Voice and Swallowing in Patients Enrolled in a Larynx Preservation Trial

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Background: The main goals of larynx preservation protocols are preservation of a functional larynx with intact voice and maintenance of normal deglutition. However, few studies have addressed functional outcomes.

Objectives: To evaluate voice and swallowing in patients enrolled in a larynx preservation protocol.

Design and Setting: Acoustic analysis of 15 patients and videofluoroscopic evaluation of 14 patients who underwent chemoradiotherapy in an attempt to preserve the larynx.

Patients: Forty-three patients with larynx or hypopharynx squamous cell carcinomas were treated with weekly paclitaxel (30 mg/m²) and cisplatin (20 mg/m²) concurrent to radiotherapy (180-rad/d fraction [1.8 Gy] to 7040 rad [70.4 Gy]). Voice was analyzed perceptually and acoustically in 15 patients. Videofluoroscopic evaluation of swallowing was performed in 14 patients, focusing on oropharyngeal motility disorders, stasis, laryngeal penetration, aspiration, and dysphagia severity.

Results: Vocal analysis produced normal results in 1 patient, mild dysphonia in 4, moderate dysphonia in 6, and severe dysphonia in 4. The mean fundamental frequency for acoustic analysis was 131.4 Hz for men and 109.8 Hz for women. Acoustic measures of perturbation and noise were above the reference limits, indicating changes in the voice signal. Swallowing analysis showed inefficient bolus preparation in 13 patients and changes in the bolus propulsion in 12. Stasis was observed in all areas of the oropharynx. Five patients had reduction in laryngeal elevation, and 12 had stasis in the hypopharynx. Five patients presented with silent aspiration. We detected functional swallowing in 3 patients, mild dysphagia in 7, mild or moderate dysphagia in 2, and severe dysphagia in 2.

Conclusions: Laryngeal preservation resulted in voice and swallowing abnormalities, but they tend to be mild to moderate, allowing intelligible communication and efficient swallowing in most patients.

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THERE HAVE BEEN significant advances in the development of larynx-preserving strategies in the last decade. Results of prospective trials indicate that the larynx can be preserved without compromising overall survival. However, there is little information about the ability of these strategies to preserve a functional larynx with normal vocal and swallowing functions, and to date, few studies have analyzed functional outcomes objectively. Oral and pharyngeal motility disorders were found in videofluoroscopic swallowing analysis of 9 patients treated with radiation and chemotherapy for advanced head and neck tumors. Objective measures of voice were studied in 15 patients at varying posttreatment intervals after chemoradiation therapy for head and neck cancer. Woodson et al tried to establish criteria for evaluating vocal function in this population. They learned that laryngeal resistance during standardized phonation was a reliable objective parameter. In the present study, we evaluated a sample of patients who underwent a larynx-preserving protocol and were treated with concomitant paclitaxel, cisplatin, and radiotherapy. The objectives of the study were to characterize voice and swallowing in these patients using acoustic and videofluoroscopic analysis.

METHODS

PATIENTS

From October 14, 1999, to October 23, 2001, 43 patients with advanced squamous cell carcinoma of the larynx or the hypopharynx were included in a larynx preservation study at the Hospital do Câncer A. C. Camargo (São
Paulo, Brazil). Informed consent was obtained from all patients before enrollment. The treatment consisted of weekly paclitaxel (30 mg/m²) and cisplatin (20 mg/m²) concurrent with standard fractionation radiotherapy (180-rad/fraction [1.8 Gy]) to a total dose of 7040 rad (70.4 Gy). Of the 43 patients, voice and swallowing were studied in 10, voice only in 5, and swallowing only in 4 patients. All 19 patients had the larynx preserved and volunteered for the functional study without any prestablished selection criteria. Most patients were in speech and swallowing rehabilitation because of presence of symptoms. The main patient characteristics are depicted in Table 1. The study included 17 men (90%) and 2 women (10%), with a mean age of 59 years (range, 40-70 years). All patients had undergone voice and/or swallowing assessment within 2 to 9 months (mean, 4.7 months) after completion of treatment. No patient had a medical history of neurologic disease, gastroenterologic dysfunction, or previous head and neck cancer. No patient was taking medication that might affect voice or swallowing or had previously undergone voice or swallowing therapy.

