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Quality of life in patients with non-small cell lung cancer

Kvalitet života bolesnika sa nesitnoćelijskim karcinomom pluća

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Abstract

Background/Aim. As lung cancer is considered the greatest contributor to death among all cancer types any help might be valuable in the assessment of treatment effects. The aim of this study was for assess the quality of life (QoL) in patients with non-small cell lung cancer (NSCLC) treated with gemcitabine-cisplatin regimen as the first line of chemotherapy. **Methods.** The QoL was assessed using certified Serbian translations of the European Organization for Research and Treatment of Cancer Quality Life Questionnaire Core 30 (EORTC QLQ-C30) and Lung Cancer Module (QLQ-LC13) – version 3. The questionnaire was used before starting treatment and after the completion of the 2nd and the 4th cycle of chemotherapy. The questionnaire scales and single items were compared in order to assess the impact of treatment on the QoL. **Results.** A total of 60 patients started and 51 completed all questionnaires. There were no changes in the global health status score between the baseline, the 2nd and the 4th cycle of chemotherapy (42.78 ± 15.76, 45.56 ± 17.59, 48.20 ± 19.24, respectively; $p = 0.1$). Social function score, symptom scores: nausea and vomiting, pain, appetite loss, constipation, diarrhea and financial difficulties score differed significantly among chemotherapy cycles, indicating improved or worsened the QoL. In the lung cancer symptom score a significant difference between measurements was observed in cough, alopecia, chest pain and in using analgesics. **Conclusion.** Monitoring of changes in the QoL among patients with locally advanced and metastatic NSCLC showed that chemotherapy did not decrease the global health status but led to significant changes in the social and financial functioning of patients. Some symptoms associated with the disease reduced in the intensity but some new occurred as a result of chemotherapy. Using questionnaires to assess the QoL helped in easier identification of adverse effects and specific problems for adequate treatment.

Key words:
quality of life; carcinoma, non-small-cell lung; antineoplastic combined chemotherapy protocols; surveys and questionnaires.

Apstrakt

Uvod/Cilj. S obzirom na činjenicu da je karcinom pluća najsmrtonosniji među svim karcinomima, dragocena je svaka pomoć u proceni efekta lečenja. Cilj ove studije bio je da se proceni kvalitet života (*quality of life* – QoL) obolelih od nesitnoćelijskog karcinoma pluća (NSCLC) koji su lečeni prvom linijom hemioterapije po protokolu gemcitabin-cisplatin. **Metode.** QoL procenjivan je primenom sertifikovane srpske verzije upitnika Evropske organizacije za istraživanje i lečenje karcinoma (EORTC QLQ-C30) i dodatka koji se odnosi na karcinom pluća (EORTC QLQ-LC13) – verzija 3. Bolesnici su ispunjavali upitnik pre započinjanja lečenja i nakon kompletiranja drugog i četvrtog ciklusa hemioterapije. Rezultati su poređeni kako bi se procenio uticaj lečenja na kvalitet života bolesnika. **Rezultati.** Ukupno 60 bolesnika bilo je uključeno u istraživanje, a 51 je popunio sve upitnike. Nije bilo statistički značajnih promena ukupnog QoL između vremena pre početka lečenja, nakon drugog i nakon četvrtog ciklusa hemioterapije (42,78 ± 15,76, 45,56 ± 17,59, 48,20 ± 19,24; $p = 0,1$). U socijalnom funkcionisanju, simptomatskim skalama (mučnina i povraćanje, bol, gubitak apetita, proliv, zatvor) i finansijskim teškoćama nađene su statistički značajne razlike pre lečenja i između ciklusa, ukazujući na poboljšanje ili pogoršanje QoL. Dodatni simptom skor za karcinom pluća pokazao je značajne razlike za kašalj, gubitak kose, bol u grudima i upotrebu analgetika. **Zaključak.** Praćenje promena QoL bolesnika sa lokalno uznapredovalim i metastatskim NSCLC pokazalo je da primena hemioterapije ne narušava ukupni QoL, ali da dovodi do značajnih promena u socijalnom i finansijskom funkcionisanju bolesnika. Smanjuje se intenzitet pojedinih simptoma povezanih sa bolešću, ali se kao posledica primene hemioterapije javljaju novi simptomi. Korišćenje upitnika za procenu QoL pomaže u lakšem prepoznavanju neželjenih efekata i specifičnih problema omogućavajući adekvatno lečenje.

