

Quality of life and voice in patients treated for early laryngeal cancer

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Key words: laryngeal cancer; quality of life; Voice Handicap Index.

Summary. *Objectives.* To evaluate quality of life and voice in patients previously treated for early laryngeal cancer versus healthy controls and to assess correlations between demographic and cancer characteristics and posttreatment quality of life and voice.

Material and methods. A total of 49 patients diagnosed with early (Tis-T2N0) laryngeal carcinoma, treated by radiotherapy or endoscopic surgery at least 6 months before, who were alive and free of recurrence formed study group. Postservice with questionnaires was accomplished. Quality of life was evaluated using Medical Outcomes Study 36-Item Health Survey (SF-36), Hospital Anxiety and Depression (HAD) Scale, voice quality – by Voice Handicap Index (VHI). Normative data were obtained from database or concurrently assessed healthy adult subjects.

Results. Hoarseness was the most frequent complain. Majority of patients consider their health as fair (69.4%), one third – good or excellent. The means of summary of SF-36 scores for physical and mental health differ significantly from normative age-matched population ($P < 0.001$). Emotional distress on HAD scale was found in 40.8% of patients vs. 17.0% of healthy controls. Majority (87.8%) of patients rated their voice abnormal; vast majority of them had slight to moderate dysfunction. Mean VHI scores were slight elevated for patients and differed significantly from healthy ones. Correlation analysis revealed a significant relationship between patients' physical health and some demographic-clinic factors.

Conclusions. Quality of life in patients previously treated for early laryngeal cancer was worse than healthy subjects. Psychiatric morbidity was indicated in around of one-third of the patients. Voice changes were reported in most patients with low handicap level. Physical health perception was better for patients with higher grade of cancer differentiation, not using alcohol, and treated first.

Introduction

Laryngeal cancer is one of the commonest of all head and neck malignant tumors (1). These are usually squamous cell carcinomas, most commonly arising from the glottis. Both external beam radiotherapy and endoscopic excision offer high and comparable cure rates for the treatment of early laryngeal cancer (2, 3). In that case, recommendations and patients' counseling should consider patients' functional outcome following treatment.

The diagnosis and treatment of any cancer is frightening for patients. For patients with laryngeal cancer, the disease can affect the ability to communicate, thereby disrupting interactions with other people and resulting in considerable social and psychological

dysfunction. Therefore, communication and general health status are major concerns to patients who are undergoing treatment for laryngeal cancer (4).

To evaluate effect of disease on life, several validated instruments have been developed. One of them is Medical Outcomes Study 36-Item Short-Form Health Survey (SF-36) – instrument that was designed to quantify patients' perceptions of their general physical and mental health and is thought to reflect the relative personal burden of disease and recently applied for laryngeal cancer patients (5, 6). The SF-36 has been used for a wide range of disease-specific topics once, it was shown to be a valid measure of degree of health (5–8). For assessment of the disease impact on psychological dysfunction, the Hospital

Anxiety and Depression Scale (HAD) is frequently used (9–11). Voice specific outcomes can be utilized by the Voice Handicap Index (VHI), a validated instrument that measures patients' disability from voice disorders and recently used to assess treatment outcomes for early laryngeal cancer (12, 13).

Few studies have measured overall general well-being and handicap specifically related to voice in patients treated for early laryngeal cancer. To date we have no studies of such outcome measurement in Lithuanian patients.

The aims of this study were to evaluate quality of life (QL) and voice in patients previously treated for early laryngeal cancer *versus* healthy controls and to assess correlations between demographic and cancer characteristics and posttreatment quality of life and voice.

