

# Voice quality after radiation therapy of early glottic cancer

Irena Hočevar Boltežar and Miha Žargi

University Department of Otorhinolaryngology and Cervicofacial Surgery, Ljubljana, Slovenia

*Radiation therapy is generally accepted as a successful treatment modality for early glottic cancer offering an acceptable voice quality after the treatment. In order to evaluate objectively the voice quality in irradiated patients and to eliminate the influence of decreasing voice quality as a result of normal aging, the results of the acoustic analysis of voice in 20 patients with early glottic cancer treated with radiation therapy were compared to the results of 20 age-matched volunteers. The results established worse voice quality in the irradiated group but the difference was not significant except in amplitude perturbation quotient which expresses the instability of loudness.*

*In order to identify the factors which could influence the quality of voice after irradiation of the laryngeal carcinoma, the results of laryngoscopy and video-endo-stroboscopy, the data about the tumor extension and the biopsy extension, were correlated with the results of the perceptive voice evaluation and the results of acoustic voice analysis. No significant influence of the stated factors on the voice quality of the patients was established. Only the irregular glottic gap during phonation indicated to be connected with very hoarse voice.*

*In conclusion, radiation therapy of early glottic cancer results in an abnormal, but still satisfactory voice quality when compared to the voice quality of normal age-matched speakers. The hoarseness is the result of instability of pitch and specifically the instability of amplitude (loudness). The voice quality after the treatment can be influenced by the tumor extension and localization, the sequels of excisional biopsy, and the radiation therapy or functional disorder. All the stated factors are very intermingled and are probably acting together.*

**Key words:** laryngeal neoplasms-radiotherapy; glottis; voice quality

## Introduction

In the last twenty years, the incidence of laryngeal cancer is increasing.<sup>1</sup> According to the data of the Cancer Registry of Slovenia, there are approximately 30 new patients with early glottic cancer (T1NoMo and T2NoMo) every year.

Surgery and radiation therapy are successful treatment modalities for early glottic cancer. Similar cure rates have been reported by some authors who used either conservative surgery or radiation.<sup>2-5</sup> Accord-

ing to clinical experience, surgical treatment of early glottic cancer often results in not the best voice quality.<sup>6,7</sup> Therefore, with respect to the voice quality, radiation therapy has been generally accepted as more suitable primary treatment modality in early glottic carcinoma.

As glottic cancer is still characteristic for males after 45 years of age, the natural process of aging of the larynx and the voice should also be considered in the evaluation of the voice quality after radiation therapy.

The aim of this study was objective evaluation of the voice quality after radiation therapy of early glottic cancer. In order to eliminate the influence of decrease of the voice quality as a result of normal aging, 20 age-matched pairs of subjects were included into the study. The goal

Correspondence to: Dr. Irena Hočevar Boltežar, MD, University Department of Otorhinolaryngology and Cervicofacial Surgery, University Hospital Ljubljana, Zaloška 7, 1000 Ljubljana, Slovenia.

of the study was also to determine which factors could influence the quality of voice after irradiation of the laryngeal carcinoma.

### Patients and methods

Twenty male patients with T1 (17 patients) or T2 (3 patients) glottic cancer who were irradiated 1 to 10 years ago were included into the study. Their age ranged from 43 to 74 years (mean: 59 years).

In 10 patients, less than one half of one vocal fold was involved. Cancer extended over more than one half of one vocal fold in 7 patients and over both vocal folds in 3 patients. In 2 patients the anterior commissure was infiltrated.

For histologic evaluation of the glottic tumor, a punch-biopsy was performed in 13 patients, and an excisional biopsy was performed in 7 patients. In all of them, squamous carcinoma was assessed.

Ten patients were irradiated with 2 Gy per fraction, and 10 patients were irradiated with 2,2 Gy per fraction, five fractions per week. The prescribed tumor dose was from 61 to 68 Gy (median: 66 Gy), delivered over 33 to 48 days (median: 44 days).

The control group consisted of 20 age-matched male subjects without subjective voice disorders who were not irradiated in the neck region. Their age ranged from 42 to 74 years (mean: 58 years).

