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Management of Early Glottic Cancer

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1. Introduction

The management of early glottic cancer has evolved significantly over the past decade, with transoral laser (TOL) surgery and radiotherapy emerging as the two most prevalent treatment modalities. The selection of one modality over another continues to generate controversy. With both modalities showing similar efficacy with regard to survival and oncologic outcomes, the selection of one modality over another hinges upon vocal function, quality of life, and cost-effectiveness as the main outcomes of interest. This chapter will begin with a brief overview of the epidemiology and presentation of glottic cancer and will follow with a comprehensive overview of the contemporary literature comparing both treatment modalities.

2. Epidemiology and clinical presentation of glottic cancer

Laryngeal cancer is the most common malignancy of the upper aerodigestive tract (Fowler, 1997) with Surveillance Epidemiology and End Results (SEER) data estimating that 12,720 men and women (10,110 men and 2,610 women) were diagnosed with laryngeal cancer in 2010. This data estimated that 3600 men and women will die as a result of the disease. The age-adjusted incidence rate was 3.4 per 100,000 men and women per year, and the median age at diagnosis was 65 years of age (SEER, 2011). Squamous cell carcinoma constitutes the overwhelming majority of laryngeal malignancies, with smoking and alcohol abuse as the two most robust etiologic factors.

Malignancy most commonly affects the glottic subsite of the larynx, and the glottis accounts for two thirds of primary laryngeal cancers. Carcinomas of the glottis produce dysphonia at an early stage, and because of poor lymphatic drainage tend not to present with nodal disease (Bouquet, 1988; Groome et al., 2001; Shah et al., 1997). Both of these features allow for single modality therapy of glottic carcinoma in the majority of patients.

3. Management

Radiotherapy and conservation surgery are the two viable treatment modalities employed in the management of early glottic cancer, with concurrent chemoradiotherapy and radical surgery reserved for advanced disease. The controversy in early glottic carcinoma management lies in which modality to select.

Intensity modulated radiotherapy (IMRT) revolutionized radiation delivery to the head and neck in the early 1990s (Webb, 2003). IMRT has now become commonplace for radiation delivery to the larynx, allowing for precision targeting of glottic tumours and the avoidance of nearby critical structures. Surgical options for early glottic carcinoma include transoral laser (TOL) surgery, transoral robotic surgery (TORS), and open partial laryngeal surgery. TOL surgery is the most widely employed surgical option for early glottic carcinoma. TOL surgery was first reported by Strong and Jako (Strong & Jako, 1972) in 1972, and was further developed by others for the management of glottic carcinoma (Eckel et al., 2000). Centres with a significant experience with TOL surgery have expanded the indication to include select T3 and even T4 lesions (Steiner, 1993; Grant et al., 2007; Motta et al., 2005; Blanch et al., 2010). In the last decade TORS has evolved as a new technology for endolaryngeal surgery. The main advantage over TOL surgery is the enhanced surgical exposure, which is not restricted to direct line of sight. The main disadvantages are the increased operative time (which has been shown to improve with greater surgical experience (Genden et al., 2009)), and the significant financial cost of the surgical robot, its maintenance, and its per-case disposables. Currently there is no evidence demonstrating improved oncologic or functional outcomes with TORS compared to conventional TOL surgery. Open partial laryngeal surgery for early glottic carcinoma is on the decline (Silver et al., 2009). This is due to the growing availability of laser technology, the growing experience with TOL surgery, and the decreased morbidity and length of hospital stay with TOL surgery (Silver et al., 2009). Our institution restricts open partial laryngeal surgery to small, localized laryngeal carcinomas that have recurred after primary radiation or concurrent chemoradiation therapy (rT1, rT2).

Selection of one modality over another, be it TOL surgery or radiotherapy, is controversial because both modalities are similarly efficacious with respect to oncologic and survival outcomes. Because of this, many contemporary studies have focussed on vocal function, quality of life, and cost-effectiveness as important secondary considerations.

3.1 Oncologic and survival outcomes

A host of studies, largely consisting of case series, have reported oncologic and mortality outcomes with TOL surgery and radiotherapy. This led our group to publish a meta-analysis (Higgins et al., 2009) comparing laser excision to radiotherapy for the treatment of early carcinomas of the glottic larynx. The meta-analysis included over 7600 patients and compared local control, laryngectomy-free survival, and overall survival between modalities. No significant difference between TOL surgery and radiotherapy was found for local control (OR 0.81, 95% CI 0.51-1.3) and laryngectomy-free survival (OR 0.73, 95% CI 0.39-1.35). However, the analysis showed a significant increase in overall survival in favour of TOL surgery (OR 1.48, 95% CI 1.19-1.85).

