

LIFE QUALITY INDEXES IN NEO-ADJUVANT CHEMOTHERAPY IN LARYNGOPHARYNX CANCER PATIENTS

N. V. Grin

State Institution "A. S. Koloiychenko Institute of Otolaryngology NAMS of
Ukraine", Kiev, Ukraine

Abstract

Urgency. Cancer patients quality on life (QOL) is one on the important criteria for the effectiveness of the treatment estimation along with traditional clinical indicators: regression of the primary tumor focus and metastases, immediate and long-term results of treatment and survival. **Materials and methods.** 66 patients with morphologically confirmed squamous cell carcinoma of laryngopharynx II - IV (T2 - 4N0-2M0) stages have been examined. They got 3 cycles of neoadjuvant chemotherapy with 21 - 28 days intervals according to the following scheme: *paclitaxel* - 175 mg/m², cisplatin – 40 mg/m². The patients were divided into two groups. Both groups patients got detoxification: the group received arginine –containing drugs and enterosorbent, group of comparison got detoxification therapy with crystalloid solutions. QOL was assessed with the use of the EORTC QLQ-H and N35 questionnaire, Karnowski's index and ECOG. The patients were examined in dynamics before treatment and during chemotherapy. **Results.** QOL of laryngopharynx malignant neoplasms patients correlates with objective clinical indexes, such as tumor regression - the more the tumor volume decreases, the better QOL of each individual patient and in the groups as a whole was, the average relapse-free survival period (median survival curve is 66 months for the main and 54 months for the group of comparison). Relapse-free survival period (in the main group it makes 87% of the total survival period, and in comparison - 72%). It is completely

determined by the courses of neoadjuvant chemotherapy given. In this case, complex treatment of patients using arginine-containing drugs and enterosorption (the main group of patients) gives better results of QOL compared to the use of detoxification therapy with saline solutions in volume up to 1.5 - 2.0 liters according to the standard protocol. Karnowski's index in the main group is 21.8%, and in the comparison group 4.4%; ECOG after three treatment cycles compared with the initial value decreased by 50.0%, while for patients in the comparison group this decrease was 21.4%. **Conclusion.** The use of QOL – indexes selected and conducting a comprehensive statistical analysis at each stage of treatment makes it possible to more objectively make research, draw the necessary conclusions, make reasonable adjustments to the treatment process, increase the evidence of medicine and the effectiveness of treatment.

Key words: laryngopharynx cancer; chemotherapy; quality of life indicators; integral indicator EORTC-QLQ-H and N35; Karnowski's index; ECOG.

Cancer is the second leading cause of death in the world. For example, in 2015 it resulted in 8.8 million of fatalities [1, 2]. Cancer causes almost every sixth death in the world. Malignant neoplasms of larynx and pharynx are an urgent and socially significant medical problem among head and neck tumors. In the structure of general oncological morbidity, the incidence of laryngopharynx cancer (LPHC) is 0.4–1.5% [8, 7]. Prevalence of this type of cancer, the complexity and stability of impaired breathing, speech, and swallowing functions, accompanied by prolonged and often persistent disability, pose the issue of rehabilitation and restoration of the quality of life of patients as one of the most important medical and social problems [5, 6].

At present, the quality of life (QOL) of cancer patients is one of the important criteria for the effectiveness of treatment assessment along with traditional clinical indicators: regression of the primary tumor focus and metastases, immediate and long-term results of treatment and survival [10, 12].

The use of methodological approaches for the study of QOL provide an opportunity adequately describe and measure the complex gamut of multifaceted violations that occur at cancer patient during special treatment and after its completion [3, 4]; study the effect of the disease and antitumor therapy on a patient's QOL with malignant neoplasms of the laryngopharynx [9, 11].

Aforenamed determines the urgency of further research in the search of new and improving existing methods of chemotherapeutic treatment of this pathology, assessing its effectiveness and patients QOL [8, 9].

Objective: to study a set of QOL indicators in laryngopharynx malignant neoplasms patients, determine their value for evaluating the results of treatment and increasing its effectiveness in neoadjuvant chemotherapy with arginine-containing drugs and enterosorption.