Ključne reči:
kvalitet života; pluća, nesitnoćelijski karcinom; lečenje kombinovanjem antineoplastika, protokoli; ankete i upitnici.

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Introduction

Lung cancer (small-cell and non-small cell) has been the second most frequent malignancy in the world population for the last ten years. Among men the most common is prostate cancer, while among women breast cancer. Lung cancer includes about 13% of all newly diagnosed malignancies [1]. It is responsible for 19.4% of all deaths from malignancies and the most common cause of death from malignancy in female and male population [2]. Each year more people die from lung cancer than from breast, prostate and colon cancer together [3].

Lung cancer is usually diagnosed in the elderly population. Two-thirds of patients with this malignancy are older than 65 years, 70 years is the average age. The disease is very rare in people younger than 45 years, less than 2% [3]. Non-small cell lung cancer (NSCLC) includes adenocarcinoma, squamous cell carcinoma and "not otherwise specified" histopathological type accounts for 85% of all lung cancer cases [4]. Lung cancer retains its status as the leading cause of cancer death (26.1%) in Europe [1].

The majority of patients at the time of diagnosis is in the advanced stage of the disease. The treatment strategy for NSCLC depends on the disease stage. In the early stages the treatment of choice is surgical intervention, in locally advanced disease the therapy of choice is a combination of radiotherapy and chemotherapy, and chemotherapy alone is an option for patients with metastatic disease [5].

A growing consensus among healthcare providers and researches is that treatment efficiency should be judged not only by its effects on surviving time but also by the quality of life (QoL).

The QoL is defined as a multidimensional construct that encompasses social, physical, cognitive, and psychological domains [6, 7]. QoL assessment is an important indicator of treatment success with the traditional indicators of tumor response, progression-free survival and surviving time [8]. There are different instruments for the evaluation of QoL and some of them are specifically designed for patients with lung cancer. The European Organization for Research and Treatment of Cancer (EORTC) – Lung Cancer (LC)-13 questionnaire, a list of symptoms that is used together with the core C-30 questionnaire, is the most commonly used in studies worldwide. The Lung Cancer Symptom Scale (LCSS) is a list of 9 organ-specific symptoms, assessed by the patients and 6 symptoms which were evaluated by an outside observer. There are no items associated with the evaluation of toxicity of treatment. The Functional Assessment of Cancer Therapy – Lung (FACT-L) questionnaire consists of 41 items, includes the general health status and organ-specific symptoms [9].

The aim of this study was assessment of the QoL in patients with NSCLC treated with gemcitabine-cisplatin regimen as the first line of chemotherapy.

Methods

This prospective follow-up study included 60 patients with histopathologically confirmed NSCLC in stage IIIb and IV (according to the TNM classification of malignant tumors) [10].

In our study QoL was measured using standard questionnaires: the 30-item EORTC Quality of Life Questionnaire (EORTC QLQ-C30) and its lung cancer supplementary questionnaire – (EORTC QLQ-LC13). Inspite of the recommendation, QoL assessments have not been incorporated in clinical practice yet [11, 12].

The questionnaires in Serbian language, used in the study, had been approved and certified by the EORTC [13].

The patients were treated with gemcitabine-cisplatin regimen as the first line chemotherapy.

Inclusion criteria were as follows: age between 18 and 75 years, general condition of the patient-performance status of 0 and 1 according the scale Eastern Cooperative Oncology Group (ECOG) [14], satisfactory haematological status (number of leukocytes $\geq 3.5 \times 10^9$/L, the platelet count $\geq 100 \times 10^9$/L and hemoglobin ≥ 100 g/L), satisfactory liver and kidney function (creatinine, urea, bilirubin, transaminases within normal range), sufficient cardiac function without active arrhythmia, signs and symptoms of congestive heart failure.

