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Treatment Considerations for Early Glottic Carcinoma: Lessons Learned and a Primer for the General Otolaryngologist

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Abstract

In this commentary, we review our experience with early glottic carcinomas in an attempt to identify points to consider when developing a treatment protocol and technical considerations in oncologic resection to maintain laryngeal function. We highlight several consistent themes: (1) difficult exposure is not always a contraindication to endoscopic resection; (2) depth of invasion may be apparent only intraoperatively; (3) radiation therapy should be offered for deeply invasive cancers requiring extensive cordectomy or for patients who cannot afford lengthy vocal downtime; however, (4) radiation therapy leads to acute dysphagia and collateral damage to the contralateral vocal fold that is avoided with surgery; (5) good voice can be obtained after healing if resection is limited to intramuscular cordectomy; (6) the key to optimal vocal results is adequate glottal closure; and (7) second look operations are occasionally necessary, and therefore preoperative counseling should include this possibility. Since both surgery and radiation therapy achieve excellent oncologic control, a patient-centered approach is preferred in management.

Keywords

glottic cancer, laryngeal dysplasia, endoscopic laryngectomy, voice outcomes, swallowing outcomes, radiation therapy

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Introduction

The goal in treatment of early laryngeal cancers is to preserve sufficient anatomy to maintain voice and safe swallow function without compromising cure. Standard treatment options include partial laryngectomy and radiation therapy (RT). Many studies have reported equivalent cure rates for these modalities; thus, debate continues as to the optimal therapeutic approach for early glottic carcinoma.

The goals for endoscopic resection include: (1) excellent laryngeal exposure, (2) sufficient margins (1 mm for glottic cancer), (3) preservation of lamina propria, and (4) post-operative glottic closure.¹ The following is a primer in treating glottic cancer with an eye to the aforementioned goals while highlighting a patient-centered approach. Using representative cases, we identify common clinical challenges and lessons learned based on treatment decisions made.

Institutional Review Board approval was obtained from the University of California, Los Angeles for this review.

Scenario 1: Difficult Laryngeal Exposure

A 71-year-old obese man with hoarseness was referred following attempted direct laryngoscopy, which was aborted due to inadequate exposure. Office laryngoscopy demonstrated a T1a lesion of the left mid-membranous vocal fold (**Figure 1**). In the operating room (OR), a Dedo laryngoscope could not be advanced beyond the tongue base due to a small mandible and very large tongue. A Holinger anterior commissure (AC) laryngoscope was advanced, albeit with difficulty, and the mid- and posterior larynx was eventually exposed via external cricoid pressure. ELS type I-II resection (based on the European Laryngological Society cordectomy classification) was performed using a microscope-mounted carbon dioxide (CO₂) laser.² After 2.5 years, the patient remains disease free with a highly satisfactory voice result (mildly rough vocal quality) and symmetric mucosal waves.

Lesson 1. Small, mid-membranous cancers can be removed endoscopically in most patients—even when exposure of

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Figure 1. T1a lesion of the left mid-membranous vocal fold.



Figure 2. Moderate to severe dysplasia of the vocal folds progressed to form a right vocal fold mass and ipsilateral immobility in a patient who was lost to follow-up for 8 months.

the commissure is limited—with excellent voice and oncologic control and avoidance of RT. A Holinger laryngoscope is not ideal for laser surgery, due to monocular vision; other laryngoscopes that enable AC exposure with binocular vision, such as an Ossoff-Pilling or Kleinsasser laryngoscope, should be considered, if available. Another option is use of flexible laser bronchoscopy, employing the potassium-titanyl-phosphate (KTP), CO₂, or other lasers.³

Scenario 2: Chronic Dysplasia

A 39-year-old teacher presented after many years of hoarseness. Biopsies demonstrated moderate to severe dysplasia of both vocal folds. The following 3 years, periodic laser ablations of the dysplasia were performed. He was lost to follow-up for 8 months, then returned with a right vocal fold mass and ipsilateral immobility (**Figure 2**). Neck exam revealed a palpable lymph node on the right. Magnetic resonance imaging showed fullness and enhancement of the vocal fold with

infraglottic extension of a mass filling the cricothyroid membrane. Following biopsy, he was staged with T3N1 squamous cell carcinoma (SCCA) and referred for chemoradiation therapy (CRT). He developed marked dysphagia following CRT lasting 6 months, although he maintained an oral diet. Fifteen months later, he remains free of disease, with some return of right vocal process mobility.

