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Quality of Life in Patients with Advanced Non-Small-Cell Lung Cancer Receiving Palliative Chemotherapy

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Abstract

The goal of this study was to explore quality of life in patients with advanced non-small-cell lung cancer (NSCLC) in an attempt to single out features that could help predict the possibility of non-completion of chemotherapy. The survey tool was the Quality of Life Questionnaire Core-30 (QLQ-C30) with the module Lung Cancer 13 (LC-13) developed by the European Organization for Research and Treatment of Cancer. The assessment of quality of life (QoL) was performed in 58 patients with advanced NSCLC before palliative chemotherapy and it was repeated in 43 patients who completed at least three cycles of chemotherapy. We found that the patients who failed to complete the chemotherapy course distinctly showed, in contradistinction to those who completed it, poor physical functioning in (67.6 ± 16.3 vs. 78.3 ± 21.3 points, respectively, $p < 0.05$) and the lack of appetite (27.1 ± 38.0 vs. 48.9 ± 37.5 points, respectively $p < 0.05$). At the end of palliative chemotherapy alopecia, sore throat, and constipation significantly worsened QoL, but global health status remained unchanged. In conclusion, poor physical functioning and loss of appetite seem to harbinger a risk of non-completion of chemotherapy in advanced NSCLC.

Keywords

Cancer symptoms · Health status · Lung cancer · Palliative chemotherapy · Physical functioning · Quality of life

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1 Introduction

Most of patients with non-small-cell lung cancer (NSCLC) are diagnosed late in the course of disease, i.e., in stage III or IV according to the TNM classification system (Broggio and

Bannister 2016). Palliative chemotherapy remains the only method of treatment in such patients, which may extend the survival rate by a matter of weeks. In case of contraindications to platin-based combination chemotherapy, mono-chemotherapy can be advised. Both in poly- and mono-chemotherapeutic regimens, the patient should receive at least three cycles of treatment. Balanced effectiveness and tolerance of treatment is of crucial meaning (Lemonnier et al. 2014). The assessment of quality of life (QoL) enables the estimation of disease influence on everyday functioning and is recommended by international expert groups, as a constituent of chemotherapy evaluation, next to survival and side effects of treatment (Losanno and Gridelli 2016; Mak et al. 2016; Quinten et al. 2009).

One of the research tools used to estimate QoL in the course of lung cancer is the Quality of Life Questionnaire Core-30 (QLQ-C30) with the module Lung Cancer 13 (LC-13) developed by the European Organization for Research and Treatment of Cancer (EORTC) (Fiteni et al. 2016; Aaronson et al. 1993). The QLQ-C30 enables the assessment of QoL in functioning scales (physical, role, cognitive, emotional, and social), in multi- and single-item scales of common cancer symptoms, in the scale of disease impact on the patient's economic condition, and in the scale of global health status/QoL. The QLQ-LC13 assesses the symptoms associated with lung cancer.

Although chemotherapy in advanced NSCLC aims to maintain current QoL (Losanno and Gridelli 2016), data on its effectiveness are contentious. Some studies show a deterioration of QoL in the domains of physical, role, emotional, and social functioning (Liu et al. 2013) and other show stabilization of QoL (Wintner et al. 2013). There also are studies showing an improvement in QoL in the domain of social functioning, with inappreciable changes in other domains (Dai et al. 2017), and *vice versa*, an improvement in individual domains but a deterioration in physical functioning (de Oliveira et al. 2013). Therefore, the aim of this study was to use the QLQ-C30 and QLQ LC-13 questionnaires to assess QoL of patients with advanced, stage III or IV, NSCLC receiving palliative chemotherapy and to determine whether this kind of assessment before treatment could help predict the completion of at least three cycles of chemotherapy planned for a patient.

2 Methods

There were 58 consecutive patients (30 women and 28 men), aged 50–81 years, enrolled into the study from October 2014 to June 2015. All of them had the diagnosis of NSCLC; 37 patients were in the stage III and 21 patients in stage IV of the disease, according to the TNM classification system (Broggio and Bannister 2016). The general health condition of the patients was 0–2 according to the Zubrod performance scale (Oken et al. 1982). All of the patients were slated to receive palliative chemotherapy, 46 of them received poly-chemotherapy based on platin (cisplatin or carboplatin with navelbine, vepesid, or pemetrexed) and 12 received mono-chemotherapy (with navelbine, docetaxel, or pemetrexed).