Exclusion criteria were: pregnancy, previously applied chemotherapy or radiotherapy, estimated survival less than three months, the presence of metastases in the central nervous system, the simultaneous presence of other malignant disease or systemic connective tissue disease, patients with adenocarcinoma with activating mutation of epidermal growth factor receptor (EGFR) gene, they were treated with tyrosine kinase inhibitors as the first line therapy [15].

The questionnaire and its purpose were explained to each patient in individual interviews and it was self-completed by each patient. It is necessary to avoid any involvement by health professionals. The patients were informed on the confidentiality of all data obtained and their right not to respond either partially or totally.

The patients personally completed the EORTC QLQ-C30 and QLQ-LC13 (version 3.0). The QLQ-C30 consists of multi-item scales and single-item measures. There are 5 functional scales, 3 symptom scales, a global health status/QoL scale, and 6 single items. Multi-item scales include a different set of items. A specific item occurs in only one scale.

All measurements ranged from 0 to 100 due to easier comparison. High scores on the global health status and functional scales indicate a high level of functioning – good QoL, while on the symptom scales low scores represent less intense symptom experience and consequently a higher QoL [14]. The QLQ-LC13 is intended for use among lung cancer patients varying in disease stage and treatment modality (surgery, chemotherapy and radiotherapy) and consisting of 13 items. It should always be complemented by the QLQ-C30. It consists of questions for assessing lung cancer-associated symptoms (cough, hemoptysis, dyspnea and site specific pain), side effects of the therapy (sore mouth, dysphagia, peripheral neuropathy and alopecia) and use of pain medication [16].

A total of 60 patients started, but 51 completed all three questionnaires. The patients filled questionnaires before sta-

rting the treatment, and after completing 2th and 4th cycle of chemotherapy. There was a 21-day interval between the cycles. Nine patients did not complete all the questionnaires. They were excluded during the study because of the progression of the disease after two cycles of chemotherapy and then chemotherapy regimen was changed. Unfortunately, one patient died after the second cycle of chemotherapy. Monitoring took four months for each patient. Tumor response was evaluated by the Response Evaluation Criteria in Solid Tumors (RECIST 1.1) [17, 18].

Statistical analysis

Data are presented as counts (%) or the mean ± standard deviation, depending on their type. The linear mixed model was used to assess differences between three measurements (baseline, second and fourth month). The linear mixed model was used to analyse changes in all scales. It has flexibility to model time effect and, the most important, it can handle missing data. *Post hoc* test with Bonferroni correction was used to assess significant differences between each measurement. All *p* values less than 0.05 were considered significant. All data were analyzed using SPSS 20.0 (IBM Corp.) statistical software. Our study has a number of outcomes. That is the reason for not performing multivariate analysis.

Results

Between April 2012 and August 2015, a total of 60 patients were analyzed. The average age was 62.9. Most of the patients were males. A half of the sample had adenocarcinoma and a half squamous cell carcinoma. Stage III was more frequent than stage VI and the performance status ECOG 1 was more frequent than ECOG 0 (Table 1).

A response to the applied chemotherapy was: no one patient had complete response, 32 patients had partial response after two and 19 after four cycles of chemotherapy. Stable disease was found in 20 of the patients after two and 24 after four cycles of chemotherapy. Progression of disease was found in 8 of the patients after two, and 8 of the patients after four cycles of chemotherapy (according to RECIST 1.1). In the patients with progression of the disease after second cycle, chemotherapy was not continued by the same protocol.

Table 2 represents the distribution of the patients concerning the response to chemotherapy after the cycles 2 and 4. The most frequent status was partial response after 2 and the stable disease after the cycle 4. There was a highest percent of the stable disease status of the total number of responses.

The global health status**,** functional scale scores and symptom scores in the three examination periods are presented in Table 3.

