DOI: 10.12991/201317380

ORIGINAL RESEARCH

Quality of life assessment of patients with metastatic lung cancer receiving platinum-based chemotherapy

Beril G. Kıvrak-Bernardelli[3], Çağlar Macit[1], S. Beril Kadıoğlu[1], Taflan Salepci[2], Philip M. Clark[1]

ABSTRACT

AIM: The aims of the study were to investigate, possible changes in quality of life (QOL) during chemotherapy, which factors might affect QOL and the relationship between QOL and performance status.

MATERIAL AND METHODS: The study was conducted at the oncology clinics of Dr. Lutfi Kirdar Kartal Training and Research Hospital, Istanbul, Turkey. Patients diagnosed with advanced small-cell lung cancer or stage IV non-small cell lung cancer were enrolled in the study. They were given platinum-based chemotherapy. The QOL EORTC core questionnaire QLQ–C30 (version 3.0) and the lung cancer module QLQ-LC13 were conducted on four separate occasions. Data related to the patients' clincal and performance status (Karnofsky Performance Status Scale (KPS) and ECOG) were recorded throughout the study.

RESULTS: With treatment, significant increases in chemotherapy related side-effects and in symptom scales related both to adverse drug reactions and disease progression were recorded. A strong, significant, negative correlation ($r = -0.71$, $p < 0.05$) between ECOG performance and all domains of EORTC QLQ-C30 was observed, similar to that between KPS and EORTC QLQ-C30 ($r = -0.74$, $p < 0.05$).

CONCLUSION: This research indicates a lack of benefit in terms of QOL from platinum-based chemotherapy in patients with metastatic lung cancer. Routine QOL assessment in this patient population may encourage the development of treatment programs which minimize chemotherapy side-effects, while maximizing patients' well being.

KEYWORDS: Small-Cell-Lung-Carcinoma, Non-Small-Cell-Lung-Carcinoma, Quality of Life, Karnofsky Performance Status Scale, Chemotherapy

AFFILIATIONS
[1]Yeditepe University, Clinical Pharmacy, Istanbul, Turkey
[2]Ministry of Health Dr. Lutfi Kirdar Research and Training Hospital, Oncology, Istanbul, Turkey
[3]University of Maryland, School of Medicine, Baltimore, USA

CORRESPONDENCE
Philip M. Clark

E-mail:
pmclark@yeditepe.edu.tr

Received:
27.09.2012
Revision:
06.02.2013
Accepted:
07.02.2013

INTRODUCTION

Epidemiology and mortality

Lung cancer has become one of the leading global causes of cancer death in both men and woman (1), and is responsible for 12.8% of all cancer cases and 17.8% of the all cancer deaths (2). The 5-year relative survival rate for lung cancer for the period of 1996 to 2003 was 16%, reflecting only a modest improvement from the 1950s (3-6). In Turkey, lung cancer incidence is increasing by 3% annually (7,8); with a male prepondrance (m/f ratio12:1). The most commonly diagnosed histological types are epidermoid carcinoma in males and adenocarcinoma in females (9).

Approximately 85% of patients with lung cancer are diagnosed at an advanced stage that is not amenable to surgical intervention. For patients with stage metastatic non small cell lung carcinoma (NSCLC) or extensive-stage small cell lung carcinoma (SCLC) the 5 year survival rate may be less than 1% (10).

Morbidity related to lung carcinomas

Besides high mortality, lung cancer is associated with high morbidity (see Appendix 1) including chest pain, cough, hemoptysis and dyspnea. (11, 12). Cough may be due to airway obstruction, post obstructive pneumonia, excessive mucus production, parenchymal metastases, or pleural effusion (13). Dyspnea occurs in most patients with lung cancer during the course of their disease due to direct impingement of the airway, underlying chronic lung disease, radiation- or chemotherapy-induced pneumonitis, infection, pleural effusion, or pulmonary embolism (14).

The commonest sites of metastases are contra-lateral lung, brain, liver, bone, adrenal gland, and extra-thoracic lymph nodes. Symptoms of brain metastases may include headache, nausea, vomiting, focal weakness, seizures, confusion, ataxia, and visual disturbances (15). In terms of bone metastasis, the axial skeleton and proximal long bones are most commonly involved. Pain due to bone metastases is present in up to 25% of patients at initial diagnosis (16).