Out of the 58 patients, 43 received at least three cycles of chemotherapy, with 13 patients receiving three cycles, 22 patients – four cycles, 6 patients – five cycles, and 2 patients – six cycles. Fifteen patients failed to complete the treatment, among them 10 patients received only one cycle and five patients received two cycles of chemotherapy. The reason for discontinuation of treatment were the following: deaths (2 patients), not turning-up after the first cycle of chemotherapy (2 patients), progression of lung cancer (8 patients), and severe side effects of chemotherapy (3 patients).

The patients filled out the QLQ-C30 and QLQ-LC13 questionnaires, either by themselves or with the help of medical staff when required. A comparative analysis conducted concerned the questionnaire before chemotherapy onset and the second time questionnaire distributed to patients before at least the third cycle of chemotherapy. In both questionnaires, the answers are scored in a 4-point scale, with the lowest value (1 = not at all) meaning no problems in particular area and the highest value (4 = very much) representing significant intensity of a problem. There also are two

items concerning the global health status that are scored in a 7-point scale, with the lowest value representing very bad result and the highest meaning an excellent result. According to EORTC recommendations, raw scores were mathematically transformed to the 0–100 range (Fayers et al. 2001). Thus, the higher the score in the functional and global health status the better was the level of function and better QoL; it was to the opposite concerning the scale for symptoms.

Data were presented as means ±SD, and medians with interquartile range (IQR). Differences between the starting and concluding scores were considered moderately significant when ≥10 points, highly significant when ≥11–20 points, and distinctly significant when ≥21 points after Osoba et al. (1998). A score ≤ 50 points was taken as indicating a low global health status after Arraras et al. (2016). The Mann Whitney U test was used for ordinal data comparisons. A p-value ≤0.05 defined statistically significant differences. The analysis was conducted using a commercial statistical package of Statistica v12 (StatSoft, Tulsa, OK).

3 Results

Tables 1 and 2 show a comparison of QoL scores before chemotherapy and before the last conducted, at least third, cycle of it in 43 patients who completed the planned treatment. There were no significant changes in the scores, either in functioning scales, with the mean pre–post chemotherapy difference of 5.0 points (range 1.2–7.3 points) or in global health status/QoL, with the pre–post chemotherapy difference of 1.6 points. However, before the last cycle of chemotherapy, the impact of symptoms such as alopecia and constipation on QoL, significantly increased, with the pre–post chemotherapy increase as high as 31.8 and 14.0 points, respectively. There also was a small, clinically not meaningful, albeit a significant increase by 3.9 points in the sore throat scoring at the end chemotherapy. On the other side, we found statistically insignificant, but clinically favorable improvements, concerning the sleep disorders (a decrease by 12.4 points), arm pain (a decrease by 11.6 points), and cough (a decrease by 9.3 points). Other changes in QoL domains in the course of treatment were neither significant not clinically meaningful.

Comparison of QoL before chemotherapy in 43 patients who completed chemotherapy to that in 15 patients who did not is shown in Tables 3 and 4. Those who failed to complete chemotherapy had a lower score, i.e., worse physical functioning and a higher one i.e., severer symptoms regarding loss of appetite and dysphagia.

The three main symptoms influencing QoL before chemotherapy were insomnia, cough, and fatigue in the patients who completed chemotherapy, and appetite loss, insomnia, and cough in those who failed to complete it. In turn, the three main symptoms influencing QoL at chemotherapy completion were fatigue, alopecia, and insomnia.