VOICE ANALYZATION

Voice was analyzed perceptually and acoustically in 15 patients. All these patients were comfortably positioned standing upright at a 15-cm distance from a microphone (Lyric 8700; Shure, São Paulo, Brazil). We recorded sustained vowel phonation and connected speech for each patient. For the sustained vowel phonation recording, each patient was asked to take a deep breath and sustain the vowel “A” at a comfortable pitch and intensity, as long and as steadily as possible, 3 times. For connected speech recording, the patient was asked to talk about his or her family. All these samples were acquired on a digital audiotape recorder.

Three trained listeners (E.C.A. and A.P.B.B.) recorded the samples of each patient for blind assessment. Listeners rated each vowel sample with respect to the GRBAS (grade, roughness, breathiness, asthenia, and strain) scale, 6 which includes grade of alteration (0, normal; 1, mild; 2, moderate; 3, severe), roughness, breathiness, asthenia, and strain. Acoustic analysis was performed via multidimensional voice program (model 4300B; Kay Elemetrics Corp, Lincoln Park, NJ) to determine 9 acoustic parameters: fundamental frequency, standard deviation of fundamental frequency (STD), jitter (PPQ), shimmer (APQ), noise-to-harmonic ratio (NHR), voice turbulence index (VTI), degree of voice breaks, degree of subharmonics, and degree of unvoiced segments (DUV).

VIDEO EVALUATION

Videofluoroscopic evaluation of swallowing was performed using radiographic equipment (model 1600E; GE Medical Systems, Milwaukee, Wis) and was performed jointly by a radiologist and a speech pathologist (A.P.B.B.). Patients stood during the examination, and the lips defined the focus of the fluoroscopic image: anterosuperiorly by the hard palate, posteriorly by the posterior pharyngeal wall, and inferiorly by the bifurcation of the airway and esophagus at the level of the seventh cervical vertebra. Different types and quantities of material were given during the anteroposterior and lateral views. The material used was liquid and paste barium. The patients were instructed to swallow 2 or 3 types of material 3 times each (liquid, paste, and solid) in variable amounts. The patients were instructed to swallow both the liquid and the paste in quantities of 5, 10, and 20 mL. For the solid material, the patients were instructed to masticate the material well before swallowing. The videotapes were analyzed jointly by 3 trained speech pathologists (E.C.A. and A.P.B.B.). Videofluoroscopy of swallowing was performed in 14 patients. We focused on oropharyngeal motility disorders, stasis, laryngeal penetration or aspiration, and dysphagia severity. Laryngeal penetration and aspiration were evaluated according to the criteria of Rosenbek et al 7 (Table 2). Dysphagia severity was analyzed according O’Neil et al. 8

1. Severe (feeding tube): unable to tolerate any oral contrast safely
2. Moderate to severe (not permitted oral intake): maximum assistance or use of strategies with partial oral contrast only (tolerates at least 1 consistency safely with total use of strategies)
3. Moderate (modified diet and/or independence): total assistance, supervision, or strategies, 2 or more diet consistencies restricted