Table 1

Basic characteristics of patients with non-small cell lung cancer (NSCLC)

Patient's characteristics	Patients
Demographic	
age (year), $\bar{x} \pm SD$	62.9 ± 8.1
gender, n (%)	
male	45 (75)
female	15 (25)
Clinical	
HP*, n (%)	30 (50)
adenocarcinoma	30 (50)
squamous cell	
Stage**, n (%)	
IIIb	35 (58.3)
IV	25 (41.7)
PS ECOG***	
0	17 (28.3)
1	43 (71.7)

***Histological type (HP) of NSCLC World Health Organisation – WHO histological classification of tumors of the lung) [18];**
****Disease stage (7th Edition of the tumor, node, metastasis (TNM) classification of malignant tumors) [12];**
*****Performance status for the Eastern Cooperative Oncology Group (PS ECOG) [14].**
$\bar{x}$ – mean; SD – standard deviation.

Table 2

Response to chemotherapy in patients with non-small cell lung cancer (NSCLC) according to Response Evaluation Criteria in Solid tumors (RECIST) 1.1 [18]

Chemotherapy cycle	Patients, n (%)		
	PR	SD	PD
After 2nd	32 (53.3)	20 (33.3)	8 (13.3)
After 4th	19 (37.3)	24 (47.1)	8 (15.7)

PR – partial response; SD – stable disease; PD – progression of disease.
Note: no one patient had complete response.

Table 3

Global health status, functional scores, symptoms scores and changing from the baseline to post-chemotherapy scores for the 30-item Quality of Life Questionnaire (QLQ-C30)

Parameters	Scores, $\bar{x} \pm SD$			*p*-value
	Baseline (I)	After the 2nd cycle of CT (II)	After the 4th cycle of CT (III)	
Global health status	42.78 ± 15.76	45.56 ± 17,59	48.20 ± 19.24	0.100
Physical function	71.78 ± 19.61	73.00 ± 18.51	76.34 ± 19.34	0.064
Role function	53.33 ± 22.72	52.22 ± 22.23	56.54 ± 23.11	0.108
Emotional function	71.81 ± 17.77	71.81 ± 19.59	74.02 ± 21.64	0.910
Cognitive function	90.28 ± 17.97	90.28 ± 18.49	88.89 ± 20.18	0.260
Social function	58.33 ± 24.06[a,b]	52.22 ± 23.46	52.94 ± 28.23	0.016*
Fatigue	39.81 ± 18.33	41.11 ± 20.69	36.17 ± 19.86	0.323
Nausea	4.17 ± 9.01[a,b]	23.61 ± 19.23	19.93 ± 17.64	< 0.001*
Pain	26.94 ± 22.98[b]	25.00 ± 20.70[c]	19.28 ± 19.54	0.001*
Dyspnea	10.56 ± 17.88	11.11 ± 16.99	8.50 ± 16.12	0.718
Insomnia	20.56 ± 24.62	22.78 ± 22.54	20.26 ± 24.11	0.537
Appetite	27.78 ± 31.99[a,b]	35.00 ± 29.06	33.99 ± 27.07	0.015*
Constipation	12.22 ± 26.01[b]	17.22 ± 24.92	20.92 ± 28.25	0.036*
Diarrhea	0.56 ± 4.30[a,b]	4.44 ± 12.97	5.23 ± 15.45	0.013*
Financial difficulties	18.33 ± 23.31[a,b]	30.00 ± 27.24	32.03 ± 29.03	0.000*

Significant difference between [a]I *vs* II, [b]I *vs* III, [c]II *vs* III; *significant *p*-value;
Note: A higher score represents a high level of functioning and better quality of life (QoL) in the global health status and functional scores. A higher symptom score represents a higher level of symptom.
$\bar{x}$ – mean value; SD – standard deviation; CT – chemotherapy.

Changes in global health status during the monitoring period are presented in Figure 1.

A significant difference was observed in social function, nausea, pain, appetite loss, constipation, diarrhea and financial difficulties. In *post hoc* testing, using the Bonferroni correction, the first measurement was significantly different from second or third, while only in a few comparisons the second one was significantly different from the third.

There was a deterioration in the social functioning of patients and more financial difficulties during the follow-up period.

Nausea, appetite loss, constipation and diarrhea were the symptoms which worsened and pain, a symptom that significantly improved during monitoring period.

In the LCSS significant difference between measurements was observed in cough, alopecia, chest pain and using analgesics. *Post hoc* testing, using Bonferroni adjustment, revealed significant differences between the first and third measurement, and the second and third in only one case (Table 4).