Table 1 Quality of life questionnaires (QLQ)-C30 and LC13 at baseline before initiation of chemotherapy and later before the completing cycle of chemotherapy

QLQ	Baseline before chemotherapy (n = 43)		Before the completing cycle of chemotherapy (n = 43)		p
Physical functioning	80 (67–97)	78.3 ± 21.3	73 (60–87)	71.0 ± 22.9	ns
Role functioning	100 (67–100)	78.7 ± 33.4	83 (50–100)	72.9 ± 31.5	ns
Emotional functioning	83 (46–92)	68.8 ± 30.9	83 (67–96)	75.0 ± 24.1	ns
Cognitive functioning	83 (67–100)	78.7 ± 25.5	83 (75–100)	83.3 ± 21.5	ns
Social functioning	100 (67–100)	76.0 ± 34.2	83 (58–100)	74.8 ± 28.5	ns
Global health status/QoL	50 (42–67)	55.2 ± 21.9	50 (50–67)	56.8 ± 18.5	ns

Data are medians (IQR interquartile range) and means ±SD
QoL quality of life, *ns* nonsignificant

Table 2 Symptom score at baseline before initiation of chemotherapy and later before the completing cycle of chemotherapy

Symptom score	Baseline before chemotherapy (n = 43)		Before the completing cycle of chemotherapy (n = 43)		p
Fatigue	22 (11–44)	30.2 ±30.0	33 (22–61)	37.7 ±27.2	ns
Nausea and vomiting	0 (0–0)	7.0 ±18.6	0 (0–17)	10.5 ±15.9	ns
Pain*	0 (0–33)	22.1 ±31.6	0 (0–33)	19.4 ±26.2	ns
Dyspnea*	0 (0–33)	27.1 ±36.6	0 (0–33)	22.5 ±27.9	ns
Insomnia	33 (0–67)	41.1 ±37.0	33 (0–33)	28.7 ±28.7	ns
Appetite loss	0 (0–33)	27.1 ±38.0	33 (0–33)	27.1 ±30.2	ns
Constipation	0 (0–0)	13.9 ±31.1	33 (0–33)	27.9 ±33.3	<0.01
Diarrhea	0 (0–0)	4.7 ±15.6	0 (0–0)	3.1 ±9.8	ns
Dyspnea **	11 (11–44)	25.8 ±27.1	22 (11–44)	28.2 ±23.3	ns
Cough	33 (33–67)	39.5 ±30.2	33 (0–33)	30.2 ±34.0	ns
Hemoptysis	0 (0–0)	7.0 ±21.3	0 (0–0)	1.5 ±7.1	ns
Sore throat	0 (0–0)	2.3 ±15.3	0 (0–0)	6.2 ±15.0	<0.05
Dysphagia	0 (0–0)	4.7 ±17.2	0 (0–0)	2.3 ±9.0	ns
Peripheral neuropathy	0 (0–33)	17.8 ±26.6	0 (0–33)	18.6 ±27.5	ns
Alopecia	0 (0–0)	1.5 ±7.1	0 (0–67)	33.3 ±39.8	<0.001
Chest pain	33 (0–33)	26.4 ±31.3	0 (0–33)	17.1 ±25.6	ns
Arm pain	0 (0–0)	22.5 ±33.1	0 (0–33)	10.9 ±18.9	ns
Pain in other body parts	0 (0–33)	20.2 ±33.4	0 (0–33)	18.6 ±25.5	ns
Financial problems	0 (0–33)	20.9 ±30.9	33 (0–33)	27.9 ±29.0	ns

Data are medians (interquartile range; IQR=Q3 – Q1) and means ±SD. Medians equal 0 (0–0) indicate that all the non-zero values measured were placed between 75th and 100th percentiles, i.e., in Q4
ns nonsignificant; *in QLQ-C30; **in QLQ-LC13

Table 3 Quality of life questionnaires (QLQ)-C30 and LC13 at baseline before initiation of chemotherapy in patients who later completed it and those who failed to complete chemotherapy

QLQ	Patients who completed chemotherapy (n = 43)		Patients who discontinued chemotherapy (n = 15)		p
Physical functioning	80 (67–97)	78.3 ±21.3	67 (57–80)	67.6 ±16.3	<0.05
Role functioning	100 (67–100)	78.7 ±33.4	83 (58–100)	80.0 ±23.7	ns
Emotional functioning	83 (46–92)	68.8 ±30.9	83 (70–96)	79.4 ±23.3	ns
Cognitive functioning	83 (67–100)	78.7 ±25.5	100 (75–100)	85.6 ±19.8	ns
Social functioning	100 (67–100)	76.0 ±34.2	100 (92–100)	91.1 ±16.5	ns
Global health status/QoL	50 (42–67)	55.2 ±21.9	50 (46–67)	53.9 ±14.7	ns

