Addressing an unmet need in oncology patients: rehabilitation of upper aerodigestive tract function

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Received 21 May 2010; revised 6 October 2010 & received 5 November 2010; accepted 19 November 2010

Background: Laryngeal dysfunction in the oncology population is common and may detract from quality of life (QoL) due to vocal restriction and aspiration. Therapies to address this complex issue have not been explored to date. We examined the outcomes among oncology patients treated with a minimally invasive office-based surgical approach for the rehabilitation of laryngeal dysfunction.

Patients and methods: A retrospective analysis was carried out of oncology patients referred for laryngeal dysfunction. Patients who underwent minimally invasive injection laryngoplasty (IL) were selected. Subjective outcome measures, objective voice analysis parameters, and swallowing studies were annotated.

Results: Sixty-one patients underwent IL for the management of laryngeal dysfunction. Lung cancer was the most common cancer diagnosis (39.3%), and 52% of patients had thoracic malignancies. All patients had a self-reported improvement in vocal function with a single injection, and 55 patients (90%) reported lasting effects at 3 months. In patients with pre- and postoperative voice analysis, phonatory function increased from 5.0 to 10.5 s, more than twofold improvement compared with baseline functioning. Seventy-one percent of patients who aspirated before injection no longer required a modified diet. There were no major complications.

Conclusions: Interventions to improve the QoL in oncology patients continue to evolve. We report significant improvements in both subjective and objective measures of laryngeal function after IL for vocal fold dysfunction that are both immediate and sustained. We conclude that IL is a safe and efficacious procedure for the treatment of laryngeal dysfunction in oncology patients, resulting in palliation and improved QoL.

Key words: injection, laryngoplasty, oncology, palliative care, upper aerodigestive tract, vocal cord paralysis

introduction

Laryngeal dysfunction in the oncology population is multifactorial and may arise from: (i) iatrogenic vagal or recurrent laryngeal nerve injury in either the neck or chest; (ii) neural compression from tumors in the thoracic or cervical compartments; and (iii) metastasis to the skull base. The impact of this dysfunction can be profound and may detract from quality of life (QoL) due to vocal restriction, reduced exercise tolerance, and aspiration [1]. In decades past, many cancer patients with true vocal cord paralysis and aspiration were relegated to permanent tracheostomy and/or enteric feeding tubes, as well as poor vocal quality, with restoration reserved for those who had been ‘cured’ of their cancers.

The development of office-based injection laryngoplasty (IL) has provided patients a minimally invasive approach to vocal cord rehabilitation without the need for general anesthesia [2]. While others have reported their success with this approach, most previous publications focus on the nononcology patient (with the exception of thyroid cancer) [3–5]. The role of office-based IL in oncology patients has received little attention. The indications for use, functional benefits, and improved QoL have been overshadowed by the number of challenges unique to this population presents as a result of ongoing treatments, anticoagulation, general deconditioning, and end-of-life foci.

We reviewed our experience with office-based management of vocal fold paralysis among patients with ongoing cancer treatment to determine the success and complications of IL in the oncology setting.

patients and methods

The study was approved by the human studies Institutional Review Board at the University of Texas MD Anderson Cancer Center (MDACC). Permission to obtain and/or utilize de-identified pictures located within this ‘Abstract/Manuscript’ was obtained from participants, as part of the informed consent process for standard of care procedures that took place within the Section of Speech Pathology/Audiology at MDACC.
The medical records of oncology patients treated at MDACC with office-based vocal fold augmentation for vocal fold paralysis during January 2007 to February 2009 were reviewed. Sixty-one patients were identified for analysis.

The patients included in the study had vocal fold paralysis and were referred to the Head and Neck Surgical Service at MDACC for intervention to treat their laryngeal dysfunction. Patients were offered IL if they had a documented vocal cord paralysis by videostroboscopic examination and had symptoms associated with these findings, as described below. Patients who were severely debilitated, candidates for permanent medialization thyroplasty (MT), or excessive gag reflex that could not be suppressed with topical anesthesia were not injected.