Symptoms which improved during a follow-up period were cough and chest pain. A significantly was reduced use of analgesics. Only alopecia progressively worsened during the study.

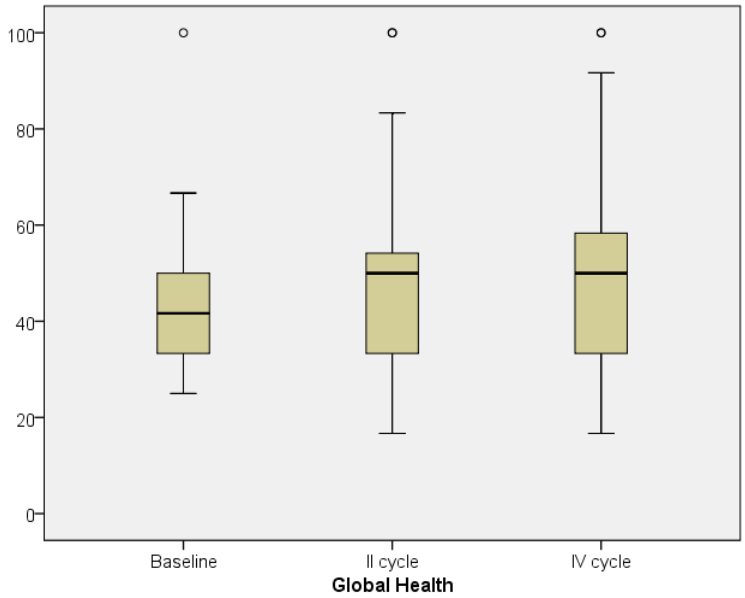

Fig. 1 – Changing of the global health status during chemotherapy. There were no statistically significant changes between baseline, 2nd and 4th cycle of chemotherapy.

Table 4

Lung cancer symptom scale (LCSS) and changing from the baseline to post-chemotherapy scores for the lung cancer (LC)-13 module

Parameters	Scores, $\bar{x} \pm SD$			*p*-value
	Baseline (I)	After the 2nd cycle of CT (II)	After the 4th cycle of CT (III)	
Dyspnea	27.22 ± 18.12	26.30 ± 18.75	22.66 ± 18.32	0.408
Cough	36.11 ± 24.77[b]	32.22 ± 22.94	25.49 ± 22.69	0.012*
Hemoptysis	2.78 ± 9.29	2.78 ± 9.29	2.61 ± 11.24	0.886
Sore mouth	4.44 ± 12.97	4.44 ± 11.43	3.92 ± 10.85	0.996
Dysphagia	5.56 ± 13.95	6.11 ± 14.38	5.23 ± 12.24	0.845
Neuropathy	5.56 ± 13.95	8.33 ± 15.80	8.50 ± 16.12	0.150
Alopecia	1.11 ± 6.03[a,b]	32.22 ± 26.73[c]	39.87 ± 29.83	< 0.001*
Chest pain	32.78 ± 27.10[b]	30.56 ± 26.25[c]	22.22 ± 20.73	0.005*
Arm pain	7.78 ± 17.75	7.22 ± 16.34	5.23 ± 13.94	0.148
Other	20.00 ± 22.30	20.00 ± 23.13	15.69 ± 20.39	0.240
Analgesics use	10.56 ± 15.64[a,b]	19.44 ± 16.57	14.38 ± 16.67	< 0.001*

Significant difference between [a]I *vs* II, [b]I *vs* III, [c]II *vs* III; *significant *p*-value; CT – chemotherapy; $\bar{x}$ – mean value; SD – standard deviation.

Note: A higher score represents a higher level of symptom.