Data are medians (IQR; interquartile range) and means ±SD
QoL quality of life, *ns* nonsignificant

4 Discussion

This study demonstrates that patients with stage III and IV NSCLC remained, generally, in a stable QoL, with inappreciable deterioration in physical, role, and social functioning and with slight improvements in the emotional and cognitive functioning at the end of palliative chemotherapy. Also, global health status/QoL hovered above the satisfactory level of 50 points, according of the criteria of Arraras et al. (2016).

Sleep disorders are common in patients with lung cancer. They appear in over half (56%) of patients with NSCLC (Nishiura et al. 2015) and are usually manifest by insomnia (Dean et al. 2015). Poor sleep efficiency, having a strong impact on QoL as measured by EORTC QLQ-C30, is present especially in lung cancer patients who are heavy smokers (Gu et al. 2018). Sleep studies, using

Table 4 Symptom score at baseline before initiation of chemotherapy in patients who later completed chemotherapy and those who failed to complete chemotherapy

Symptom score	Baseline in patients who completed chemotherapy (n = 43)		Baseline in patients who discontinued chemotherapy (n = 15)		p
Fatigue	22 (11–44)	30.2 ±30.0	33 (22–39)	35.6 ±21.5	ns
Nausea and vomiting	0 (0–0)	7.0 ±18.6	0 (0–0)	5.6 ±12.1	ns
Pain	0 (0–33)	22.1 ±31.7	33 (0–42)	31.1 ±32.0	ns
Dyspnea*	0 (0–0)	27.1 ±36.6	33 (17–33)	31.1 ±26.6	ns
Insomnia	33 (0–67)	41.1 ±37.0	33 (33–67)	46.7 ±32.9	ns
Appetite loss	0 (0–33)	27.1 ±38.0	67 (17–67)	48.9 ±37.5	<0.05
Constipation	0 (0–0)	13.9 ±31.1	0 (0–67)	28.9 ±39.6	ns
Diarrhea	0 (0–0)	4.6 ±15.6	0 (0–0)	2.2 ±8.6	ns
Dyspnea**	11 (11–44)	25.8 ±27.1	22 (11–28)	25.2 ±23.6	ns
Cough	33 (33–67)	39.5 ±30.2	33 (33–67)	44.0 ±32.5	ns
Hemoptysis	0 (0–0)	7.0 ±21.3	0 (0–0)	6.7 ±19.7	ns
Sore throat	0 (0–0)	2.3 ±15.2	0 (0–0)	2.2 ±8.6	ns
Dysphagia	0 (0–0)	4.6 ±17.2	0 (0–33)	13.3 ±21.1	<0.05
Peripheral neuropathy	0 (0–33)	17.8 ±26.6	33 (0–33)	24.4 ±29.5	ns
Alopecia	0 (0–0)	1.5 ±7.1	0 (0–0)	8.9 ±26.6	ns
Chest pain	33 (0–33)	26.4 ±31.3	33 (0–50)	31.1 ±36.7	ns
Arm pain	0 (0–33)	22.5 ±33.1	33 (0–67)	35.6 ±36.7	ns
Pain in other body parts	0 (0–33)	20.2 ±33.4	33 (0–33)	26.7 ±31,4	ns
Financial problems	0 (0–33)	21.0 ±30.9	0 (0–17)	13.3 ±27.6	ns