Lesson 2. Laryngeal dysplasia is a chronic condition. Unless a small area is involved that can be completely excised, voice-preserving surgical approaches and continued vigilance is necessary. Of all patients who undergo excisional biopsy of dysplasia, 14% will have recurrences, with progression to cancer in 6% (with moderate or high grade). The latency period between initial diagnosis and cancer is approximately 4 years for mild, 3 years for moderate, and 2 years for severe dysplasia.⁴

Lesson 3. Posttreatment dysphagia occurs in 50% to 60% of patients as a result of RT and CRT due to multiple factors, including trismus, fibrosis, and stricture. Swallowing continues to evolve over the first year after treatment. After this time, additional improvement in swallowing is unlikely, particularly without intervention. In our experience, the bulk of spontaneous symptom improvement in swallowing occurs after the initial 6 months, and the patient should be counseled accordingly. Of course, this will vary with radiation dosing parameters. Participation in a swallow preservation program helps maintain a functional swallow, thereby limiting adverse effects on quality of life (QOL).⁵

Scenario 3: Balancing Voice and Cancer Treatment

A 42-year-old physician presented with 3 months of persistent hoarseness. Laryngoscopy, poorly tolerated due to a strong gag reflex, demonstrated a superficial left vocal fold mass, and office biopsy was notable for “at least carcinoma in situ.” Goals established during pretreatment counseling included curing cancer, minimizing vocal downtime, avoiding significant decrement in vocal quality, and allowing this physician-patient to quickly resume his clinical responsibilities. Given the disease’s superficial appearance, he opted for surgical excision. Intraoperatively, the mass was more endophytic than suspected, with extension to the vocal ligament. ELS type II resection was performed. Permanent section confirmed a diagnosis of moderate to well differentiated SCCA. The anterior margin contained moderate dysplasia.

Several laser procedures were performed over the following 4 months to address the dysplasia. The patient was taken back to the OR for a second look and repeat biopsy, which demonstrated mild dysplasia. Three months later, he developed a 5 mm mass of the anterior left vocal fold, at the site of known dysplasia. ELS type II resection was performed, and deep margin frozen section biopsy of the vocalis muscle contained “atypical squamous epithelium.” In order to minimize the patient’s vocal downtime, however, deeper resection (ELS type III) was not performed. Final

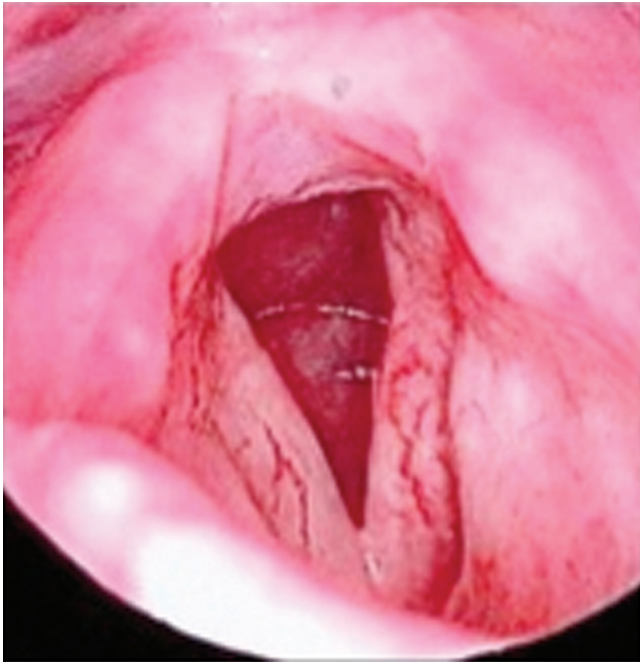


Figure 3. Bilaterally edematous and hypervascular-appearing true vocal folds following radiation therapy for a glottic carcinoma.

section confirmed atypia and further stated, “Cannot rule out SCCA.” After discussion with the patient, he was referred for RT.

From a QOL perspective, he was able to resume his busy surgical schedule and continued to work throughout his RT. He also developed dysphagia symptoms lasting 6 months, although he was able to maintain an oral diet. Surveillance examination shows bilateral mildly edematous and hypervascular-appearing true vocal folds (**Figure 3**). His voice is mildly rough, and he is able to maintain his clinical duties with avoidance of voice overuse. Interestingly, since completing RT, he tolerates laryngoscopy without his previous intense gag reflex.

In addition to reinforcing lessons 2 and 3, the following new lessons are illustrated by this case.

Lesson 4. While improved post-RT tolerance of office laryngoscopy may not be of immediate oncologic or functional concern, it is notable because nerve damage is a well-known morbidity of head and neck irradiation. It may result in any number of cranial neuropathies, and sensory nerves are susceptible to injury as well, as illustrated here.⁶ Sensory neuropathy is a significant sequela of RT, affecting long-term swallowing function.^{7,8} Of course, patients who undergo multiple laryngoscopies may also eventually learn to tolerate any uncomfortable sensation, and thus improve their tolerance as well.

Lesson 5. Sometimes, depth of invasion may not be apparent until operative microlaryngoscopy, despite careful preoperative examination. The endophytic nature of this lesion likely contributed to deeper tumor extent and recurrence. For the



Figure 4. A small mass is noted following ELS type II resection of glottic carcinoma, at the resection site. Pathology demonstrated granulation tissue without evidence of dysplasia or carcinoma.

patient with deeply invasive disease who cannot afford lengthy vocal downtime following extensive cordectomy, surgery in combination with RT or RT alone is an option. CO₂ laser salvage cordectomy is an important therapeutic option in cases of persistent or recurrent disease following RT and should be discussed preoperatively as well.