Constitutional symptoms, such as depression, fatigue, anxiety, insomnia, anorexia, and cachexia, cause significant debility in patients with lung cancer. Depression and psychological distress are very common, but are infrequently recognized or treated (17).

Less frequently encountered, paraneoplastic syndromes describe the effects of cancer that occur systemically or at sites distant from tumor such as symptoms related to hypercalcemia (18), hyponatremia (19), Cushing's syndrome (20), Lambert-Eaton syndrome, and other neurologic disorders.

Treatment of advanced lung cancer

The cornerstone of treatment of patients with extensive stage SCLC is multiagent chemotherapy. Stage IV non-small cell lung cancer (NSCLC) is largely incurable using present-day therapies. For most patients under age 75 years with good performance status, the best first approach is double-agent chemotherapy utilizing carboplatin plus a second agent, usually paclitaxel, gemcitabine, or docetaksel (21) (see Appendix 2).

It has been surmised that patients who have an ECOG performance status of 0 or 1 may benefit more than patients with performance status 2, from the combination of a platinum agent, either cisplatin or carboplatin, and a second agent (22).

Quality of life assessment in lung cancer

Quality of life (QOL) can be defined as the effect of an illness and its therapy upon a patient's physical, psychological, and social well being as perceived by the patient themselves (23). QOL assessments should be given due priority whenever it is expected that the survival differences between the treatment groups is going to be small, or when the difference in at least one factor predicting QOL is expected to be large. The effect of two different therapeutic modalities on QOL and overall survival helps select the better modality. In fact, a particular treatment may be preferred if it improves the QOL, even if the survival is not superior (24).

QOL is closely linked to symptom burden and severity in lung cancer. Loss of physical functioning, psychological events such as depression, and reduced overall QOL are associated with uncontrolled symptoms (25, 26). In addition, depression has been found to be an independent prognostic factor for lung cancer, irrespective of stage (27).

The European organization for the treatment and research of cancer quality of life questionnaire, EORTC QLQ-C30, (see Appendix 3) includes five functional scales (physical, role, cognitive, emotional, and social), three symptom scales (fatigue, pain, nausea, and vomiting), and one global health and QOL scale. This instrument has demonstrated a high reliability and validity across the continents (28). The EORTC QLQ-LC 13 questionnaire (see Appendix 4) was developed as a lung cancer specific supplementary to the EORTC QLQ-C30. It assesses lung cancer related symptoms, treatment related side-effects, pain, and pain medication (29). The Turkish language versions of both EORTC QLQ-C30 and QLQ-LC13 have been validated for use in lung cancer patients. (30, 31)

Performance status (PS)

PS is the patient's ability to perform certain physical activities, especially related to mobility, work, and self-care. The most well established tools are the Karnofsky Performance Scale (KPS) (see Appendix 5), and the Eastern Cooperative Oncology Group (ECOG) (see Appendix 6). KPS is a simple and widely used numerical instrument for rapidly quantifying the PS of an individual based on patients' level of independence (38). Studies have demonstrated a direct relationship between KPS and the perceived QOL in patients with cancer, including lung cancer (27, 35). Similarly, the ECOG is a five-grade observer rating of patients' physical ability (35, 37). Both instruments (KPS and ECOG) have been found to be valid (37) including the Turkish language versions. (32, 33)

The aims of the study were to determine how QOL is affected by chemotherapy, which other factors affect QOL apart from chemotherapy in this patient group and the relationship between QOL and performance status.

MATERIAL AND METHOD

The study was a prospective-randomised research conducted in the oncology out-patient clinics of Dr. Lutfi Kirdar Kartal Training and Research Hospital, a 750-bed ministry of health facility located in Istanbul, Turkey.

Inclusion criteria required for patients were: diagnosis of metastatic [stage IV] lung cancer; inclusion within two weeks of diagnosis; not having yet received treatment. All participants were Turkish-speaking, conscious, and fully informed of their diagnosis. Additionally, mortality before completion of the third cycle of chemotherapy was accepted as an exclusion criterion.

A total of 17 out of 28 patients diagnosed with advanced SCLC, or stage IV NSCLC, and who were to receive platinum-based chemotherapy, fulfilled the criteria above, gave their consent and participated fully at every stage in this study. Four patients declined to give their consent; five patients who previously gave their consent decided not to participate before the first, second, third, or fourth chemotherapy treatment; and two patients died during the course of the study.