Table 1. Patient Characteristics

<table>
<thead>
<tr>
<th>Patient No./ Age, y/ Sex</th>
<th>TNM Stage</th>
<th>Tumor Site</th>
<th>Months Since Radiotherapy</th>
<th>Days With Tracheotomy</th>
<th>Days With Feeding Tube</th>
<th>Current Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>1/51/M</td>
<td>T4 M2a M0</td>
<td>Piriform sinus</td>
<td>2</td>
<td>0</td>
<td>81</td>
<td>Alive, larynx preserved</td>
</tr>
<tr>
<td>2/67/M</td>
<td>T3 N0 M0</td>
<td>Transglottic</td>
<td>2</td>
<td>278</td>
<td>234</td>
<td>Death</td>
</tr>
<tr>
<td>3/54/M</td>
<td>T3 N0 M0</td>
<td>Transglottic</td>
<td>4</td>
<td>150</td>
<td>0</td>
<td>Alive, larynx preserved</td>
</tr>
<tr>
<td>4/51/M</td>
<td>T3 N2b M0</td>
<td>Supraglottic</td>
<td>6</td>
<td>0</td>
<td>60</td>
<td>Total laryngectomy</td>
</tr>
<tr>
<td>5/66/M</td>
<td>T3 N1 M0</td>
<td>Glottic</td>
<td>3</td>
<td>0</td>
<td>49</td>
<td>Total laryngectomy</td>
</tr>
<tr>
<td>6/57/M</td>
<td>T2 N0 M0</td>
<td>Supraglottic</td>
<td>4</td>
<td>0</td>
<td>0</td>
<td>Total laryngectomy</td>
</tr>
<tr>
<td>7/67/M</td>
<td>T3 N0 M0</td>
<td>Glottic</td>
<td>9</td>
<td>0</td>
<td>37</td>
<td>Alive, larynx preserved</td>
</tr>
<tr>
<td>8/62/F</td>
<td>T3 N0 M0</td>
<td>Transglottic</td>
<td>9</td>
<td>0</td>
<td>156</td>
<td>Alive, larynx preserved</td>
</tr>
<tr>
<td>9/70/F</td>
<td>T3 N0 M0</td>
<td>Transglottic</td>
<td>6</td>
<td>213</td>
<td>173</td>
<td>Alive, larynx preserved</td>
</tr>
<tr>
<td>10/66/M</td>
<td>T3 N0 M1</td>
<td>Piriform sinus</td>
<td>3</td>
<td>36</td>
<td>...</td>
<td>Gastrostomy</td>
</tr>
<tr>
<td>11/41/M</td>
<td>T4 N0 M0</td>
<td>Transglottic</td>
<td>2</td>
<td>110</td>
<td>0</td>
<td>Alive, larynx preserved</td>
</tr>
<tr>
<td>12/64/M</td>
<td>T3 N0 M0</td>
<td>Transglottic</td>
<td>6</td>
<td>290</td>
<td>2</td>
<td>Alive, larynx preserved</td>
</tr>
<tr>
<td>13/65/M</td>
<td>T4 N2c M0</td>
<td>Transglottic</td>
<td>6</td>
<td>9</td>
<td>157</td>
<td>Alive, larynx preserved</td>
</tr>
<tr>
<td>14/60/M</td>
<td>T4 N2b M0</td>
<td>Supraglottic</td>
<td>9</td>
<td>59</td>
<td>0</td>
<td>Alive, larynx preserved</td>
</tr>
<tr>
<td>15/40/M</td>
<td>T4 N0 M0</td>
<td>Transglottic</td>
<td>6</td>
<td>88</td>
<td>72</td>
<td>Total laryngectomy</td>
</tr>
<tr>
<td>16/59/M</td>
<td>T3 N2b M0</td>
<td>Piriform sinus</td>
<td>3</td>
<td>6</td>
<td>193</td>
<td>Death</td>
</tr>
<tr>
<td>17/56/M</td>
<td>T3 N0 M0</td>
<td>Glottic</td>
<td>2</td>
<td>0</td>
<td>104</td>
<td>Alive, larynx preserved</td>
</tr>
<tr>
<td>18/60/M</td>
<td>T4 N1 M0</td>
<td>Supraglottic</td>
<td>3</td>
<td>89</td>
<td>42</td>
<td>Alive, larynx preserved</td>
</tr>
<tr>
<td>19/65/M</td>
<td>T3 N2b M0</td>
<td>Piriform sinus</td>
<td>6</td>
<td>0</td>
<td>60</td>
<td>Total laryngectomy</td>
</tr>
</tbody>
</table>
4. Mild to moderate (modified diet and/or independence): intermittent supervision or cueing, 1 or 2 consistencies restricted
5. Mild (modified diet and/or independence): distant supervision, may need 1 diet consistency restricted
6. Within functional limits or modified independence (normal diet): patient may have mild delayed swallowing reflex, stasis spontaneously cleared, and there is no penetration or aspiration
7. Normal (normal diet): normal in all situations and the patient does not need strategies or extra time