Laryngeal dysfunction was defined as any one of the following: dysphonia, weak cough, poor airway protection, or aspiration as a result of unilateral vocal fold paralysis. Pre- and postprocedure voice analysis data were collected using the Kay Emetrics Computerized Speech Lab (KayPENTAX, Lincoln Park, NJ). The average maximum phonation time (MPT) was selected and recorded before and after IL to evaluate phonatory efficiency. Laryngeal videostroboscopy was carried out in all cases [6].

All patients underwent office-based vocal fold augmentation with the transthyroidal IL technique using either Cymetra (Lifecell, Branchburg, NJ) or Radiesse (Bioform, San Mateo, CA) [7], as previously described [8]. Informed consent was obtained before the procedure. The affected vocal fold was injected using a 23-gauge needle using videoendoscopic guidance (Supplementary data - video clip, available at Annals of Oncology online). The amount of implant material used ranged from 0.5 to 2 cc. All patients were placed on complete voice rest for 24–48 h after the procedure. All patients were seen in follow-up after the procedure (average 4 weeks) and evaluated by the surgeon and speech pathologist. Patients were queried at their posttreatment visit for subjective improvement in voice quality or volume. Videostroboscopy documented vocal fold closure during phonation. The average MPT was collected after the procedure in the majority of the patients. The pre- and postinjection average MPT was entered and analyzed using SPSS (SPSS version 16; SPSS Inc., Chicago, IL). The paired samples t-test was used to determine statistical significance between pre- and postinjection mean phonation time. P < 0.05 was considered statistically significant.

results

We identified 61 patients who underwent office-based IL for glottic insufficiency during the study period. There were 44 males and 17 females, who reported an average of 6.4 months of symptomatic dysfunction (Table 1). An iatrogenic injury to either the recurrent laryngeal nerve or vagus nerve was the likely etiology in 26 patients (42.6%). Lung cancer was the most common cancer diagnosis, followed by head and neck cancer (Figure 1). No allergic reactions were noted.

All patients (100%) self-reported improvement in their laryngeal dysfunction (voice and/or airway protection), results that were persistent in 90% of patients at an average of 3 months of follow-up (Table 1). Videostroboscopic findings also confirmed improvement in true vocal fold closure after vocal fold injection (Figure 2). In patients with pre- and postoperative voice analysis (n = 33), MPT showed a twofold increase, from 5.0 to 10.5 s in duration (Figure 3). There was no statistical difference in outcomes among patients when the following variables were tested: materials utilized, oncological diagnosis, or oncological treatments.

Among patients with preinjection aspiration symptoms, 10 of 14 (71.4%) patients no longer required a modified diet. Three patients were able to have their tracheostomies decannulated as a result of the improvement in pulmonary toilet. Only seven patients required a secondary injection (11.5%), and all experienced subjective and objective improvement. Five patients underwent a subsequent permanent MT due to the long-standing nature of the paralysis. In the study group, 17 patients (28%) were being treated with either antiplatelet or anticoagulant medications, and none experienced bleeding or bruising complications at the time of

Table 1. Patient demographics and outcomes

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>60.5 (range: 25–81)</th>
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</thead>
<tbody>
<tr>
<td>Gender, n(%)</td>
<td>Male 44 (72.1)</td>
</tr>
<tr>
<td></td>
<td>Female 17 (27.9)</td>
</tr>
<tr>
<td>Duration of symptoms (months)</td>
<td>6.4</td>
</tr>
<tr>
<td>Prior surgery, n(%)</td>
<td>26 (42.6)</td>
</tr>
<tr>
<td>Documented vagal/recurrent laryngeal nerve injury, n(%)</td>
<td>15 (24.6)</td>
</tr>
<tr>
<td>Material used, n(%)</td>
<td>Radiesse 33 (54.1)</td>
</tr>
<tr>
<td></td>
<td>Cymetra 28 (45.9)</td>
</tr>
<tr>
<td>Average volume injected (cc)</td>
<td>1.1 (range: 0.5–2)</td>
</tr>
<tr>
<td>Length of follow-up (months)</td>
<td>3.2</td>
</tr>
<tr>
<td>Improvement, n(%)</td>
<td>61 (100.0)</td>
</tr>
<tr>
<td>Durable improvement (&gt;3 months)</td>
<td>55 (90.2)</td>
</tr>
<tr>
<td>Multiple injections, n(%)</td>
<td>7 (11.5)</td>
</tr>
<tr>
<td>Complications, n(%)</td>
<td>Major 0 (0.0)</td>
</tr>
<tr>
<td></td>
<td>Minor 2 (3.3)</td>
</tr>
<tr>
<td>Permanent thyroplasty, n(%)</td>
<td>5 (8.2)</td>
</tr>
</tbody>
</table>