Setting, sample and analizing

1. After obtaining verbal consent, the patients' demographic data was collected (age, gender, smoking history).

2. Structured interviews, each of which lasted between 30 to 90 minutes, were conducted based on the EORTC core questionnaire for quality of life in cancer patients QLQ–C30 (version 3.0), and the specific lung cancer module questionnaire EORTC QLQ-LC13. Interviews were conducted in outpatient clinics or by telephone, using validated Turkish translations of the above

questionnaires on four separate occasions, pre-treatment and before the second, third and fourth cycle of chemotherapy.

3. Data related to the patients' clincal and performance status (KPS and ECOG) were also recorded on four occasions during the study.

4. Statistical analysis was carried out using Prism® (version 5 for Mac OS X 2009). QOL differences between the baseline, first, second and third chemotherapy were analyzed using repeated-measures one-way analysis of variance (ANOVA). Pair-wise, post hoc comparison was performed between the groups at the baseline, first, second, and third chemotherapy applying the Tukey test. Correlation coefficients between global health status and age/smoking habit/ECOG/KPS were calculated using Pearson correlation analysis.

RESULTS

Demographics

Table 1 provides demographic details of the patient group included in the study.

Quality of life

As seen in both Figure 1 and Table 2, there was a continuous downward trend in General/ Global Health Status, from the baseline to the third chemotherapy. The decreases between the baseline and third chemotherapies ($p< 0.005$) and the second and third chemotherapies ($p< 0.005$) were statistically significant ($F= 1.520$).

Other changes in QOL scores, according to assessment of the QLQ-C30 instrument, are summarized in Table 2. Regarding functional scales there were statistically important losses in all the functional areas: physical functioning decreased significantly between the baseline and third chemotherapies ($p< 0.05$, $F= 3.336$); role functioning between the baseline and third chemotherapies ($p< 0,05$, $F= 1.016$); emotional function between the baseline and third chemotherapies ($p< 0.05$, $F= 3.173$); cognitive functioning between the baseline and second chemotherapies, the baseline and third chemotherapies, and the first and third chemotherapies ($p< 0.005$, $F= 4.152$); and social functioning decreased significantly between the baseline and third chemotherapies and the first and third chemotherapies ($p<0.05$, $F=6.14$).

TABLE 1. Patients' Demographics and Clinical Characteristics

Variables	N= 17 (%)
Age, yr (mean±SD)	59.29 ± 1.73
Gender, No	
Male	14 (82.35)
Femaie	3 (17.64)
Histology	
Small cell	3 (17.64)
Non-small cell	14 (82.35)
Adenocarcinoma	11 (64.70)
Others	3 (17.64)
Metastatic area	
Hemotorax	9 (52.94)
Bone	3 (17.64)
Brain	1 (5,88)
Liver	1 (5.88)
Other	3 (17.64)
Biopsy area	
Bronchoscopy	14 (82.35)
Bronchoscopy+Transthorasic tru-cut biopsy	3 (17.64)
Treatment	
paclitaxel+ carboplatin	6 (35.29)
cisplatin+ etoposide	8 (47.05)
cisplatin+ gemcitabine	2 (11.76)
docetaxel+ cisplatin	1 (5.88)
Smoking	
20 pack/ years	10 (58.82)
25 pack/ years	3 (17.64)
50 pack/ years	4 (23.52)

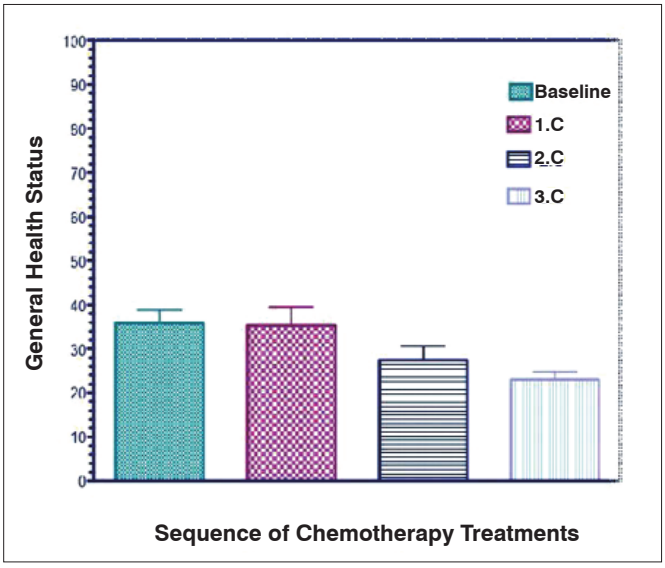

FIGURE 1. General health status scores at the four assessments
*With respect to GHS, there was a continuous downward trend from the baseline to the third chemotherapy. The decreases between the baseline and third chemotherapies ($p< 0.005$) and the second and third chemotherapies ($p< 0.005$) were significant. ($F= 1.520$)