**STATISTICAL ANALYSIS**

Statistical analysis was performed using the t test (2-tailed, unpaired) to verify the differences between the variables STD, PPQ, APQ, NHR, DSH, and DUV and the reference values (Kay Elemetrics database) with a 95% significance level. The nonparametric Kruskal-Wallis test was preferred to verify the differences among median values for acoustical analysis and grade of dysphonia (0, normal; 1, mild; 2, moderate; and 3, severe).

**RESULTS**

All 19 patients selected for this study had a complete response to chemoradiotherapy, with no detectable tumor at the date of the functional evaluation. Eleven patients (58%) underwent a tracheotomy at some point during the treatment (range, 0-290 days; mean±SD, 69.9±96.9 days). Fourteen patients (74%) required a feeding tube placement for nutrition at some point (mean±SD, 78.9±47.4 days). At the time of this analysis, 6 patients still had a tracheotomy and 6 patients were still using a feeding tube.

In the follow-up period of 10 to 32 months (mean, 20.5 months), 11 patients (58%) were alive with an intact larynx, 1 patient (5%) was using a gastrostomy tube, 5 patients (26%) underwent a salvage total laryngectomy, and 2 patients (10%) died of cancer.

A normal voice was observed in 1 (7%) of the 15 patients, mild dysphonia in 4 (27%), moderate in 6 (40%), and severe in 4 (27%). The vocal parameters of roughness or breathiness were the most frequent abnormalities (87% and 78%, respectively). The most frequent vocal quality was rough and breathy voice in 47% of the patients. Only 3 patients (20%) presented with strain and/or instability in vocal quality.

Values of acoustic STD, PPQ, APQ, NHR, and DUV were significantly above the reference limits (Table 3). Mean±SD fundamental frequencies of 131.4±36.8 Hz (range, 85.5-212.8 Hz) for the men and 109.8±4.3 Hz for the women were found. There was a wide range of values in all parameters analyzed. Acoustical measures were abnormal, and the measures of STD, PPQ, APQ, NHR, VTI, and DUV demonstrated a significant correlation with the perceptual grade of dysphonia (Table 4).

The Figure shows the events observed during oral and pharyngeal swallowing and the presence of aspiration or penetration (the entry of food to the level of the vocal folds) of each patient. Regarding the swallowing mechanism of these patients, we observed reduced oral swallowing with reduced bolus formation in 13 patients (93%) and reduced bolus propulsion in 12 patients (86%). Stasis was observed in all areas of the oropharynx, in the oral cavity in 13 patients (93%) and in the hypopharynx in 12 (86%). Stasis was especially noticeable in the valleculae and the superior esophageal sphincter (SES). In addition, we observed a reduction of the laryngeal elevation in 5 patients (36%) and, consequently, a reduction of the SES opening. Regarding aspiration, the material did not enter the airway in 3 patients (21%) (score 1 of the penetration/aspiration scale, Table 5). In 6 patients (43%), material entered the airway...
Preservation of normal speech and/or swallowing in patients with advanced laryngeal cancer was unusual in the past. Recent trials combining chemotherapy and irradiation showed that the preservation of the anatomic larynx might be possible without compromising survival. However, preservation of the anatomy does not necessarily result in the preservation of adequate function. Postirradiation xerostomia, fibrosis, edema, and mucositis could have a negative impact on both voice and swallowing functions. The addition of chemotherapy may exacerbate the detrimental effects of radiotherapy.