Three recent single-arm series on radiotherapy for early glottic carcinoma have been published after our 2009 meta-analysis. New series by Tateya et al (Tateya et al., 2010) (150 patients with T1 and T2 disease) and Sjogren et al (Sjogren et al., 2009) (316 patients with T1 disease) noted excellent local control and overall survival rates with radiotherapy, and these results were in keeping with the published literature. Hafidh et al (Hafidh et al., 2009) reported a recent 150-patient Canadian series with 5-year T1 and T2 local control rates of 71.0% and 63.3%, respectively. The pooled T1 and T2 local control rate observed in this

study was lower than those observed in the single-arm radiotherapy case series included in our meta-analysis¹⁵, which ranged from 77.4% to 88.0%.

TOL surgery has since been studied in two single-arm series. A series by Rucci et al (Rucci et al., 2010) included 81 patients. Over one third of tumours involved the anterior commissure, a known poor prognosticator for local control with either TOL surgery or radiotherapy. The reported local control rate was 74.1% and was out of the 75.1% to 93.7% range observed in our meta-analysis (Higgins et al, 2009). Another recent series by Ansarin et al (Ansarin et al., 2010) looked specifically at patients aged 70 years or older, and documented excellent local control and overall survival rates in keeping with the published literature.

Most importantly, three studies published after our 2009 meta-analysis compared TOL surgery and radiotherapy head-to-head. Two of these studies (Mahler et al., 2010; Schrijvers et al., 2009) demonstrated a significant increase in laryngectomy-free survival (LFS) in the TOL surgery groups. The third study (Kujath et al., 2011) found a trend for increased LFS with TOL surgery.

Overall, recent single-arm series may serve to strengthen existing data which demonstrate excellent local control and survival for both modalities, but offer little new information. Two of the three head-to-head comparison studies (Mahler et al., 2010; Schrijvers et al., 2009) have demonstrated that laryngectomy-free survival may be better with TOL surgery than with radiotherapy.

3.2 Voice and quality of life

A recent systematic review (Spielmann et al., 2010) sought to determine whether there was a difference in voice outcomes and quality of life between TOL surgery and radiotherapy. The authors determined that voice outcomes and global quality of life (QOL) outcomes were comparable between modalities and stressed the need for uniform use of specific voice and QOL measurement tools to reliably make comparisons between studies. Of the fifteen studies included in the objective voice outcome analysis of the Spielmann et al review, only three demonstrated significantly better objective voice outcomes with radiotherapy. Each of these three studies used electroacoustic analysis, the criticism being that this form of objective analysis may not correlate well with subjective vocal function and QOL. Of the nine studies in the review that reported QOL outcomes, four used the Voice Handicap Index (VHI). One of these studies (Peeters et al., 2004) reported a significant improvement in the overall VHI score with TOL surgery. The remaining three studies demonstrated no significant difference in overall VHI scores between modalities. Looking again at the Spielman et al review, two of the nine studies included in the QOL analysis employed the European Organisation for Research and Treatment of Cancer (EORTC) QLQ C30 and QLQ H&N 35 questionnaires. One of the two studies (Stoekli et al., 2001) demonstrated improved swallowing, salivary function, and dental health with TOL surgery.

Two recent Canadian studies (Kujath et al., 2011; Osborn et al., 2011) have compared voice outcomes between TOL surgery and radiotherapy. The study by Kujath et al was discussed previously with regard to oncologic outcomes, but also looked at subjective voice outcomes in a subset of 79 patients. Two tools were used to measure voice outcome. Patients who underwent TOL surgery were less likely to have an understandability score of 100 or more

(Performance Status Scale for Head and Neck Cancer Patients), and were more likely to have a Voice Handicap Index (VHI-10) score of 10 or more. However, another Canadian study by Osborn et al demonstrated a non-significant trend for increased voice-related quality of life (V-RQOL) among patients who underwent radiotherapy as opposed to TOL surgery.