Materials and methods

66 patients with morphologically confirmed squamous cell carcinoma of the laryngopharynx of the III-IV (T2 - 4N0-2M0) stages, who received 3 cycles of neoadjuvant chemotherapy, participated in the study. Through randomization, patients were divided into the main group (n = 33) and the comparison group (n = 33). Both groups patients received neoadjuvant chemotherapy cycles with 21 - 28 days intervals according to the scheme: *paclitaxel* - 175 mg/m², *cisplatin* - 40 mg/m². The main group detoxification therapy consisted of arginine-containing drugs and enterosorbent, and the comparison group patients got crystalloid solutions detoxification therapy [4].

QOL was assessed by EORTC QLQ-H and N35 questionnaire, Karnowski's index and ECOG. Patients were examined in dynamics before treatment, and at the stages of chemotherapeutic treatment [8, 9]. Student's coefficient, Wilcoxon's test, χ^2 square [8, 9, 11] were used as statistical methods.

When assess QOL with the use of EORTC QLQ-H and N35 questionnaire, mainly patients' subjective assessments of their condition were taken into account, whereas Karnowsky's and ECOG index are more often used by doctors to assess the condition of an oncological patient and take into account, in addition to subjective parameters of QOL, objective indicators of the patients' condition [1, 3, 7, 9, 11].

Results and discussion

When study QOL according to the questionnaire, censored patients amounted to 10%. According to EORTC QLQ-H and N35 questionnaire, Karnowski's index and ECOG scale, a high score indicates a worsening situation (high level of severity of symptoms).

QOL analysis of patients with head and neck cancer according to EORTC-QLQ-H and N35 questionnaire for groups of patients is shown in Table 1.

Table 1

Analysis of the quality of life of patients with head and neck cancer according to EORTC-QLQ –H & N35

Treatment cycles	Main group, n=33	Comparison group, n=33	P
Before	42.9 ± 1.8	43.5 ± 1.1	0.165
First	35.9 ± 1.4	37.9 ± 0.9	0.229
Second	31.0 ± 0.6	34.1 ± 0.9	0.014
Third	29.0 ± 0.6	36.6 ± 1.4	0.007

It was found that QOL average values in the first and second groups before treatment did not differ significantly ($p > 0.05$).

Comparison of the dynamics of indicators according to the EORTC-QLQ-H & N35 questionnaire during the treatment period is given in the figure below.



Fig. 1. Dynamics of indicators according to EORTC-QLQ-H and N35 questionnaire during treatment in the main (first) group and the comparison group (second) of patients

From these data it follows that the initial values of the indicator in the main (first) group (42.9) and in the comparison group (second) (43.5) were comparable. During treatment, this ratio has changed markedly: in the first group it became 29.0 versus 36.6 in the other ($p = 0.007$). It should be noted that a lower value of the integral indicator corresponds to the better condition of the patient. An analysis of the quality of life of patients with head and neck cancer determined by Karnowski's index for groups of patients is given in table 2.

Table 2.

Analysis of the quality of life of patients with head and neck cancer by determining Karnowski's index

Treatment cycles	Main group, n = 33	Comparison group, n = 33	P
Before	63.1 ± 2.5	65.0 ± 2.4	0.583
First	70.6 ± 2.0	86.6 ± 2.3	0.492
Second	75.0 ± 1.9	72.1 ± 2.0	0.292
Third	76.9 ± 2.1	67.9 ± 2.9	0.013*

* -p< 0.05

According to the accepted gradation, the average value in the patients' groups under study before the treatment corresponds to the state when a patient is quite independent, although his normal activity is impossible. As it seen from the tables, the initial condition of the patients of the first and second groups is almost the same.

After treatment, the improvement of their condition was different. For the first group patients who got arginine-containing drugs and for whom enterosorption was used, Karnowsky's index rose significantly higher (see table).

Karnowsky's index for three treatment cycles increased compared with the initial value for the first group by 13.8 units, or 21.8%, while for patients of the second group this increase was 2.9 units, or 4.4%.



Fig. 2. Dynamics of the average Karnowsky's index

If we use the previously introduced indicator for the patient's condition improvement, then according to Karnowsky's index we have:

- Indicator of improvement in the main group: 21.8%;
- Indicator of improvement in the comparison group: 4.4%.

Table 3.

