Objective: To evaluate the voices of irradiated patients with early glottic carcinoma and to compare these with the voices of healthy volunteers.

Design: Case-control study.

Setting: University Department of Otorhinolaryngology and Cervicofacial Surgery, University of Ljubljana, Ljubljana, Slovenia.

Subjects and Methods: The voice samples (sustained vowel) of 50 patients (44 men and 6 women) who had been irradiated for T1 (43 subjects) or T2 (7 subjects) glottic squamous carcinoma at least 1 year prior to the study were analyzed with the Multi-Dimensional Voice Program (Kay Elemetrics Corp, Lincoln Park, NJ) and compared with those of a normal group of 50 age- and sex-matched volunteers. Average fundamental frequency, jitter, shimmer, noise-to-harmonic ratio, and degree of voiceless elements were determined. In the irradiated group, videostroboscopy was performed. The patients assessed their voice fatigue.

Results: The irradiated subjects demonstrated significantly higher values for jitter, shimmer, and degree of voiceless elements than did the healthy volunteers. The values for noise-to-harmonic ratio were higher in the irradiated group, but the difference was not significant ($P = .08$). The values for fundamental frequency were almost equal in both groups. In most of the irradiated subjects, some irregularities of the vocal fold vibration were noticed. Many of these patients also reported voice fatigue.

Conclusions: Radiation therapy for early glottic cancer results in poorer voice quality compared with normal age-and sex-matched speakers. In most of the irradiated patients, greater than normal effort in voice production was found based on patient assessment. This may result from stiffness of the vibratory source and inadequate compensatory maneuvers in phonation. We suggest that voice therapy during and after radiation therapy may result in better voice quality.

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Laryngeal cancer is quite common in Slovenia. It represents 3% of all malignant diseases in males. In approximately one third of patients with laryngeal cancer, the malignant tumor appears on the vocal folds. In 80% of patients with glottic cancer, the disease is diagnosed early while still in a localized stage.

By clinical definition, “early glottic cancer” comprises Tis, T1, and T2 tumors without metastases. When the treatment results of radiotherapy and surgery for early glottic cancer are comparable, the functional results of radiotherapy are superior. Generally, voice quality improves a few months after irradiation. In earlier studies, some authors reported normal voice in most of their patients at least 1 year after treatment. However, because of improvements in diagnostic criteria and methods, more recent studies on voice quality of irradiated patients report abnormalities in almost all patients.

The aim of our research was to assess objectively the quality of voice in subjects irradiated for early glottic cancer and to compare it with the voice characteristics in healthy volunteers.

RESULTS

The results confirmed that the voices of the irradiated patients demonstrated significantly higher JIT, SH, and DUV than did the voices of the age- and sex-matched volunteers. The mean values of fundamental frequency were almost identical in both groups. Although there was a slight difference between the groups in NHR in the analyzed vocal samples, it was not significant ($P = .08$) (Table 1).
SUBJECTS AND METHODS

The results of acoustic analysis of the voice samples of 50 irradiated patients (44 men and 6 women) were compared with the analysis of the voices of 50 healthy age- and sex-matched volunteers. The control subjects had no history of subjective voice disorders or irradiation in the head and neck region. Controls ranged in age from 20 to 84 years (mean ± SD, 58.8 ± 13.8 years). Six control subjects were smokers; 35 did not smoke or had given up smoking more than 1 year before data collection. For 9 control subjects, information about smoking was not available.

Study patients had been irradiated for early glottic cancer 1 to 10 years before the present assessment. Their age ranged from 20 to 86 years (mean ± SD, 59.6 ± 13.2 years). Eight irradiated subjects were smokers; 42 subjects did not smoke or had given up smoking more than 1 year previously.

Forty-three irradiated subjects had T1 tumors and 7 had T2 tumors. All tumors were pathologically diagnosed as squamous carcinoma. Twenty-one patients were irradiated with 2-Gy daily fractions and 29 with 2.2-Gy daily fractions, receiving 5 fractions per week. The prescribed tumor dose ranged from 61 to 68 Gy (median, 64.4 Gy).