Discussion

Most of the patients in our study were male according to the global statistics for NSCLC [2]. The number of patients with adenocarcinoma and squamous cell carcinoma was equal. Although adenocarcinoma is more common in developed countries, in our country this is not so because of the widespread habit of cigarette smoking which is strongly related with squamous cell carcinoma (Institute of Public Health of Serbia "Dr Milan Jovanović-Batut") [19]. The patients were treated with gemcitabine/cisplatin regimen as the first line chemotherapy. The gemcitabine-cisplatin is one of the most effective regimens against advanced NSCLC [20]. A response to chemotherapy (according to RECIST 1.1) in our patients was similar to previously published studies [16, 21]. Despite advances in treatment, survival of patients with IIIb and IV stage of NSCLC is relatively short [22]. In Europe, for IIIb stage of NSCLC the median survival time with treatment is 13 months, while a 5 year survival rate is 5%. For IV stage the median survival time is about 8 months, and a 5 year survival rate is 1% (European Society for Medical Oncology – ESMO 2010) [23]. Many studies show a short survival of these patients inspite of treatment, and for last ten years there has been no significant improvement.

A median survival in our study was not calculated because of a relatively short follow-up period and a certain number of patients who left the study because of changing chemotherapeutic regimen after progression of disease.

Chemotherapy offers the possibility to control or decrease cancer-associated symptoms [24]. QoL scores at the start of treatment, and subsequent changes in those scores, may predict survival duration independently of the treatment group, performance status, and treatment response [25].

There were no significant changes in the global health status of the patients between the baseline, the 2nd and 4th cycle of chemotherapy (Figure 1).

Wintner et al. [26] found that chemotherapy alone, regardless of the number of cycles, had no impact on the QoL of patients with lung cancer.

Our results are different from Braun et al. [27] who demonstrate that the QoL is worse in previously treated patients than in newly diagnosed patients, suggesting that chemotherapy has a negative impact on QoL.

Hollen et al. [28] reported that the QoL at baseline may be of greater prognostic value than disease stage or performance status.

We found a significant deterioration in the social functioning of the patients during treatment. Studies [29, 30] that examined the emotional and social experiences of patients with lung cancer established that these patients reported a higher level of stress, compared with people who suffered from different types of cancer. Several cross-sectional studies showed that a high level untreated stress leads to a lower QoL, less satisfaction with the medical services, lower adherence to treatment, and shorter patient survival [30].

During chemotherapy, gastrointestinal toxicity is very common and leads to a reduced dose of drugs, disposal treatment and interruption of treatment, unfortunately. We found a significant increase in the incidence of diarrhea and constipation after the start of chemotherapy compared to a baseline. The causes of diarrhea during the course of disease and treatment are numerous and complex. Diarrhea can be directly related to cancer treatment and according to the pathophysiological mechanism may be exudative, secretory, osmotic, malabsorption, and due to motility disorders. A percentage of patients with diarrhea or constipation as a result of their treatment estimated to be about 10% of patients with advanced cancer [31]. The mechanisms underlying chemotherapy-induced constipation remain poorly defined. Often it is secondary to drugs that are given to control other chemotherapy or cancer-induced symptoms such as antiemetics and opioids [32]. These symptoms should be treated non-pharmacologically or pharmacologically, because they significantly deteriorate the QoL.

Nausea and vomiting were significant problems for the patients treated with highly emetogenic chemotherapy. The patients who received first line cisplatin-based chemotherapy had a higher level of symptoms: fatigue, nausea and vomiting, appetite loss and constipation in relation to carboplatin-

based chemotherapy. Our results, showing a significant increase in the level of of nausea and vomiting compared with the baseline agree with the results of other studies [33, 34]. Early detection and control of these symptoms is very important part of treatment to avoid development of anticipatory nausea and vomiting [35].

The loss of appetite is typically present in 15–25% of all cancer patients at diagnosis and may also occur as a side effect of treatment. It can be exacerbated by chemotherapy and radiation therapy side effects such as taste and smell changes, nausea, and vomiting [36]. Xara et al. [37] report that a number of lung cancer related symptoms such as the loss of appetite were associated with worse QoL among 56 patients with NSCLC. Increased appetite loss is associated with shorter survival [28]. Our study show that in the second measuring these symptoms were most expressed. Better scores at the third measuring were the result of timely application of symptomatic therapy.

The study showed a significant increase in financial difficulties in the second and especially in the third measuring. Patients during the course of the disease in most cases are unable to work and spend their financial resources to the increased cost of living due to the disease. The results of our study are consistent with those from a large database study by Buzaglo et al. [38] which reported that lung cancer patients had the highest rate (> 8%) of serious financial consequences and personal bankruptcy in relation to all other malignancies.