Figure 1. Distribution of treated patients based upon primary oncological diagnosis.
injection. Complications were few: only one patient required admission to the hospital for subjective dyspnea, but no evidence for obstruction was noted on fiberoptic laryngoscopy. The patient was treated with steroids, and no further intervention was necessary. Another patient developed transient mild dyspnea that was treated conservatively with a short course of oral steroids as an outpatient.

discussion

Despite the significant impact on QoL and function that vocal cord paralysis has on this population, the role of IL in the oncology patient has received little attention to date. IL is a well-described procedure that has been demonstrated to improve glottic function in patients with vocal cord paralysis or paresis mostly as a result of benign disease and is often carried out in the operating room [3, 9, 10]. In this study, we demonstrate that minimally invasive office-based IL can be carried out safely and provide significant improvements in the laryngeal function of patients with cancer. More importantly, no treatment breaks were required, and nearly all patients experienced quantifiable enhancement in speech and, in some cases, elimination of aspiration and improved diet. These findings support the use of this approach more broadly to improve QoL among patients with cancer.

Oncology patients with recurrent laryngeal or vagus nerve injuries experience significant morbidity as a result of this upper aerodigestive tract dysfunction [11]. This can be manifested by changes in vocal quality, decreased phonatory abilities, limited exercise tolerance, chronic aspiration, and poor airway protection [12]. Not only can this impact daily function at home and the workplace by limiting communication with caregivers and co-workers, there is a concern for the development of aspiration-related pneumonia. Managing these issues for those patients who are actively undergoing chemotherapy or radiation therapy, or for patients who experience laryngeal dysfunction as a result of their tumor or the cancer surgery, can be challenging.

For the oncology patient, a number of barriers exist that limit treatment options for vocal fold paralysis. Most importantly, symptoms of limitations in communication are not often solicited by oncologists, and these symptoms are not captured by most QoL measures in the oncology population [13–15]. Other issues include: (i) ongoing chemotherapy and/or radiotherapy, (ii) the need for chronic anticoagulation, (iii) failure to thrive and severe deconditioning, and (iv) focus on end-of-life issues. These factors limit operative interventions, particularly the use of MT [16]. The less-invasive IL also has its limitations in this population when it is carried out in the operating room as it often requires a treatment break from either radiation or systemic therapy in order to anesthetize the patient and perform the procedure. The advantages of the office-based IL, in comparison, include: (i) performance under local anesthesia; (ii) the ability to perform the procedure during the treatment schedule; and (iii) it does not require reversal of anticoagulation. These important advantages have led us to offer this therapeutic modality as a standard approach, with good success and minimal complications.

From a functional standpoint, our results compare favorably with other studies, albeit in a unique and complex patient population. The majority of patients experienced both subjective and objective improvement in vocal function. Only a small percentage of patients went on to receive a second injection, and only five patients underwent a subsequent MT. MT offers a permanent solution to vocal fold paralysis with a more favorable voice outcome, but does require general anesthesia and a transcervical approach for implantation of a foreign body. Thus, we offered a conversion to MT only to those who had achieved durable disease control and had favorable performance scores. Overall, complications were rare, and only one patient required overnight observation and steroids due to mild airway edema, and another with mild dyspnea was treated with oral steroids as an outpatient. No patient required operative removal of the injectate. These
results also compare favorably with other reported studies [4, 5, 17–19].