The patients assessed their voice fatigue after talking for 10 minutes (1 indicates no fatigue; 2, minor fatigue; 3, marked fatigue; and 4, unable to talk because of voice fatigue). In the irradiated patients, videostroscopy was conducted. Postirradiative morphologic lesions on the vocal folds were assessed (1 indicates no lesion; 2, minor lesions; 3, moderate lesions; 4, severe lesions; and 5, very severe lesions). Both the irradiated patients and the control subjects had a voice analysis performed. A voice sample of the sustained vowel /a/ at habitual pitch and loudness, in duration of 3 seconds, was analyzed with the Multi-Dimensional Voice Program (Kay Elemetrics Corp, Lincoln Park, NJ). Average fundamental frequency (F0) for the voice sample, jitter (JIT), shimmer (SH), noise-to-harmonic ratio (NHR), and degree of voiceless elements (DUV) were determined. JIT indicates the period-to-period variability of the pitch period. The threshold value for JIT is 83.2 µs. SH represents the period-to-period variability of the peak-to-peak amplitude (loudness) within the analyzed voice sample. Its threshold value is 0.35 dB. NHR is the average ratio of energy of nonharmonic components in the range 1500 to 4500 Hz to energy of harmonic components in the range 70 to 4500 Hz, and represents a general evaluation of noise presence in the analyzed signal. The threshold value for NHR is 0.19%. DUV is an estimated relative value of nonharmonic areas (where F0 cannot be detected) in the voice sample. Any presence of DUV in the vocal sample is not normal.

In every irradiated patient and control subject, 5 live voice samples were analyzed. The mean values for F0, JIT, SH, NHR, and DUV were then used for further evaluation. The results of voice analysis in the irradiated patients were compared with the results in the control subjects. Analysis of variance, nonparametric Kruskal-Wallis test, and χ² test using the statistical package Epi Info, version 5 (Centers for Disease Control and Prevention, Atlanta, Ga), were used.

The study was in accordance with the ethical standards of the State Committee on Human Experimentation in Slovenia.

We then compared the results of the acoustic analyses of voice samples with threshold values for different variables. We noted that in the irradiated group there were significantly more subjects with abnormal JIT and SH (P = .003 and .009, respectively) (Table 2).

In the irradiated group, there were 8 smokers and 42 non- or ex-smokers. In the control group, there were 6 smokers and 35 non- or ex-smokers. For 9 control subjects, information about smoking was not available. The groups did not differ significantly (χ² = 0.01, P = .87).

Ten irradiated patients felt no fatigue after talking for 10 minutes. Seventeen patients felt minor fatigue, and 23 felt marked fatigue. No patient was unable to continue to talk because of voice fatigue.

Among 50 irradiated patients, 11 had severe postirradiative morphologic lesions on the vocal folds (edema or atrophy of the mucosa, tissue defects, or scars). Twenty-five subjects had moderate lesions and 14 had minor mucosal lesions on the vocal folds. The lesions were almost always present on the side of the original lesion, but in most patients postirradiative changes were also visible on the contralateral fold.

Videostroboscopic findings were normal in 4 irradiated patients (8%). According to voice analysis, these 4 had normal voices. In all other irradiated patients, the amplitudes of vocal fold vibration were reduced or absent, and the mucosal wave was restricted or absent on one (15 patients) or both vocal folds (31 patients). Of the 50 irradiated subjects, 24 were noted to have irregular closure of the glottis. Some degree of extraneous supraglottic activity was seen in 31. All 31 patients reported marked (23 patients) or mild (8 patients) voice fatigue. Irregular phase symmetry in the vibratory pattern was noted in 15 irradiated subjects.

The results of the present research confirmed that voice quality in the patients irradiated for early glottic cancer was poorer than in the sex- and age-matched control subjects.

As glottic cancer characteristically is diagnosed in patients 45 years and older, the natural process of aging must be considered in the evaluation of voice quality after radiation therapy. With increasing age, there are structural changes in the cartilage, ligaments, muscles, and mucous membranes of the larynx; a decrease in pulmonary function; degenerative changes in the resonance tract; and deterioration of the nervous control of breathing, phonation, and resonance. This results in changes of pitch, decrease in loudness and pitch range, increased instability of pitch and amplitude, and voice fatigue.15,16 In the

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**Table 2**

<table>
<thead>
<tr>
<th>Lesion Type</th>
<th>Irradiated Subjects</th>
<th>Control Subjects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe</td>
<td>11</td>
<td>0</td>
</tr>
<tr>
<td>Moderate</td>
<td>25</td>
<td>2</td>
</tr>
<tr>
<td>Minor</td>
<td>14</td>
<td>35</td>
</tr>
<tr>
<td>None</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

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**COMMENT**

The results of the present research confirmed that voice quality in the patients irradiated for early glottic cancer was poorer than in the sex- and age-matched control subjects.
present study, in order to exclude the influence of aging on voice quality, the voices of irradiated patients were compared with the voices of sex- and age-matched volunteers. Thirty of 50 irradiated patients and an equal percentage of control subjects were older than 60 years. The acoustic analyses of voice samples of the older subjects in both the irradiated and volunteer groups identified at least minor abnormalities in most of them, which confirmed the deterioration of voice quality with aging. Nevertheless, the measured JIT, SH, and DUV were significantly higher in the irradiated group.