Material and methods

Patients

Patients diagnosed with early laryngeal carcinoma (carcinoma in situ – Tis, T1N0 and T2N0) in a department of Otorhinolaryngology of Kaunas University of Medicine between 2000 and 2006 years and treated by radiotherapy or endoscopic surgery at least six months before formed study group. Patients who were older than 80 years at the time of making diagnosis, had recurrence, or were treated by laryngectomy following recurrence were excluded from the study. A total of 72 patients met inclusion-exclusion criteria to whom general health and voice quality related questionnaires were sent twice: with intervals of two to four weeks. Fifty-six of the 72 patients (77.7%) or their relatives responded to the questioning. Six patients died: one patient due to the laryngeal cancer, while others due to comorbid diseases. One patient declined to completed questionnaire because of illness, leaving 49 patients aged 42–79 years in the study group who data were analyzed.

Demographic data, cancer characteristics, method of treatment of enrolled patients were obtained from the records of Department of Otorhinolaryngology of Kaunas University of Medicine. Disease of the patients was staged according the International Classification of Diseases for Oncology and TNM classification (14). Recurrence of the disease was stated from the endoscopic examination of the larynx at the follow-up during period of investigation or from the latest examination from recorders, also by anamnesis and telephone interviewing. Questionnaires were sent to the patients included study-specific questionnaire to assess present complains, unhealthy habits; two

quality of life questionnaires: Medical Outcomes Study 36-Item Short-Form Health Survey and Hospital Anxiety and Depression Scale, and voice-specific questionnaire – voice handicap index. The time after the end of treatment and the questionnaire survey ranged from 6 to 78 months, with a mean of 27.7 ± 20.7 months.

Normative data for SF-36 were obtained concurrently and from database of Kaunas University of Medicine from generally healthy (no heavy chronic disease, not being on tablets, not acute disease at the time of investigation) age-matched 191 adults: 89 (46.6%) males and 102 (53.4%) females aged 47 to 83 years (mean age, 59.6 ± 8.4 years). Normative data for HAD and VHI were obtained from database and included 94 healthy voice subjects: 22 (23.4%) males and 72 (76.6%) females aged from 23 to 67 years (mean age, 37.7 ± 10.8 years).

The study was conducted with the approval of the Ethics Committee of Kaunas University of Medicine.

Treatment. Patients were treated by two methods: with radical radiotherapy as their primary treatment and received conventionally fractionated radiation therapy to a biologically equivalent dose of 55 to 68 Gy in 4 to 6 weeks, when the larynx was the target volume or had undergone endoscopic excision of the cancer under general anesthesia at Kaunas University of Medicine.

Questionnaires

Study-specific questionnaire contained five self-reported questions related to education, smoking, alcohol use habits (yes/no), weight, use of medicines, as well as eight questions we considered to be of specific interest to laryngeal carcinoma patients. Symptoms (hoarseness, dysphagia, odynophagia, difficulties in breathing, head-neck pain) were evaluated using 100 mm (1 mm = 1 point) visual analogue scale (VAS).

SF-36. Status of the general health was investigated by the SF-36 (5). This self-report survey consisted of eight scales for physical functioning, physical limitations, bodily pain, general perception of health, mental health, emotional limitations, social functioning, and vitality. Subscores in these 8 areas are pooled into 2 composite summary scores representing overall physical health (first four scales subscores) and mental health (last four scales subscores). These are the physical component summary (PCS) and the mental component summary (MCS) (7). PCS and MCS scores are normalized on a scale of 0 to 100, with higher scores representing better functioning. Only these two

parameters were analyzed in this study. Questionnaire is validated and translated into 40 languages including Lithuanian (7, 8).

Hospital anxiety and depression scale. The HAD is a self-rated scale found to be valid and reliable for detecting depression and anxiety disorders (15). It has been used in studies of head and neck cancer patients (9, 10). HAD contained a 14-item questionnaire with four response categories, measuring the level of anxiety and depression in two separate subscales. Scale scores range from 0 (no symptoms) to 21 (maximum of distress). Scale cut-off has been established as follows: possible depression or anxiety morbidity, 8 to 10 on either scale, and probable psychological distress, more than 10 on either scale.