Although true vocal fold (TVF) paralysis is frequently linked to aspiration among medical professionals, it is of note that unilateral TVF paralysis is rarely the cause of aspiration in patients with an otherwise intact oropharyngeal functioning. Adequate airway protection is often maintained despite TVF immobility because of the duplicity of airway protection mechanisms [20]. The literature reports a prevalence of aspiration in patients with unilateral TVF immobility between 23% and 38% [21, 22]. In our study, instrumental swallowing evaluations were carried out before injection in approximately half (28/61) of the patients. Twenty-eight percent (17/61) of patients had evidence of aspiration on modified barium swallow (MBS) studies before injection. This aligns with cited prevalence data.

In our tertiary oncology setting, the focus of many referrals for vocal fold augmentation is different from the focus in traditional otolaryngology practices. It is frequently the case that the referral is made before the patient is medically ready for instrumental evaluation (MBS or functional endoscopic evaluation of swallowing) for the sole purpose of improving glottic competency for cough as prevention from possible aspiration. Forty-three percent of patients were referred for iatrogenic injury with the sole aim of TVF approximation. Given the medical complexity and fragility of these surgical patients, many physicians prefer to avoid even the risk of food or barium into the surgical site. Furthermore, aspiration status has been shown to correlate with findings such as the relative position of the affected TVF and size of the resulting glottic gap [23], as well as concurrent physiological impairments including reduced hyolaryngeal excursion or pharyngeal range of motion [21, 22, 24, 25]. These findings were considered during laryngeal videostroboscopic examination and were used to guide the selection of those individuals for whom instrumental dysphagia examination was indicated. Among patients who aspirated, 50% who returned for MBS postinjection had resolution of aspiration or improved sensation and clearance. Seventy percent of preinjection aspirators who did not return for postinjection instrumental evaluation were lost to follow-up. The palliative purpose of injection likely explains these cases.

It is important for oncology patients with laryngeal dysfunction to be identified and referred to an otolaryngologist and speech pathologist for diagnosis and treatment. Not every patient with glottic insufficiency will require or even desire an intervention, but our series demonstrates that IL offers a simple and efficacious office-based therapy to appropriately selected patients interested in improving glottic efficiency. These findings highlight the success of the IL technique in a patient population with poor overall oncological outcomes, one that has a significant impact on function during the last few months of life.

Our long-term results are limited as some of these patients were treated in the palliative setting and, thus, follow-up data are lacking. Many providers are reluctant to perform procedures in terminally ill patients, but an increased awareness of palliative care and end-of-life issues has prompted a reexamination of the role of definitive intervention for patients suffering from cancers, at all stages of their disease, with the goal of maximal rehabilitation using minimally invasive techniques. The technique utilized in this series, transcervical IL, offers a safe office-based approach to improve vocal quality and airway protection. Our experience suggests that patients who are treated for end-of-life palliation receive improvements in overall vocal function. Longer follow-up of surviving patients will be necessary to determine the durability of these results.

**Conclusion**

In conclusion, IL is a safe and efficacious technique for augmenting glottic function in select patients with vocal fold paralysis or paresis. Morbidity is minimal, and many patients experience improvements in upper aerodigestive tract function. The procedure can be carried out in an office-based setting, offering several advantages to the oncology patient. This minimally invasive approach obviates the need for interruptions in chemotherapy or radiotherapy. The procedure also eliminates associated blood loss. Although favorable outcomes were observed for patients who aspirated, the aim of vocal fold augmentation in the palliative care setting may be solely to achieve glottic competency for a productive cough to minimize potential for aspiration.

**Acknowledgements**

We thank Francisco Serna for technical support and Terri Astin for administrative assistance. This study was presented in part at the 13th World Conference on Lung Cancer (July 2009, San Francisco, CA) and at the Annual Meeting of the American Academy of Otolaryngology-Head and Neck Surgery (October 2009, San Diego, CA).

**Funding**

MEK has received an honorarium and a travel grant from Bioform Medical, Inc. (San Mateo, CA).

**Disclosure**

The opinions and assertions of the authors contained herein are the private views of the authors and are not to be construed as reflecting the views of the Department of Defense or the Department of the Army. All remaining authors have declared no conflicts of interest.

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