Analysis of ECOG status of laryngopharyngeal cancer patients

Treatment cycles	Main group, n=33	comparison group, n=33	p
Before	1.6 ± 0.8	1.6 ± 0.8	0.999
First	1.2 ± 0.7	1.5 ± 0.8	0.110
Second	0.9 ± 0.7	1.2 ± 0.7	0.086
Third	0.8 ± 0.8	1.4 ± 1.0	0.009

* $-p < 0.05$

It is important to note that before treatment, ECOG score in the main group and comparison group patients is almost the same (about 1.6) and corresponds to Karnowski's index values (about 65).

As a result of treatment, the improvement of the patients condition was different. For the patients who received arginine-containing drugs and enterosorption, ECOG score decreased significantly more (see the Table).

ECOG score for three treatment cycles compared to the initial value decreased for the main group by 0.8 units (from 1.6 to 0.8), or by 50.0%, while for patients in the comparison group this decrease was 0.2 units (from 1.6 to 1.4) or 21.4%.

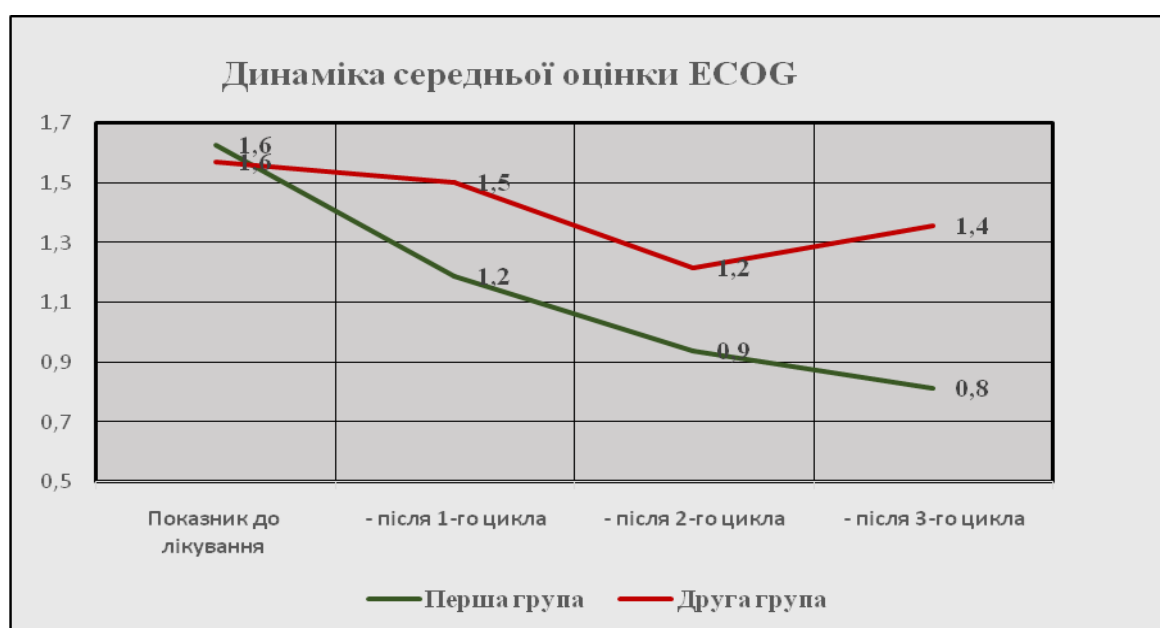


Fig. 3. ECOG dynamics of patients in the main group and the comparison group

From the data presented it follows that at each stage of treatment, the group average value (the lower is ECOG, the better) for the patients of the main group decreased more than the corresponding average value for patients in the comparison group. This indicates that treatment in the main group was more effective.