Voice handicap index. This patient self-assessment consists of 10 items in three domains: emotional, physical, and functional aspects of voice disorders and measures the impact of voice problems on a person's life (12). Subjects rate each statement frequency on 5-point equal-appearing scale, with the following values: 0 – never and 4 – always. The VHI generates a total score ranging from 0 to 120. The higher the standard score, the worse the VHI. Overall judgment of voice disturbances was assessed using 5-point Likert scale from 1 (normal) to 4 (severe dysfunction).

Statistical analysis was performed with SPSS statistical software (version 10 for Windows; SPSS Inc, Chicago). *t* test was used for normally distributed

quantitative parameters, Mann-Whitney U test – for not normally distributed and nonparametric data. Multiple comparisons were assessed using an ANOVA model. Chi-square test was used to compare proportions. Correlation analysis was made with Pearson correlation coefficient (*r*). Results were considered significant at $P < 0.05$. We used such notations: * $P < 0.05$; ** $P < 0.01$; *** $P < 0.001$.

Results

General characteristics of the 49 patients included in this study are given in Table 1. Their mean age was 62.2 ± 8.6 years, and the vast majority of them (91.8%) were men. Most of the patients (98.0%) had cancer localized in glottis (Fig. 1); 98.0% of patients had histologically proven squamous cell carcinoma. The median time from the diagnosis establishing and the beginning of treatment was 30 days. Two-thirds of the patients (67.3%) had Tis or T1N0 carcinoma, one-third – T2N0. Thirty patients were treated with radical radiotherapy, and 19 patients underwent endoscopic excision.

Questionnaires

Study-specific questionnaire revealed that the most frequent complains of patients treated at least 6 months before were hoarseness (63.5%) and head-neck pain (36.7%), but symptoms were not severe in their nature: 42.0 ± 28.7 points and 27.1 ± 22.5 on a 100-point VAS

Table 1. Demographic and cancer characteristics in 49 patients treated for early laryngeal cancer

Characteristic	n (%)
Age, mean, years	62.2
Male/female	45 (91.8)/4 (8.2)
Smokers: before/after treatment	30 (61.2)/12 (24.5)
Alcohol users: before/after treatment	28 (57.1)/23 (46.9)
Cancer localization Supraglottis/glottis/subglottis	1 (2.0)/47 (96.0)/1 (2.0)
Cancer stage In situ (TisN0M0) I (T1N0M0) II (T2N0M0)	3 (6.1) 30 (61.2) 16 (32.7)
Grade of cancer differentiation (G) G1 (high) G2 (moderate) G3 (low)	31 (63.3) 14 (28.6) 1 (2.0)
Method of treatment Radiotherapy Endoscopic resection	30 (61.0) 19 (39.0)

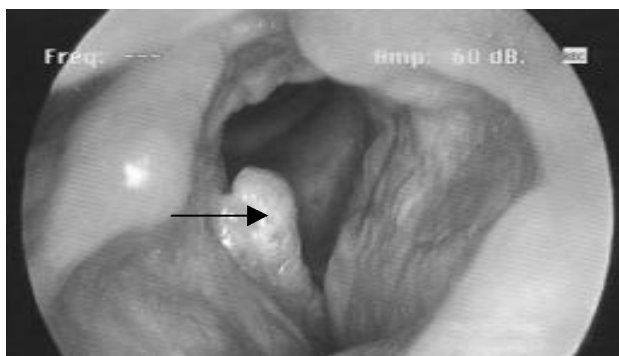


Fig. 1. Videoendoscopic view of early right vocal fold carcinoma (arrow)

scale, respectively.