Our meta-analysis (Higgins et al., 2009) demonstrated a trend for improved voice quality with radiotherapy, yet this was a non-significant finding. Currently, the major argument in favour of radiotherapy is improved voice quality, but this has yet to be born out in large-scale systematic studies. It is also difficult to link electroacoustic analytic outcomes with subjective vocal function and QOL outcomes.

3.3 Cost effectiveness

Our group (Higgins, 2011) recently published a cost-utility analysis comparing TOL surgery to radiotherapy and demonstrated an almost two-fold increase in cost with radiotherapy. The TOL surgery cost \$2475.65 CAD/case, generating 1.663 QALYs, whereas radiation cost \$4965.85 CAD/case, generating 1.506 QALYs. Another Canadian cost analysis was reported by Philips et al (Philips et al., 2009) and concluded that radiotherapy was four times as costly as TOL surgery. A recent Dutch study (Goor et al., 2007) also demonstrated the increased cost of radiotherapy. The total cost of radiotherapy and TOL surgery was 8322 euros and 4434 euros, respectively. In addition, an American study by Brandenburg et al (Brandenburg et al., 2001) demonstrated increased costs associated with radiotherapy compared to TOL surgery. In contrast, a single Belgian study (Gregoire et al., 1999) documented an increased cost of TOL surgery compared to radiotherapy. However, this study reported a 30% positive margin rate in the TOL surgery group, and positive margins were managed with adjuvant radiotherapy instead of re-excision.

Overall, the majority of studies point to an increased cost with radiotherapy compared to TOL surgery. However, it is worthwhile to note that each of these five studies did not include patients undergoing robotic TOL surgery, which may impact significantly on cost effectiveness.

4. Conclusion

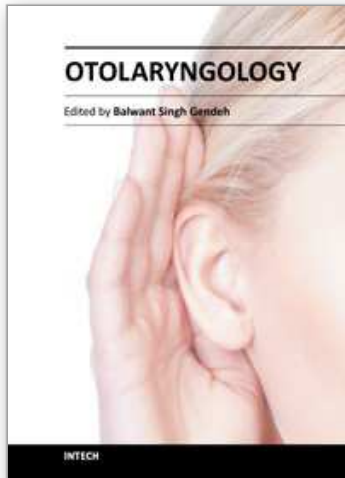
The management of early glottic cancer is controversial, with no head to head randomized controlled trials comparing oncologic/survival or functional/QOL outcomes between modalities. The majority of studies in the literature consist of single arm retrospective series, with few head to head retrospective series. A meta-analysis by our group (Higgins et al., 2009) showed a significant increase in overall survival with TOL surgery, and similar local control and laryngectomy-free survival between modalities. Voice outcomes were similar between modalities, but with an overall tendency for improved voice outcomes with radiotherapy. Three recent head-to-head studies have been published since our analysis, with two of these studies (Mahler et al., 2010; Schrijvers et al., 2009) showing a significant increase in LFS with TOL surgery. A recent systematic review (Spielmann et al., 2010) was unable to find clear differences in voice outcomes and QOL measures between modalities. The review demonstrated improved electroacoustic scores in some patients treated with radiotherapy, but did not demonstrate improvement in voice QOL. The most striking difference between treatment modalities is financial, with four of five recent studies

(Higgins, 2011; Philips et al., 2009; Goor et al., 2007; Brandenburg et al., 2001) showing TOL surgery to be more cost-effective. It is also worthwhile to note that TOL surgery is less time consuming for patients. Patients undergoing TOL surgery convalesce over a matter of days while patients undergoing radiotherapy are treated over four or more weeks. In summary, it is our view that although TOL surgery and radiotherapy may share similar oncologic, voice, and QOL outcomes, TOL surgery offers the distinct advantages of reduced health care costs and shorter duration of treatment.

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This book emphasizes on different aspects of otolaryngology - the medical sciences of diagnosis and treatment of ENT disorders. "Otolaryngology" is divided into various clinical sub-specialities, namely otology, rhinology, laryngology, and head and neck. This book incorporates new developments, as well as future perspectives in otolaryngology. I would like to dedicate this book to those of you who will pick up the torch and by continued research, close clinical observation and the highest quality of clinical care, as well as by publication and selfless teaching, further advance knowledge in otolaryngology from this point forward. It is intended to be a guide to other books to follow. Otolaryngologists, researches, specialists, trainees, and general practitioners with interest in otolaryngology will find this book interesting and useful.

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