In the patients with glottic cancer who were treated with radiation therapy, mirror laryngoscopy and stroboscopy with video-telescope Storz and stroboscope Atmos were conducted to assess the morphologic changes on vocal folds (ranging from 1=no changes to 5=very severe), the vibration of the vocal folds and the glottic closure during phonation (1=complete closure, 2=narrow gap, 3=irregular gap). Signs of laryngeal muscles misuse during phonation were established as present or absent.

In the patients and the control subjects, a voice analysis was performed. A voice sample of sustained vocal "a" in duration of 3 seconds was recorded for further analysis in terms of determination of its pitch, stability of pitch and amplitude (loudness), and presence of noise. The sample was analysed with a Multi-Dimensional Voice Program (Computerized Speech Lab, Kay Elemetrics, USA) and 6 different variables were measured. First of the variables was the mean fundamental frequency (Fo). The second was the pitch pertur-

bation quotient (PPQ) which measures the short-term (cycle-to-cycle) irregularity of pitch. The third variable was the coefficient of Fo (vFo) which reflects the very long-term variation of Fo within the analysed voice sample. The fourth was the amplitude perturbation quotient (APQ) which measures the short-term irregularity of the peak-to-peak amplitude (loudness) of the voice. The fifth variable was the coefficient of amplitude variation (vAm) which reflects the very long-term amplitude variation within the analysed voice sample. The last variable was noise-to-harmonic ratio (NHR) which is a general evaluation of noise present in the analysed signal.

The voices of the irradiated patients were evaluated by an experienced phoniatrician. The perceptive evaluation ranged from 1 for normal voice to 5 for aphonia.

The results of voice analysis in the irradiated patients were compared to the results in the control subjects. In order to identify the factors which could influence the quality of voice after irradiation of the laryngeal carcinoma, the results of laryngoscopy and video-endostroboscopy, the data about the tumor extension and the biopsy extension, were correlated with the results of the perceptive voice evaluation and the results of acoustic voice analysis. The t-test for pairs and different regression models of the statistical package Statistica v.5.0 were used.

### Results

The results of voice analysis showed that all the studied variables were more abnormal in the irradiated patients than in the control subjects but no significant difference was assessed in most of them. The only variable that showed significant difference was APQ. (Table 1).

**Table 1.** Comparison of the variables of the acoustic voice analysis in the patients with glottic cancer who were irradiated (N=20) and in the control subjects (N=20)

Variable	Irradiated patients mean value (stand. dev.)	Control subjects mean value (stand. dev.)	p
Fo	147.55 (35.13)	141.50 (31.61)	0.51
PPQ	0.70 (0.51)	0.49 (0.37)	0.18
vFo	3.26 (4.86)	1.46 (0.72)	0.12
APQ	3.84 (1.74)	2.54 (1.18)	0.00*
vAm	14.52 (7.02)	11.88 (5.52)	0.20
NHR	0.14 (0.05)	0.14 (0.02)	0.92

According to the phoniatrician's perceptive evaluation of the voices of the irradiated patients, 1 subject had normal voice, 8 subjects had slightly hoarse voices, 9 subjects had hoarse voices and 2 subjects had very hoarse voices.

Signs of laryngeal muscles misuse were present in 13 subjects among 20 irradiated patients.

Almost no differences were found when the results of the perceptive evaluation of the patients' voices were correlated to the tumor extension, to the biopsy extension, to the morphologic changes on vocal folds, and to the signs of laryngeal muscles misuse during phonation. The only notable difference was found with the correlation of the perceptive voice evaluation to the completeness of the glottic closure. The difference could not be considered as statistically significant because of the small number of the studied patients. (Table 2).

**Table 2.** Correlation of the results of the perceptive voice evaluation to the tumor extension, to the biopsy extension, to the morphologic changes on vocal folds, to the signs of laryngeal muscles misuse during phonation, and to the completeness of the glottic closure in the group of irradiated patients (N=20)

Correlated variable	Normal or slightly hoarse voice (No. of patients)	Hoarse or very hoarse voice (No. of patients)
<i>Tumor extension:</i>		
less than 1/2		
of one vocal fold	4	5
more than 1/2		
of one vocal fold	5	6
<i>Biopsy extension:</i>		
punch-biopsy	6	7
excisional biopsy	3	4
<i>Morphologic changes on vocal folds:</i>		
slight	5	3
severe and very severe	4	8
<i>Laryngeal muscles misuse:</i>		
present	5	8
absent	4	3
<i>Glottic closure:</i>		
complete closure		
or narrow gap	8	8
irregular gap	1	3

With the correlation of the results of the acoustic analysis of the voice samples of the irradiated patients to the tumor extension, to the biopsy extension, to the morphologic changes on vocal folds, to the signs of laryngeal muscles misuse during phonation, and to the completeness of the glottic closure, no differences were showed. (Table 3).