Lesson 6. During RT, the contralateral larynx receives a nearly full dose of radiation, leading to its associated complications, unlike endoscopic resection. This merits pretreatment dialogue with the patient when a discussion of risks and benefits of various treatment options occurs.

Scenario 4: New Mass Following Endoscopic Cancer Resection

A 78-year-old man presented with several months of dysphonia and a biopsy reporting moderately differentiated SCCA of the right true vocal fold. ELS type II resection using the CO₂ laser was performed, with negative margins. Three months later, vocal quality diminished, and laryngoscopy revealed a small mass at the resection site (**Figure 4**). He was taken back to the OR. Excisional biopsy was performed. Pathologic section revealed granulation tissue, with no carcinoma. Despite scarring of the right vocal fold, his postoperative voice improved markedly, with mild roughness and normal projection. He remains disease free 18 months postoperatively.

Lesson 7. Granulation tissue can occur after laser resection. Surgical evaluation and excision are necessary if any oncologic concerns remain. Preoperative counseling should include the possibility of a “second look” to provide close surveillance. This is especially important in previously irradiated patients, as high levels of background inflammation may prevent accurate office examination. Laser cordectomy is an excellent salvage option in those patients found to have persistent/recurrent disease.

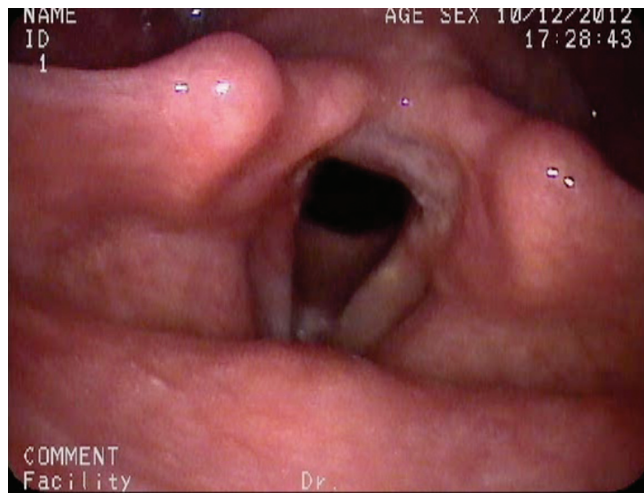


Figure 5. Tissue regeneration 16 months following near-total right cordectomy.

Lesson 8. If glottic closure can be achieved, a good voice result can be obtained—even if only one vocal fold generates mucosal waves. In fact, subligamentous cordectomy may produce better postoperative voice and stroboscopic results than subepithelial cordectomy. Therefore, a more aggressive resection to achieve a straight vocal fold edge should be considered if cancer reaches the vocal ligament and only minimal lamina propria can be preserved.⁹

Scenario 5: Extensive Resections

A 37-year-old man presented with 6 months of dysphonia. Office laryngoscopy, challenging due to marked gagging, demonstrated tumor involvement of the right vocal fold from the vocal process to the AC. An outside biopsy demonstrated SCCA. Following discussion of the risks and benefits of surgery and RT, the patient opted for surgical excision, with the understanding that a prolonged period may be necessary for voice recovery.

Intraoperatively, the tumor was bulky and deep with muscular invasion. ELS type Va cordectomy was performed, including near total right cordectomy, and excision of the AC and left anterior vocal fold. Postoperatively, no remnant right vocal fold was visible on laryngoscopy. His voice was markedly rough and breathy, consistent with the large glottic gap. Sixteen months postoperatively, he remains disease free. The vocal fold slowly healed, with tissue regeneration (**Figure 5**). Vocal quality increased with improving glottic closure; his most recent speech evaluation notes mild breathiness and roughness, and the patient describes his voice as “nearly normal.” Laryngoscopy continues to be poorly tolerated in this non-irradiated patient.

Lesson 9. Extensive cordectomy (ELS type III-Va) does not necessarily lead to a poor voice result, as long as one has the patience to wait for tissue regeneration. Generally, ELS type I-III cordectomies will have favorable voice results, following healing. Vocal quality after ELS types IV and V cordectomies is less favorable, based on analysis of

maximal phonation time, jitter, shimmer, noise-to-harmonic ratio, and voice-handicap index.¹⁰ However, with preservation of paraglottic space and some lateral vocal fold tissue, the glottis has an ability to regenerate and provide glottic closure for voice regeneration. Therapeutic options for improving voice after treatment of early glottic cancer, such as injection or medialization thyroplasty, are available.

Conclusion

Many articles have been published presenting oncologic and voice results of endoscopic resection and RT. Cure rates for both modalities are excellent, although there is ongoing controversy regarding morbidities associated with each. In addition, however, it is helpful to have a practical, patient-centered perspective on planning therapy in various clinical situations. This commentary is meant to provide that perspective for the otolaryngologist who does not routinely care for patients with glottic cancer.

Author Contributions

Nausheen Jamal, project design, acquisition and interpretation of data, writing, revising, and final approval of manuscript; **Elazar Sofer**, project design, acquisition and interpretation of data, drafting and final approval of manuscript; **Dinesh K. Chhetri**, project conception and design, data interpretation, critical revision and final approval of manuscript.

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