Concerning symptom scales there were significant increases in the reported incidence of the following clinical signs: nausea and vomiting increased significantly between the baseline and second chemotherapies and between the baseline and third chemotherapies ($p< 0.05$, $F= 1.301$); dyspnea symptoms increased from the first chemotherapy to the third ($p< 0.023$, $F= 1.931$); insomnia between the baseline and second chemotherapies and the baseline and third chemotherapies ($p < 0.05$, $F= 1.523$); and appetite loss increased significantly between the baseline and second chemotherapies, baseline and third chemotherapies, and between the first and third chemotherapies ($p < 0.003$, $F= 1.668$). Non - significant increases in fatigue, pain, constipation, diarrhoea and financial difficulties were observed.

Table 3 summarizes the trends in QOL with progressing treatment according to the lung cancer specific questionnaire (QLQ-LC13). Regarding treatment-related side effects, significant increases were recorded in all areas as follows: incidence of sore mouth increased significantly between the baseline and first, second, and third chemotherapies ($p < 0.05$, $F= 1.085$); dysphagia between the baseline and second and third chemotherapies ($p < 0.05$, $F= 6.559$); peripheral neuropathy between the baseline and first, second, and third chemotherapies ($p < 0.05$, $F= 7.040$); and alopecia increased significantly between baseline and first, second, and third chemotherapies, between first and second, and between first and third chemotherapies ($p < 0.05$, $F= 0.9904$).

TABLE 2. QLQ scores according to QLQ-C30 at the four assessments

EORTC QLQ-C30 (n=17)			(mean ± SD)	
Areas	**Baseline**	**1st Chemotherapy**	**2nd Chemotherapy**	**3rd Chemotherapy**
Global Health Status/ QLQ	35.78± 2,81	35.29 ± 3,86	27.45 ± 2,97	23.04 ± 0,87
Functional scales*				
Physical functioning (○)	53.73 ± 3,83	49.02 ± 2,86	43.14 ± 2,91	38.04 ± 2,86
Role functioning (○)	52.94 ± 5,94	41.18 ± 2,95	38.24 ± 3,92	35.29 ± 2,76
Emotional functioning (○)	62.25 ± 5,64	57.35 ± 3,76	50.00 ± 5,89	40.69 ± 5,94
Cognitive functions (○,◊,□)	64.71 ± 7,96	61.76 ± 6,92	45.10 ± 3,86	35.29 ± 4,84
Social functioning (○,□)	44.12 ± 4,98	43.14 ± 2,84	32.35 ± 2,75	23.53 ± 3,93
Symptom scales**				
Fatigue	56.21 ± 3,98	55.56 ± 2,78	60.13 ± 2,98	66.67 ± 2,62
Nausea and vomiting (○,◊)	17.65 ± 5,94	33.33 ± 3,86	43.14 ± 5,64	47.06 ± 3,95
Pain	54.90 ± 5,67	55.88 ± 3,72	60.78 ± 4,76	68.63 ± 3,84
Dyspnea (□)	56.86 ± 3,73	45.10 ± 3,77	54.90 ± 2,82	62.75 ± 3,68
Insomnia (○,◊)	49.02 ± 6,82	62.75 ± 8,88	78.43 ± 2,95	78.43 ± 2,81
Appetite loss (○,◊,□)	49.02 ± 7,91	58.82 ± 7,96	76.47 ± 5,94	88.24 ± 3,86
Constipation	41.18 ± 5,91	35.29 ± 4,93	39.22 ± 2,75	41.18 ± 3,97
Diarrhea	19.61 ± 4,68	21.57 ± 3,68	23.53 ± 4,81	27.45 ± 5,78
Financial difficulties	27.45 ± 5,76	31.37 ± 5,82	37.25 ± 2,94	39.22 ± 3,82