General health SF-36 questionnaire. The mean physical component summary and the mental component summary scores are shown in Fig. 2. Majority of patients treated for early stage laryngeal cancer consider that their health at the time of investigation was fair (69.4%) or good and excellent (26.6%) and did not change over the last year (59.2%) or improved (30.6%). However, the summary SF-36 scores for physical and mental health in treated laryngeal cancer patients differ significantly from normative population: 58.5 ± 23.1 vs. 76.9 ± 14.1 and 65.4 ± 19.5 vs. 77.0 ± 13.0 , respectively ($P < 0.001$, Fig. 2).

HAD scale. The psychiatric morbidity is shown in Table 2. The anxiety was predominant in probable emotional distress evaluation and involved approxima-

tely one-fifth of the patients. However, depression was dominant in possible clinical case of the disease. The percentage of cancer patients scoring as possible or probable case of anxiety and depression was much higher than in healthy subjects' group: 40.8% vs. 17.0% ($P < 0.05$).

Voice-specific questionnaire: Voice Handicap Index. A high percentage of patients treated for early laryngeal cancer reported voice problems: 87.8% of them rated their voice abnormal in overall rating. However, the majority of the patients (77.6%) had slight to moderate dysfunction, only 10.2% of the patients reported severe voice problems. Fig. 3 shows the mean VHI scores for total, functional, emotional, and physical domains. A slight, but significant elevation in means of all VHI subscales was found in patients' group than compare to healthy subjects with physical component being worse. The mean value of total VHI score was 35.5 ± 26.0 points vs. 5.7 ± 8.7 points ($P < 0.001$).

Quality of life and voice in patients treated for early stage laryngeal cancer appears similar despite stadium and treatment arms.

Correlation analysis between demographic and cancer characteristics and posttreatment quality of life and voice

Correlation analysis was accomplished between patients' physical and mental component summary, HAD anxiety and depression, VHI subscale scores

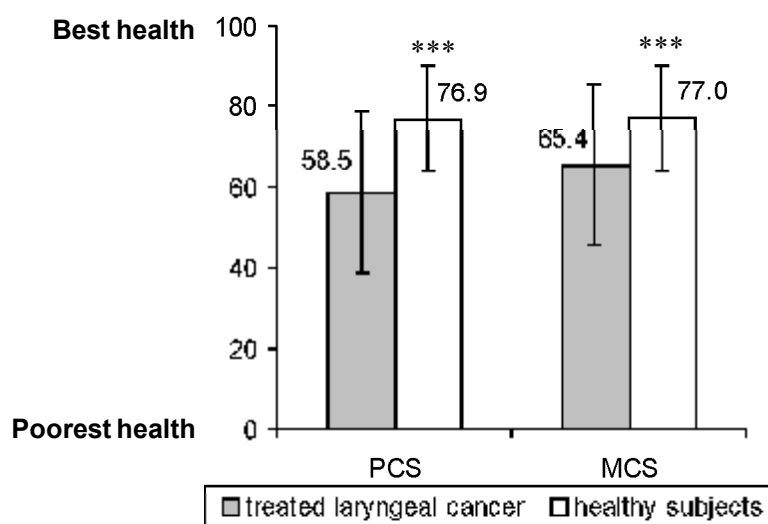


Fig. 2. The means of physical component summary (PCS) and mental component summary (MCS) scores

***Statistically significant difference between patients previously treated for early laryngeal cancer (N=49) and healthy (N=191) subjects, $P < 0.001$.