**Table 3.** Correlation of the results of the acoustic analysis of the voice samples to the tumor extension, to the biopsy extension, to the morphologic changes on vocal folds, to the signs of laryngeal muscles misuse during phonation, and to the completeness of the glottic closure in the group of irradiated patients (N=20)

Correlated variable	Fo p	PPQ p	vFo p	APQ p	vAm p	NHR p
Extension of the tumor	0.78	0.35	0.48	0.89	0.41	0.15
Extension of the biopsy	0.64	0.25	0.98	0.19	0.08	0.15
Morphologic changes on the vocal folds	0.42	0.63	0.64	0.84	0.25	0.19
Laryngeal muscles misuse	0.99	0.52	0.35	0.77	0.19	0.06
Glottic closure	0.92	0.54	0.44	0.47	0.17	0.52

## Discussion and conclusions

The results of the study assessed that in the patients who were irradiated because of early glottic cancer, the voice quality was slightly worse than in the age-matched control subjects. Only in one variable - APQ which expresses the instability of amplitude (loudness) of the voice showed to be statistically significant.

The results of the present study did not confirm the influence of the cancer extension, the biopsy extension, the signs of laryngeal muscles misuse during phonation, and the morphologic changes on vocal folds on the voice quality. The completeness of the glottic gap indicated to be important for the voice quality, the irregular gap being connected with hoarse voice.

Most of the authors reporting about the voice quality after the radiation therapy of early glottic cancer assessed abnormal voice after the treatment. Better results were obtained when the patients themselves evaluated their voices. They assessed normal or nearly normal voice in 76%<sup>8</sup> or even in 83% of them.<sup>9</sup> Worse results were established when the voices were evaluated by a professional. Morgan et al.<sup>10</sup> reported that speech and language therapists had found voice abnormalities in all studied irradiated patients. Similar results were established in the present study where the voice of only one patient was evaluated as normal.

As glottic cancer is still characteristic for males after 45 years of age, the natural process of aging of the voice should also be considered in the evaluation of the voice quality after radiation therapy. The

structural changes in the cartilages, ligaments, muscles, mucous membranes of the larynx, the decrease of pulmonary function, the degenerative changes in the resonance tract, the deteriorating nervous control of breathing, phonation and resonance appear and result in changes of pitch, decrease of loudness and pitch range, increasing instability of pitch and amplitude, and voice fatigue.<sup>11</sup> In the present study, the voices of irradiated patients were compared to the voices of age-matched volunteers. The acoustic analysis of all the studied voice samples of the patients and the volunteers established at least minor abnormalities in the stability of pitch and amplitude. The voices of irradiated patients were more unstable but the differences were not significant. Only APQ which expresses short-term irregularity of amplitude (loudness) showed to be significantly worse in the irradiated patients.

The results of other studies are similar. Hirano *et al.*<sup>12</sup> reported about abnormal APQ in one third of the irradiated patients. Lehman *et al.*<sup>13</sup> established significant difference in stability of pitch and amplitude of the voices of the irradiated patients in comparison with the voices of the volunteers. However, they found no differences in Fo in both groups of the studied subjects, as was also the case in the present study.

Some authors tried to evaluate which factors influenced the quality of voice after the radiation therapy of early glottic cancer. Lehman *et al.*<sup>13</sup> studied the influence of irradiation technique, the depth of biopsy, and the tumor localization on the results of acoustic analysis of voice and established no significant differences. The signs of laryngeal muscles misuse during phonation was assessed in 13 among 20 studied subjects. On the other hand, Benninger *et al.*<sup>14</sup> showed that complications during irradiation, the excisional type of biopsy, and the bilateral involvement of vocal folds are connected with bad voice quality.