Perceptual analysis of voice quality has been used in prior studies of laryngeal cancer in patients with stage T1 glottic cancer treated with exclusive radiotherapy. In a previous study by our group, 42.9% of patients with stage T1 and T2 glottic cancer treated with radiotherapy had normal voices. Our current results in perceptual analysis with chemoradiation revealed 5 patients (33%) with a perceptually normal voice or mild dysphonia, 6 patients (40%) with moderate dysphonia, and 4 patients (27%) with severe dysphonia. Most of the patients had a mild or moderate dysphonia that did not affect oral communication. Only 4 patients had a severe impairment in vocal quality that had a real impact on oral communication.

The vocal parameters of roughness (n = 16; 87%) or breathiness (n = 15; 78%) were the most frequent abnormalities. The most frequent vocal quality was rough and breathy voice (n = 9; 47%). Only 3 patients (20%) had strain and/or instability in vocal quality. Besides perceptual analysis, most studies that address the effects of radiation therapy for laryngeal tumors on vocal quality have used acoustic measures.

Our results showed a wide range of fundamental frequency values of the 13 male patients, with a mean ± SD of 131.4 ± 36.8 Hz (range, 85.5-212.8 Hz; reference range, 80-150 Hz). The 2 female patients had fundamental frequencies of 106.7 and 112.8 Hz, which are below reference values for women (150-250 Hz). Although we did not correlate laryngeal data with fundamental frequency, low values of frequency might be related to the laryngeal edema frequently found in these patients. High values of fundamental frequency would be explained by increased stiffness of the vocal folds due to the effects of radiotherapy and scarring at the original tumor site.

Acoustical measures of STD, PPQ, APQ, NHR, and DUV were significantly above the reference limits in patients who underwent laryngeal preservation. This finding may be due to both edema and stiffness of vocal folds. Another possible abnormality in this population would be glottic incompetence due to loss of vocal fold tissue or to paralysis or fixation of the vocal fold away from the midline. Vocal chinks generate increased transglottic airflow and consequently turbulence noise in high frequencies. Our results did not show statistically increased values of VTI.

According to Woodson et al, acoustic measures, although useful in describing vocal quality as measured in the voice laboratory, do not necessarily reflect the functional outcome in terms of communication in daily life. The authors studied various acoustical measures and only found a correlation between PPQ scores and listener...
ratings of perceived voice quality. Contrary to this, we found measures of STD PPQ, APQ, NHR, VTI, and DUV to be significantly correlated with perceptual grade of dysphonia.

Both perceptual and acoustical analyses were reliable parameters for vocal quality evaluation in patients undergoing laryngeal preservation strategies. Acoustical measures seemed also to be useful to describe vocal quality and reflect functional outcome in terms of communication in daily life. In addition, these tests could be useful in evaluating the impact of voice therapy in these patients.

As far as swallowing, studies by Lazarus' and Koch et al. have shown severely impaired swallowing in patients with oral and pharyngeal cancers who underwent chemotherapy and radiation therapy for organ preservation. These studies focused on swallowing-related sequelae that were present within the first 6 months after the completion of therapy. Lazarus et al. demonstrated reduced laryngeal elevation and a significant difference in temporal and distance measures of pharyngeal structure movement of the patients compared with healthy patients. They studied 9 patients, noting aspiration in 8 (89%) of them, and described 3 patients each who could tolerate liquids only, liquids and puree, or all bolus consistencies. They concluded that radiotherapy to the base of the tongue or larynx could adversely affect swallowing. Koch et al. also demonstrated impaired laryngeal elevation, epiglottic movement, and pharyngeal stripping.