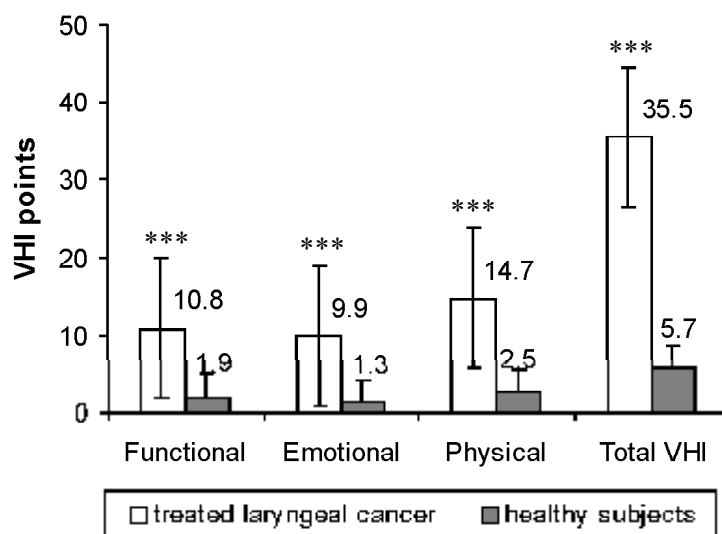


Fig. 3. The means of voice handicap index scores

***Statistically significant difference between patients previously treated for early laryngeal cancer (N=49) and healthy (N=94) subjects, $P<0.001$. Note: the higher score, the worse the voice handicap index (VHI).

Table 2. Results from the HAD scale

Emotional status	Treated laryngeal cancer patients (N=49), N (%)	Healthy subjects (N=94), N (%)
Possible ^a anxiety	8 (16.3)	8 (8.5)
Possible depression	11 (22.4)*	4 (4.3)
Probable ^b anxiety	8 (16.3)	6 (6.4)
Probable depression	1 (2.0)	2 (2.1)
Total No. of possible and probable cases of anxiety and depression	20 (40.8)*	16 (17.0)

^a Possible anxiety disorder, number of patients scoring 8–10 on anxiety scale; possible depression disorder, number of patients scoring 8–10 on depression scale; ^b Probable anxiety disorder, number of patients scoring ≥ 11 on anxiety scale; probable depression disorder, number of patients scoring ≥ 11 on depression scale.

*Statistically significant difference between patients previously treated for early laryngeal cancer patients vs. healthy subjects ($P<0.05$).

with these factors: gender, age, disease stadium, histological grade of cancer differentiation, time from the diagnosis establishing and beginning of treatment, method of treatment, use of alcohol, and smoking habits. Significant correlation from slight to moderate was found between physical health and histological grade of cancer differentiation ($r=-0.27$, $P<0.05$), use of alcohol ($r=0.27$, $P<0.05$), and time from the diagnosis establishing and beginning of treatment ($r=-0.36$, $P<0.01$). Patients with higher cancer differentiation grade, not using alcohol, and treated first reported their general physical health better than others. No other significant relationships were found.

Discussion

Quality of life is an important outcome measure in oncology. Quality of life is both subjective, including the patient's view, and multidimensional, covering a broad spectrum of the patient's life aspects (16). Major concerns of early laryngeal cancer patients are well-being in general and voice quality, because such patients in general have a good prognosis with a 5-year disease-specific survival rate of more than 90% for T1 tumors and more than 70% for T2 tumors despite of treatment modality (1). In this study, we included patients with early laryngeal cancer from Tis to T2N0 stadium treated by radiotherapy or endo-

scopic surgery at least six months before, who were free of recurrence, and not older than 80 years at the time of cancer diagnosis. We excluded patients with recurrence because such condition could have significant impact on QL and voice measurements. Patients older than 80 years at the time of diagnosis we consider may have difficulties to complete questionnaires and participate in the study.

Data of our study showed that most frequent complain was hoarseness, reported by 63.5% of patients. One-third of the patients had not severe head and neck pain. These two symptoms were directly connected with the received treatment modalities – external beam of radiotherapy to the larynx and endoscopic excision of tumor – and could be expected. Hoarseness as being one of leading symptom was also reported in previous studies with laryngeal cancer patients (9, 10).

