and/or with minor thyroid cartilage erosion; b) T4a may include LSCC with transmural erosion of the

thyroid cartilage, and/or massive involvement of the extralaryngeal soft tissues, and/or extension to the trachea and/or hypopharynx [6]. Such heterogeneous subcategories are associated with different therapeutic options and prognosis, and should be considered separately, though the International Classification of Diseases for Oncology, 3<sup>rd</sup> Edition (ICD-O-3) does not distinguish them [3-6].

When considering "larynx preservation" treatments, the exact meaning of "preservation" (i.e. not having undergone total laryngectomy) should be kept in mind: the definition of "organ preservation" protocol implies the alternative surgical treatment is only total laryngectomy [7]. A part from specific and rare contraindications (i.e. severe bronchopulmonary chronic obstructive disease, neurological problems impairing the ability to expectorate and/or swallow), most T3 and selected T4a LSCC can be successfully managed by OPHLs [3-6]. Obviously, partial laryngectomy is a larynx- preserving treatment. Considering a nonsurgical treatment as organ preservation protocol, when a partial laryngectomy is feasible, does not seem appropriate.

# "Larynx Preservation" Protocols: Lessons Learnt from the Past

During the last decades, LP has been the cornerstone of advances in larynx cancer therapy. Since the early Veterans Affairs laryngeal study, neoadjuvant therapy has been believed to achieve organ preservation without compromising survival in most patients (66%) with locally advanced LSCC [2]. This finding was further supported by the European Organization for Research and Treatment of Cancer larynx preservation study [8]. Afterwards, the Radiation Therapy Oncology Group (RTOG) 91-11 trial found a higher rate of LP after concurrent platinum-based chemoradiotherapy (hazard ratio, 0.46; 95% CI, 0.30-0.71), resulting in the adoption of this approach as the treatment of choice for LP in most western countries [7]. Despite such favorable results, the most effective multimodal regimen leading to LP without increasing mortality has, however, remained elusive, and questions persist as to the multimodal regimen of choice for LP. This uncertainty stems from several factors: even though locoregional control and LP were significantly improved in the chemoradiotherapy group compared with the induction or radiotherapy alone group in the RTOG 91-11 trial, more deaths were classified as unrelated to larynx cancer or treatment in the chemoradiotherapy group (30.8%) compared with induction (20.8%) and radiotherapy alone (16.9%), raising concerns for long-term treatment-induced toxic effects in the chemoradiotherapy group [7].

Furthermore, even though no significant difference in LP existed when comparing radiotherapy alone with induction, induction was slightly favored. This finding, together with a higher disease-related mortality in the radiotherapy group *vs.* the induction group, raises questions about whether the induction regimen ought to be

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a reasonable compromise between the high overall mortality in the chemoradiotherapy group on one hand and the higher disease-related mortality in the radiotherapy-only group on the other. Regardless of the single protocols, it is worth noting the recent information from the National Cancer Database and the Surveillance, Epidemiology, and End Results Program, which shows overall survival (OS) for patients with laryngeal cancer has decreased in the United States from 1975 to 2010 [9], after the introduction of chemoradiotherapy approaches for LP. Given these facts, we should probably conclude that a onesize-fits-all approach (chemoradiotherapy) is probably wrong and that OPHLs approach may be a viable alternative both in terms of OS and laryngeal function preservation. Succo et al report a 5-year OS among patients with T3 glottic carcinoma treated with OPHLs of 87.8%, which is extremely promising when compared with the results obtained with non-surgical treatments [4]. As to functional outcomes, in their recent study Al-Gilani et al [10] reported a gastrostomy dependence rate of 30.6% among patients receiving "unspecified" surgery plus Radiotherapy (RT), while Succo et al reported 98.6% of their patients submitted to OPHLs without radiotherapy were free of feeding tube/gastrostomy one year after treatment. The high rate of gastrostomy dependence Al-Gilani found in his study was attributed by the author to the additional side effects of surgery and radiotherapy in terms of tissue fibrosis and neuromuscular dysfunction. On the contrary, OPHLs offer wide margins of resection, with a consequent rarer indication to postoperative RT on the residual larynx, which may explain the lower rate of dysphagia noticed by Succo et al [4,5].

#### **Conclusion**

#### Lessons for the future and teachings to our trainees

As a practitioner working in the 21st Century, re-assessing standardized protocols and critical analysis of treatment results are the foundations of progressive laryngeal oncology. The recent information from the National Cancer Database and the Surveillance, Epidemiology, and End Results Program (suggesting a modest but significant survival disadvantage associated with nonsurgical therapy) should raise questions as to whether the widely used chemoradiotherapy approach in the United States is leading to increased mortality and should suggest considering OPHLs surgery as a valid alternative to non-surgical LP protocols.

As junior laryngeal surgeons learn their skills, they inevitably emulate their masters and should pass through a learning curve that leaves them feeling comfortable with any kind of laryngeal surgery, including OPHLs. Learning such techniques requires time and energy. However, if we are to make progress, the results of LP treatments should be re-visited and the role of partial laryngeal surgery should be underlined. The guiding principle for the best treatment for each patient is adapting the treatment to the disease in every single patient

(and not adapting the disease/patient to standard protocols). If we want to offer our patients the best treatment option, the surgeon of the Head & Neck Multidisciplinary Team should be able to perform all types of laryngeal surgery. Therefore, the role of LP protocols should be limited to those cases where the alternative surgical treatment is only total laryngectomy (i.e. no OPHL is applicable).

We also may need to accept a lower rate of organ preservation in exchange for maintaining a better overall survival and quality of life at least for some patients, since a dead patient does not really care whether his or her larynx is intact.

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