Our study confirmed significant oral and pharyngeal dysfunction in all 14 patients studied. Abnormalities observed were characterized by reduced oral swallowing, including reduced bolus formation (n = 18; 93%) and inability to move the bolus through the pharynx (n = 16; 86%). When the salivary glands are included in the irradiation field, the resultant xerostomia and hypolacation further impair mastication and the initiation of the swallowing reflex. Stasis was observed in all areas of the oropharyngeal tract, including the oral cavity (n = 13; 93%) and the hypopharynx (n = 12; 86%); stasis was especially noticeable in the valleculae and the SES. Because of xerostomia and reduced posterior lingual retraction, there is a damping of the bolus propulsive force into the pharynx. Consequently, bolus transit through the pharynx alters its progression and may lead to vallecular retention and piriform sinus stasis. Pharyngeal stasis may also be explained by fibrosis of the pharyngeal muscles, with resultant impairment of pharyngeal contraction. In addition, hypopharyngeal stenosis may occur due to severe fibrosis that is associated with radiation injury. We also observed a reduction of laryngeal elevation in 5 patients (36%) and, consequently, a reduction of the SES opening. Altered laryngeal motion suggests fibrosis of the soft laryngeal tissues.

Regarding aspiration, the material did not enter the airway in 3 patients (score 1 of the penetration/aspiration scale) (Table 5). In 6 patients (43%), material entered the airway above the vocal folds (scores 2 and 3), in 5 it was ejected, and in 1 it remained in the supraglottic space. Laryngeal penetration of food was observed during swallowing in 2 patients, after swallowing in 4, and during and after swallowing in 3. The occurrence of aspiration in patients with a preserved larynx has been reported previously. Contrary to the high aspiration rate reported by Lazarus' and the low incidence reported by Koch et al., we found aspiration in 5 patients (36%). In all patients, aspiration was asymptomatic during swallowing, 3 after swallowing, and 1 during and after swallowing. Only 1 of these patients ejected the material out of the airway (score 6); in the other 4 cases, aspiration was silent (score 8). As in the study by Smitt and Goffinet, aspiration in our patients, when present, was minimal and did not pose a significant risk or impairment. This was observed in patient 3, with mild dysphagia, and in patients 1 and 6, with mild-to-moderate dysphagia. Only patients 10 and 16 were analyzed as having severe dysphagia due to severe silent aspiration. Patient 10 was not able to rehabilitate swallowing and is using a gastrostomy tube. In summary, although not a single patient had normal swallowing, 13 (71%) had functional swallowing (level 6) or mild dysphagia (level 5). Only 2 patients (14%) had severe dysphagia.

Studies of patients' perception of the changes in swallowing function after undergoing such a preservation strategy showed a treatment-related decline in quality of life during therapy. However, this perception is reversed after 6 months following treatment completion. This was confirmed in our follow-up observation (mean, 20 months; range, 10-32 months), since 7 (50%) of 14 patients were alive with normal swallowing preserved, and only 1 patient was still using a gastrostomy tube. Most of these patients underwent swallowing therapy after the video-fluoroscopic evaluation.

Prior studies that evaluated voice and swallowing abnormalities following chemotheraphy and irradiation have been limited by small numbers of patients or by focusing on only one laryngeal function aspect. The current study sought to address both functions (voice and swallowing) in a relatively short follow-up period. All these patients underwent voice and swallowing therapy, and we plan to analyze the impact of these therapies on postrehabilitation results in the future.

In summary, although preservation of the larynx does not necessarily result in the preservation of both voice and swallowing, most of the patients analyzed in our study had mild to moderate functional impairments. In almost all patients, the vocal quality and swallowing were compatible with daily life functioning. It should be emphasized that patients with satisfactory vocal and swallowing function can have disease recurrence, need a laryngectomy, or die of the disease. Further follow-up will be necessary to assess the effects of voice and swallowing therapy in the long term.

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