The results of this study showed that majority (96%) of patients consider that their general health at the time of investigation as fair or good and excellent when mean 27.7 months after the end of treatment were passed, and did not change over the last year in two-thirds of patients or even improved (30.6%). The mean SF-36 summary scores for physical and mental health were high enough exceeding 58.5 points and 65.4 points from maximum 100 points, respectively. However, mean general physical and mental aspect scores in patients treated for early laryngeal cancer differ significantly from those of age-matched healthy subjects. The results correspond with the disease nature that is frightening for the patients and with the treatment side effects: most of the patients (30) were treated by external radical radiotherapy that commonly results to edema of the larynx and surrounding tissue following fibrosis with some limitations in physical and mental health. Equally we should remember that QL is subjective self-reported patients' perception of general health level frequently representing the gap between the perceived reality and patients expectations (16). There are only few publications regarding SF-36 scoring in laryngeal cancer patients; most of them included patients suffering not only from laryngeal, but also from other localization of the head and neck cancer. Hence, the comparison of the results is complicated. In a study by Hammerlid and Taft (17), the SF-36 scores of various stages of head and neck cancer patients 3 years after diagnosis significantly differ from the Swedish normative population only in role of physical functioning, whereas Grignon *et al.* (6) have found evident differences on summary general health scores in patients with the same diseases pattern vs. controls. Stoeckli *et al.* (18) compared QL of long-term 56 survivors after radiotherapy and

endoscopic laser surgery for T1-T2N0 laryngeal cancer and concluded that all patients, whether treated with surgery or radiotherapy, reported good global quality that is similar to our study results, except that there was no control group and other questionnaire for global QL was used.

Therefore, a high level of psychological distress in patients with head and neck cancer has been reported by other authors, we included HAD scale in this study. Our study data showed a high degree of psychological distress indicating psychiatric morbidity in a great number of patients (20 of 49) (Table 2). This finding is in agreement with that of other studies with head and neck cancer including laryngeal patients (9–11, 19). Hammerlid *et al.* (9) in the study with 48 patients with head and neck various stage cancer similarly to our study results have found that 34% of them had psychological distress after 6-month follow-up and 29% at 1-year follow-up after treatment. It has been suggested that negative outcomes associated with psychological distress could be modified by patients' social support coming from family close friends and specialists (16, 19).

Posttreatment voice quality is an important parameter for sufficient patients' social functioning. Our study showed that a high percentage of patients (87.8%) treated for early laryngeal cancer reported voice problems; however, the majority of them (77.6%) had slight to moderate dysfunction. Voice handicap level for Tis – T2N0 patients in all three VHI subscores was low, mostly elevated in physical subscale with a mean VHI value of 14.7, but differed significantly from healthy voice subjects. This indicated that such patients mostly need higher physical efforts to produce voice and feel discomfort of phonation that results in some voice problems in daily life. The mean total VHI score was found to be 35.5 points from maximum 120. Literature data are scanty on this point. Coleman *et al.* (13) accomplished meta-analysis of treatment for T1a glottic cancer and found low levels of voice handicap for such patients with mean total VHI values ranging from 11.5 to 28.5 points. VHI scores were similar regardless the type (radiotherapy or endoscopic excision) of treatment. Authors concluded that mean VHI scores of patients with T1a glottic cancer compare favorably to those of patients treated for non-neoplastic lesions that VHI score was around 26.5. A little higher total VHI score found in our study could reflect more extend stadium of the disease. In generally, this finding that voice handicap is low enough after early laryngeal cancer treatment is important to reassure laryngeal cancer patients about fair posttreat-

ment results, especially for professional voice users.

Analysis of factors related to treatment outcome showed that patients with higher grade of cancer differentiation, not using alcohol, and treated first reported their general physical health better than others. Higher histological grade is responsible for slower disease development. Use of alcohol is less generally understood. Most studies, unfortunately, investigated predictors for survival that is not case in early laryngeal cancer. Other studies suggested that continued smoking and extent of prior biopsy influence the post-treatment voice quality (20). There are data that despite of majority of patients believing that habit-related factors increased chances of having cancer, about one third continued to smoke or drink regardless of their disease (16).