In the present study, adverse influence of the tumor extension over more than one half of one vocal fold, the excisional biopsy, and very severe morphologic changes on vocal folds on voice quality was not proved. Only the irregular glottic closure during phonation (not always connected with very severe morphologic changes of vocal folds) was more often observed in very hoarse patients than in patients with better voice. What was the cause of a tissue defect or a scar at the edge of one or both vocal folds was not established. The possible factors could be: the tumor localization or deeper in-

filtration, the depth of biopsy or the individual inflammatory and scirrhous response to tumor and radiation. The signs of functional disorder were established in 13 patients, therefore, the reason for bad voice quality could also be the misuse of laryngeal muscles in phonation. We can speculate that the combination of all the stated factors influence the voice quality after radiation therapy of early glottic cancer. The results of the study can only indicate the problem due to small number of included subjects.

In conclusion, radiation therapy of early glottic cancer results in an abnormal, but still satisfactory voice quality when compared to the voice quality of normal age-matched speakers. The hoarseness is the result of instability of pitch and specifically the instability of amplitude (loudness). The voice quality after the treatment can be influenced by the tumor extension and localization, the consequences of excisional biopsy, the radiation therapy or functional disorder. All the stated factors are very intermingled and are probably acting together. The role of every factor was not established yet, for this reason, a study on greater number of patients is necessary to improve the phoniatric approach to the patients with early glottic cancer.

### Acknowledgement

The authors wish to thank to Prof. Marjan Budihna MD PhD, Hotimir Lešničar MD, Erika Šoba-Podobnik MD, Ladica Furlan MD, Boris Jančar MD from Institute of Oncology in Ljubljana for their help in the study.

### References

1. *Incidenca raka v Sloveniji* 1991. Ljubljana: Onkološki inštitut - Register raka za Slovenijo, 1994.
2. Dickens WJ, Cassisi NJ, Million RR, Bova FJ. Treatment of early vocal cord carcinoma: a comparison of apples and apples. *Laryngoscope* 1983; **93**: 216-9.
3. Pellitteri PK, Kennedy TL, Vrabec DP, Beiler D, Hellstrom M. Radiotherapy: the mainstay in the treatment of early glottic carcinoma. *Arch Otolaryngol Head Neck Surg* 1991; **117**: 297-301.
4. Million RR. The larynx... so to speak: everything I wanted to know about laryngeal cancer I learned in the last 32 years. *Int J Radiat Oncol Biol Phys* 1992; **23**: 691-704.

5. Lešničar H, Šmid L, Zakotnik B. Early glottic cancer: the influence of primary treatment on voice preservation. *Int J Radiat Oncol Biol Phys* 1996; **36**: 1025-32.
6. Wetmore SJ, Key JM, Suen JY. Laser therapy for T1 glottic carcinoma of the larynx. *Otolaryngol Head Neck Surg* 1986; **112**: 853-5.
7. Hirano M, Hirade Y, Kawasaki H. Vocal function following carbon dioxide laser surgery for glottic carcinoma. *Ann Otol Rhinol Laryngol* 1985; **94**: 232-5.
8. Karim ABMF, Snow GB, Siek HTH, Njo KH. The quality of voice in patients irradiated for laryngeal carcinoma. *Cancer* 1983; **51**: 47-9.
9. Stoicheff ML. Voice following radiotherapy. *Laryngoscope* 1975; **85**: 608-18.
10. Morgan DAL, Robinson HF, Marsh L, Bradley PJ. Vocal quality 10 years after radiotherapy for early glottic cancer. *Clin Radiol* 1988; **39**: 295-6.
11. Koopman CF Jr. Otolaryngologic (head end neck) problems in elderly. *Med Clin North Am* 1991; **75**: 1373-88.
12. Hirano M, Mori K, Iwashita H. Voice in laryngeal cancer. In: Smee R, Budger GP, eds. Laryngeal cancer. Proceedings of the 2nd World Congress on laryngeal cancer, Sydney, February 1994. Amsterdam : Elsevier, 1994: 54-64.
13. Lehman JJ, Bless DM, Brandenburg JH. An objective assessment of voice production after radiation therapy for stage I squamous cell carcinoma of the glottis. *Otolaryngol Head Neck Surg* 1988; **98**: 121-9.
14. Benninger MS, Gillen J, Thieme P, Jacobson B, Dragovich J. Factors associated with recurrence and voice quality following radiation therapy for T1 and T2 glottic carcinomas. *Laryngoscop* 1994; **104**: 294-8.