The results of some other studies are similar. Lehman and colleagues' and Dagli's and their colleagues reported higher JIT in the voices of irradiated patients when compared with the voices of controls. Lehman and coworkers also found higher SH in these patients but noted intersubject variability in their irradiated group. Hirano et al found abnormal JIT in one third of irradiated patients with early glottic carcinoma, which represents a lower percentage of patients than in the present study. McGuirt et al reported no significant difference in JIT between irradiated subjects and controls. Dagli and Hirano and their coworkers found no difference in SH in irradiated patients’ voices when compared with age-matched volunteers. The results of our study, however, agree with the findings of Lehman et al.

Regarding the presence of noise in analyzed vocal samples, Dagli et al reported similar findings in their irradiated group and controls. Lehman and colleagues found the signal-to-noise ratio to be significantly lower in irradiated subjects. Hirano et al noted an abnormal presence of noise in the voices of most irradiated patients. Our results also showed abnormal presence of noise more often in the voices of irradiated patients than in controls, but the difference was not significant (P = .08).

In the present study, voiceless elements were found in the analyzed samples significantly more often in the irradiated group than in controls (P = .03), and the degree of voiced elements was accordingly decreased. McGuirt et al also reported a lesser degree of voiced elements in the vocal samples of irradiated subjects; however, their findings normalized in the analysis of a complete sentence. Harrison and colleagues noted an abnormal degree of voiced elements in patients’ voices some months after irradiation for early glottic cancer. Nine months after treatment, however, acoustic analysis of voices showed normal findings.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Irradiated Patients</th>
<th>Control Subjects</th>
<th>Test</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>F0, Hz</td>
<td>163.32 ± 50.92</td>
<td>160.10 ± 50.03</td>
<td>F = 0.10</td>
<td>.75</td>
</tr>
<tr>
<td>JIT, µs</td>
<td>104.26 ± 81.87</td>
<td>55.12 ± 39.12</td>
<td>H = 17.66</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>SH, dB</td>
<td>0.52 ± 0.89</td>
<td>0.52 ± 0.89</td>
<td>H = 10.84</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>NHR, %</td>
<td>0.16 ± 0.08</td>
<td>0.13 ± 0.02</td>
<td>H = 3.13</td>
<td>.08</td>
</tr>
<tr>
<td>DUV, %</td>
<td>3.74 ± 11.87</td>
<td>0.53 ± 1.61</td>
<td>H = 4.56</td>
<td>.03</td>
</tr>
</tbody>
</table>

*Data are given as mean ± SD. F0 indicates fundamental frequency for voice sample; F, analysis of variance; JIT, jitter; H, Kruskal-Wallis; SH, shimmer; NHR, noise-to-harmonic ratio; and DUV, degree of voiceless elements.

Table 2. Abnormal Values of Different Variables of Acoustic Analysis in 50 Irradiated Patients and in 50 Control Subjects

<table>
<thead>
<tr>
<th>Variable</th>
<th>Irradiated Patients</th>
<th>Control Subjects</th>
<th>Chi² Test</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>JIT, µs</td>
<td>24</td>
<td>10</td>
<td>8.73</td>
<td>.003</td>
</tr>
<tr>
<td>SH, dB</td>
<td>29</td>
<td>16</td>
<td>6.83</td>
<td>.009</td>
</tr>
<tr>
<td>NHR, %</td>
<td>6</td>
<td>1</td>
<td>2.46</td>
<td>.11</td>
</tr>
<tr>
<td>DUV, %</td>
<td>15</td>
<td>7</td>
<td>7.73</td>
<td>.05</td>
</tr>
</tbody>
</table>

*Data are given as number of subjects. JIT indicates jitter; SH, shimmer; NHR, noise-to-harmonic ratio; and DUV, degree of voiceless elements.