Data are medians (interquartile range; IQR=Q3 – Q1) and means ±SD. Medians equal 0 (0–0) indicate that all the non-zero values measured were placed between 75th and 100th percentiles, i.e., in Q4
ns nonsignificant; *in QLQ-C30; **in QLQ-LC13

actigraphy and the Pittsburgh Sleep Quality Index (PSQI), have revealed poor sleep quality significantly affecting QoL in NSCLC patients receiving chemotherapy (Dean et al. 2015) or worsening of sleep problems after two cycles of chemotherapy (Liu et al. 2013). In a similar study, NSCLC patients with sleep disorders have had a diminished QLQ-C30 score of 46.3 ± 20.2 compared to the 65.2 ± 20.7 in those without such disorders (Nishiura et al. 2015). Our present findings are in line with those studies as we report that sleep disorders, particularly insomnia, were the most important symptoms adversely affecting QoL at the time of NSCLC diagnosis in patients who either completed or not the chemotherapy course. In addition, however, we noticed that insomnia improved from the clinical standpoint at chemotherapy completion. A pre–post chemotherapy difference amounted to 12.4 points downward, which was in a range of moderate clinical significance.

In the current study, cough came in second, after insomnia, as a symptom influencing QoL at the time of NSCLC diagnosis in patients who completed chemotherapy and it was in third place, after the loss of appetite and insomnia, at chemotherapy completion. Cough had an impact on QoL both before and after chemotherapy, although its unfavorable effect was somehow corrected after chemotherapy. In contrast, we found that fatigue, another essential factor having an impact on QoL at the time of diagnosis, somewhat increased before the completing chemotherapy cycle. Both cough and fatigue have been reported as common symptoms, present in over 90% of lung cancer, which curtail daily activities of patients (Choi and Ryu 2018, Iyer et al. 2013, 2014; Okuyama et al. 2001). Fatigue is sometimes reported as a non–typical paraneoplastic symptom of lung cancer (Latimer and Mott 2015; LeBlanc et al. 2015). In the QLQ C-30 evaluation of chemotherapy effects, fatigue has been reported as a symptom strongly adversely affecting influencing QoL, which may go in parallel with chemotherapy-related neutropenia

in NSCLC patients (Kristensen et al. 2018; Lemonnier et al. 2014).

In the current study we noticed a chemotherapy-related difference in the intensity of symptoms that affect QoL. Alopecia, sore throat, and constipation became intensified after chemotherapy. The first two symptoms are well known side effects of chemotherapy (Park et al. 2013), with sore throat having been reported as a symptom associated with shorter survival in NSCLC patients (Arraras et al. 2016), whereas constipation may presumably result from other drugs used for lung cancer treatment, such as opiates or codeine. Contrary to the consistent impression regarding adverse effects of chemotherapy, we failed to notice any major gastrointestinal symptoms or peripheral neuropathy that would worsen QoL. A loss of appetite remained unchanged by chemotherapy as well. Pain intensity in this study ranged, on average, from 20 points before to 29 points after chemotherapy, indicating a slight adverse effect on QoL. In fact, pain became less severe before the completing cycle of chemotherapy, with a mean score below 20. Likewise, dyspnea was rather stable throughout the course of observation, having no appreciable effect on QoL. Hemoptysis was a rare symptom, both before and after chemotherapy.

Another finding of note in this study was the presence of decreased physical functioning, loss of appetite, and dysphagia already before the commencement of chemotherapy, pointing to a risk of its non-completion. That is in line with previous studies assessing QoL and survival after chemotherapy, in which poor physical functioning at the time of NSCLC diagnosis was a strong predictor of chemotherapy non-completion and of overall unfavorable outcome (Ediebah et al. 2014; Braun et al. 2011; Movsas et al. 2009; Fielding and Wong 2007; Herndon et al. 1999; Ganz et al. 1991). In this study we did not examine the relationship between QoL and survival of NSCLC patients, but chemotherapy non-completion was related to fatal disease progression. Thus, we believe the present findings indirectly confirm the role of QoL in predicting the course of advanced NSCLC, including a risk of non-completion of chemotherapy. We conclude that the evaluation of QoL should belong to the diagnostic armamentarium in advanced NSCLC patients slated to receive palliative chemotherapy.

Conflicts of Interest The authors declare no conflicts of interest in relation to this article.

Ethical Approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. The study was approved by the Ethics Committee of Wrocław Medical University in Wrocław Poland. The authors obtained written permission from EORTC to adopt and use a Polish version of QLQ-C30 and QLQ-LC13 questionnaires.

Informed Consent Informed consent was obtained from all individual participants included in the study.

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