Symptoms associated with lung cancer which require palliative treatment may arise from the primary tumor (dyspnea, hemoptysis, pain, fatigue, etc.), symptoms of the regional spread of disease (pleural effusion, superior vena cava syndrome), and symptoms of distant metastasis (liver, brain, bone, etc). These symptoms may have significant negative effects on the QoL.

Approximately 65% of people with lung cancer have a chronic cough. Cough in lung cancer is a distressing symptom with a significant impact on the QoL, and there is no effective therapy. Persistent cough can interfere with speech, eating, and sleeping, thus impacting the QoL [39]. During our research we found a reduction in the intensity of cough compared with baseline and it is consistent with Park et al. [40] who reported that cough tends to improve during chemotherapy.

Alopecia is a very common side effect of antineoplastic drugs. The patients in our study had significant hair loss after the 2nd and even more evident after the 4th cycle of chemotherapy. Studies reported increased occurrence of alopecia after the 1st cycle of chemotherapy, a result that indicates low QoL. According to Can et al. [41], hair loss is the most devastating effect and can directly affect social and emotional aspects of the QoL of female patients undergoing chemotherapy.

Chemotherapy-induced hair loss is considered to be one of the most traumatic factors in cancer patient care. Hair loss can negatively impact individual perceptions of appearance, body image, sexuality, and self-esteem, as well as deprive patients of their privacy, because this treatment-related outcome is readily associated with having cancer by the lay public. About 47% of female cancer patients consider hair loss to be the most traumatic aspect of chemotherapy. Motivation for a comprehensive support program has the potential to improve psychological status of patients with hair loss during their cancer therapy [42].

Pain is one of the several symptoms of cancer that create a poor QoL because pain affects physical functions and has an emotional impact. For cancer patients, pain and symptom control are the best predictors of overall QoL scores because the effects of unrelieved pain and poorly managed symptoms interfere with the activities of daily living, mood, mobility, and independence. It is also the most common cause of disability and is associated with depression, anxiety, and sleep disturbances [43].

A reduction of pain is one of the most important goals in the treatment of cancer patients. In this study we found that pain was significantly lower after starting and during chemotherapy compared to the time before the treatment. Several studies such as that of Herndon et al. [44] showed that pain is the principal prognostic factor in advanced NSCLC.

During our study, the level of pain decreased due to antineoplastic therapy and use of analgesic. Successful treatment of pain includes the following: assessment of cancer pain, a review of specific cancer pain syndromes, general principles of cancer pain management, an overview of risk management in patients treated with opioids, prevention and management of opioid side effects, the clinical use of non-opioid analgesics (including nonsteroidal anti-inflammatory drugs and adjuvant analgesics), non-pharmacologic methods of cancer pain management [45].

Opioids are widely used for treatment of pain in patients with cancer because of their safety, multiple routes of administration, ease of titration, reliability, and effectiveness for all types of pain (somatic, visceral, neuropathic) [46].

We found no significant changes in the scores for dyspnea, hemoptysis, sore mouth, dysphagia and neuropathy. Literature data show a low incidence of the aforementioned symptoms when cisplatin are used in combination with gemcitabine, a factor that should be considered in the choice of drug therapy [47].

Recent studies suggest that among patients with NSCLC more lung cancer related symptoms may adversely affect both a response to the treatment and the overall survival. Cancer treatment may positively and negatively affect the QoL. Tumor response may have a positive influence on survival and QoL, but adverse effects of treatment may have a negative effect on these parameters [48, 49].

Conclusion

The influence of treatment on the QoL is ever more important when considering treatment options for patients. In this study monitoring of changes in the QoL among patients with locally advanced and metastatic NSCLC show that chemotherapy does not decrease the global health status, but leads to significant changes in social and financial functioning of patients. Some symptoms associated with the disease reduce their intensity but some new occur as the result of chemotherapy. Using questionnaires to assess the QoL during treatment helps in identifying changes of the QoL, adverse effects of therapy and specific problems for adequate treatment. Palliative treatment should not deteriorate the QoL.

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