The limitation of our study is that the statistical analyses performed in this article pointed to differences between QL and voice in all patients treated for early laryngeal cancer versus healthy controls not

separating them according different treatment modalities and stage. Such stratification gave too small study groups for precise comparisons. Future investigations on this point are needed.

Conclusions

Majority (96.0%) of patients previously treated for early (Tis-T2N0) laryngeal cancer rated their general health as fair or better; however, summary scores of overall physical and mental health were worse than healthy subjects. Psychiatric morbidity was indicated in around one-third of laryngeal cancer patients and significantly differed from healthy subjects' rate. Most (77.6%) patients reported slight to moderate voice problems in daily life with being hoarseness the most frequent complain. Factors related to cancer differentiation grade, alcohol use, and time between making diagnosis and beginning of the treatment appear to have a significant impact on patients' reported physical health status.

Pacientų, gydytų nuo ankstyvojo gerklų vėžio, gyvenimo ir balso kokybė

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Raktažodžiai: gerklų vėžys, gyvenimo kokybė, balso neįgalumo indeksas.

Santrauka. *Tyrimo tikslas.* Įvertinti ir palyginti pacientų, gydytų nuo ankstyvosios stadijos gerklų vėžio, gyvenimo ir balso kokybę su sveikų žmonių duomenimis bei nustatyti ryšius tarp gyvenimo kokybės rodiklių, demografinių ir vėžio charakteristikų.

Medžiaga ir metodai. Analizuoti 49 pacientų, kurie gydyti nuo ankstyvosios stadijos gerklų vėžio, duomenys po gydymo praėjus ne mažiau kaip 6 mėn. ir neturi atkryčių. Pacientams paštu išsiųsti klausimynai. Gyvenimo kokybė vertinta trumpuoju bendrosios sveikatos klausimynu „SF-36“; emociniai sutrikimai – nerimo ir depresijos skale; balso neįgalumas – balso neįgalumo indekso klausimynu. Parametrų norma nustatyta sutartinai tiriant sveikus žmones ir naudojantis duomenų bazės duomenimis.

Rezultatai. Užkimimas buvo pagrindinis tokių pacientų skundas. 69,4 proc. pacientų teigė, kad jų gyvenimo kokybė nebloga, trečdalis nurodė gerą ar puikią. Fizinės ir psichikos sveikatos suminių rodmenų vidurkiai nustatyti reikšmingai mažesni nei sveikų žmonių ($p < 0,001$). Emociniai sutrikimai gydytiems nuo gerklų vėžio pacientams buvo reikšmingai dažnesni nei sveikiems: atitinkamai – 40,8 proc. ir 17,0 proc. Dauguma (87,8 proc.) pacientų nurodė, kad jų balso kokybė yra pakitusi, vyrauja lengvo ir vidutinio sunkumo disfunkcija. Balso neįgalumo indekso vidurkiai reikšmingai skyrėsi nuo sveikų žmonių. Nustatyta reikšmingų ryšių tarp bendrosios fizinės paciento sveikatos vertinimo ir kai kurių demografinių bei vėžio charakteristikų.

Išvados. Bendroji sveikatos būklė nuo ankstyvosios stadijos gerklų vėžio gydytų pacientų, po gydymo praėjus ne mažiau kaip pusei metų, buvo blogesnė nei bendrosios populiacijos. Reikšmingai dažniau nei sveikiems žmonėms nustatyta emocinių sutrikimų – nerimas ir depresija. Daugumos pacientų balso kokybė buvo pakitusi, dažniausiai ji sukėlė nesunkią balso negalią. Geresnė tokių pacientų fizinė sveikata buvo reikšmingai susijusi su didesne naviko diferenciacija, alkoholinių gėrimų nevartojimu ir anksčiau pradėtu gydymu.

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Received 11 February 2008, accepted 18 April 2008

Straipsnis gautas 2008 02 11, priimtas 2008 04 18