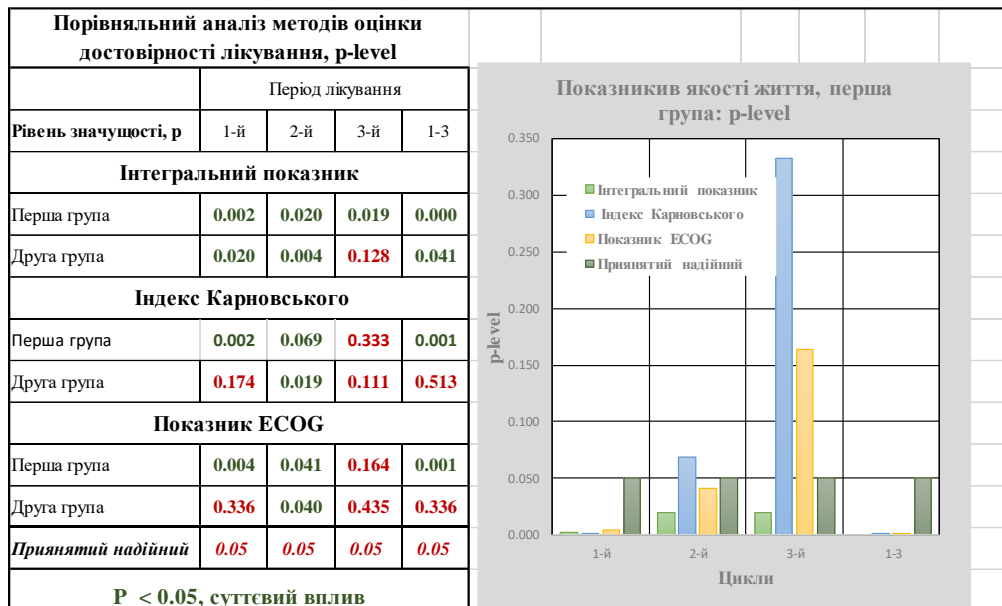


Fig. 4. Comparison of methods for assessing the quality of life to determine the effect of accompanying therapy (Wilcoxon test)

The highest level of confidence relates to the integral indicator.

Prior to treatment, in patients of both groups initially low QOL indexes were determined by all criteria that could be compared. There were no statistically significant differences ($p > 0.05$). The decrease in QOL indexes is due to the presence of a malignant neoplastic process, hospitalization to an oncological unit, information about treatment methods and terms, worsening of the patient's general condition and, as a result, depressive state, which is associated with personal anxiety about the outcome of the disease and the possibility of maintaining the previous social status.

In general, QOL of patients with malignant neoplasms of the larynx and pharynx was determined to a greater extent by the courses of neoadjuvant chemotherapy. After such special treatment, in both groups there was an improvement in physical, role and emotional functioning, decrease in the level of disease's symptoms. For almost every QOL index, the treatment performed had a positive effect, which is proved by the data in the corresponding tables, comparing the average values for the samplings before and after treatment.

Comparison of the treatment parameters in the two groups under study indicates that the complex treatment of the patients with malignant neoplasms of the laryngopharynx with arginine-containing drugs and enterosorption (main group) gives better results than the treatment with traditional means (comparison group). In the main group the indicators of overall and relapse-free survival are significantly better than those in the comparison group, where the patients received detoxification therapy with saline solutions up to 1.5 - 2.0 liters (standard protocol). The relapse-free survival period in the main group is 87% of the total survival period in the group. The relapse-free survival period in the comparison group is 72% of the total survival period in the group. The average disease-free survival period in patients in the main group is 22 months. The average disease-free survival period in patients in the comparison group is 18 months. The median survival curve is 66 months for the main and 54 months for the comparison group.

Conclusions

The research conducted has shown that QOL of laryngopharynx malignant neoplasms patients correlates with objective clinical indicators, such as tumor regression (the more the tumor volume decreases, the better QOL in each individual patient, and in the groups as a whole), the average relapse-free survival period (median survival curve is 66 months for the main and 54 months for the comparison group).

A relapse-free survival period (87 % in the main group, and 72 % in the comparison group) is completely determined by the courses of neoadjuvant chemotherapy. In this case, complex treatment of malignant neoplasms of laryngopharynx with the use of arginine-containing drugs and enterosorption gives better results of QOL improving in comparison with the use of standard protocol treatment. Karnowski's index was 21.8% in the main group, and 4.4% in the comparison group; ECOG score decreased by 50% for three treatment cycles compared to the initial value in the main group, while in the comparison group it amounted to 21.4%.

The use of QOL set of indicators (integral indicator EORTC-QLQ-H and N35, Karnowski's index and ECOG indicator) and statistical analysis done at each stage of treatment makes it possible to conduct more objective researches, draw the necessary conclusions, make reasonable adjustments to the treatment process, increase the evidence of medicine and treatment effectiveness.

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