In our research, F0 was almost identical in both the irradiated and control groups. The results of Lehman and coworkers' were similar. By contrast, Stoicheff found lower F0 in the irradiated subjects. The author hypothesizes that lower F0 was the result of edema of the irradiated vocal fold mucosa. Dagli et al, however, reported higher F0 in irradiated patients, probably as a result of fibrosis of the vocal folds. In our irradiated patients, atrophy, edema, and scarring were found on vocal folds. In many cases, one vocal fold was edematous and the other was atrophic and fibrotic. The side of the original lesion was more often fibrotic.

Presence of postirradiative mucosal lesions of the vocal folds correlated with videostroboscopic findings. Diffuse stiffness of the larynx was seen on stroboscopy in most patients irradiated for early glottic cancer. Lehman et al reported poor vibratory source, seen on stroboscopy, of irradiated vocal folds in many of their patients. Hirano and colleagues found irregularities in the vibration of vocal folds in two thirds of irradiated subjects. However, Tsunoda et al, who observed 10 patients irradiated for T1 carcinoma of the vocal fold, reported better results based on their videostroboscopic findings. One year after treatment, the mucosal wave was present in all their patients.

Postirradiative mucosal lesions of the vocal folds and stiffness of the larynx may be attributed to the well-known effects of radiation fibrosis, damage of small vessels, and breakdown of elasticity. This is even more convincing when one considers that abnormalities were observed also on the side contralateral to the tumor.

Forty of our irradiated patients reported mild or marked voice fatigue. In 31 patients with voice fatigue, some degree of extraneous supraglottic activity was also observed. Stiffness of the vocal folds may necessitate greater effort in voice production for some irradiated patients. Another explanation for excessive tension of the laryngeal muscles in voice production, however, may be inadequate voice technique that develops before, during, or after irradiation for malignant laryngeal tumor. An organic lesion in the larynx (tumor and/or radiomucositis) may result in altered laryngeal biomechanics and maladaptive compensatory maneuvers, which may continue even after the organic lesion subsides. To prove this theory, a prospective study is needed.

Excessive tension of the laryngeal muscles in voice production, manifesting as extraneous supraglottic activity, may also be the cause of the irregularities in vocal
fold vibration observed in the present study. Irregular vibration cycles result in excessive pitch and amplitude variability and greater DUV.

According to Stoicheff, the amount of talking during the treatment period of irradiation for early glottic cancer appears to affect the length of time needed for voice recovery after treatment. Rydell et al reported almost normal values for JIT and SH in a group of 18 subjects after irradiation for T1 glottic carcinoma. Their patients had received basic instructions on voice hygiene and proper phonation technique.

Patients in the present study did not receive voice therapy. We suggest that voice therapy during and after radiation therapy for early glottic cancer may result in better compensatory maneuvers in use of the affected vibratory source and, hence, better voice quality. A prospective study may confirm this hypothesis.

In conclusion, radiation therapy for early glottic cancer results in poorer voice quality when compared with that of normal sex- and age-matched speakers. Most irradiated patients require greater than normal effort to speak, possibly as a result of stiffness of the vibratory source and inadequate voice technique. An individual's inflammatory and scirrhous response to tumor and irradiation and concomitant maladaptive compensatory maneuvers in phonation are probably closely intermingled, exerting a combined effect. We suggest that a better voice outcome may be achieved if patients receive voice therapy during and after radiation therapy.

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REFERENCES


more often in recurrent tumors. Similar to the management of sinonasal papillomas, an open cavity allows easy inspection and management of local recurrence. Another alternative would be radical temporal bone resection, although the sequelae, especially of facial nerve resection, may be difficult to justify without evidence of malignancy.

REFERENCES


Submissions

Residents and fellows in otolaryngology are invited to submit quiz cases for this section and to write letters to the ARCHIVES commenting on cases presented. Quiz cases should follow the patterns established. See “Instructions for Authors.”

Material for the PATHOLOGY FORUM should be mailed to the Editor.

Reprints not available.

Correction

Error in Byline, Corresponding Author Paragraph, and Table of Contents. In the Original Article by Hocevar-Boltzar and Zargi titled “Voice Quality After Radiation Therapy for Early Glottic Cancer,” published in the September issue of the ARCHIVES (2000;126:1097-1100), the first author’s name was misspelled in the Table of Contents on page 1061, in the byline on page 1097, and in the Corresponding Author paragraph on page 1100. In each place, the first author’s name should have appeared as “Irena Hocevar-Boltzar, MD, PhD.” The journal regrets the error.