* The scores range from 0 to 100, with lower scores representing a loss of function.
** Higher scores represent a greater severity of symptoms and side effects;
filled boxes indicate significant changes from baseline values or between chemotherapy cycles ($p < 0.05$).
○ Indicates a significant difference between baseline and third chemotherapy
□ Indicates a significant difference between first and third chemotherapy
◊ Indicates a significant difference between baseline and second chemotherapy

TABLE 3. QLQ scores according to LC13 at the four assessments

QLQ-LC13				
Areas	**Baseline**	**1st Chemotherapy**	**2nd Chemotherapy**	**3rd Chemotherapy**
Symptom scales*				
Cough	58.82 ± 5	49.02 ± 4	58.82 ± 4	60.78 ± 4
Haemoptysis	37.25 ± 7	29.41 ± 8	50.98 ± 5	50.98 ± 6
Dyspnea	52.94 ± 3	54.25 ± 3	58.17 ± 2	65.36 ± 2
Pain in chest	41.18 ± 8	39.22 ± 5	54.90 ± 6	62.75 ± 5
Pain in arm or shoulder	52.94 ± 4	43.14 ± 4	50.98 ± 4	52.94 ± 4
Pain in other parts	29.41 ± 8	35.29 ± 8	33.33 ± 9	29.41 ± 8
Sore mouth	11.76 ± 4	37.25 ± 8	49.02 ± 6	56.86 ± 5
Dysphagia	29.41 ± 7	43.14 ± 6	56.86 ± 4	62.75 ± 4
Peripheral neuropathy	43.14 ± 6	62.75 ± 4	62.75 ± 2	76.47 ± 3
Alopecia	0	49.02 ± 5	78.43 ± 3	86.27 ± 4

*The scores range from 0 to 100, with higher scores representing a higher level of symptoms and side effects; filled boxes indicate significant changes from baseline values or between chemotherapy cycles ($p < 0.05$).

On the other hand non-significant increases were observed for lung cancer associated symptoms (cough, haemoptysis, dyspnea), and site specific pain (chest, arm and shoulder, and other areas).

Other findings related to factors that may affect QOL

The mean age of the patients was 59.23±1.73 (Table 1). No significant correlation was found between age and general health status. ($p > 0.05$).

All of our patients had a smoking history (Table 1) with a mean packet year = 27.94±12.75, although none were smoking after diagnosis. No correlation between the number of packet years and QOL was found in this patient group.

Performance scales

As can be observed from Table 4, there was a significant difference in the ECOG performance between the baseline and second and third chemotherapies ($p < 0.05$, $F = 0.923$). In the same way, there were significant differences between the baseline and second and third chemotherapies, and between first and third chemotherapies for KFS values ($p < 0.05$, $F = 9.507$).

Relationship between QOL and Performance status

As can be seen in Figure 2, there was a significant negative correlation between ECOG performance scale and QOL as reflected by General Health Status ($r = -0.71$, $p < 0.05$).

As shown in Figure 3, there was a significant positive correlation between KFS performance scale and GHS ($r = 0.74$, $p < 0.05$).

DISCUSSION

Effect of chemotherapy on QOL

It was observed in our study that as treatment progressed, there were significant increases in chemotherapy related side-effects

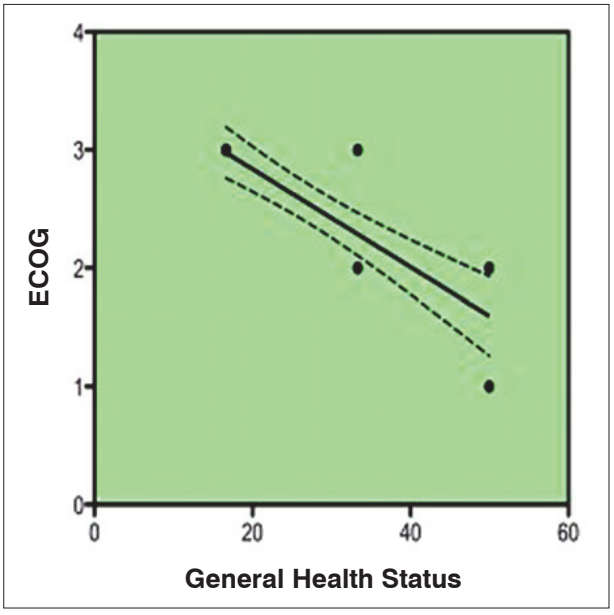

FIGURE 2. Correlation between ECOG performance scale and Global Health Status

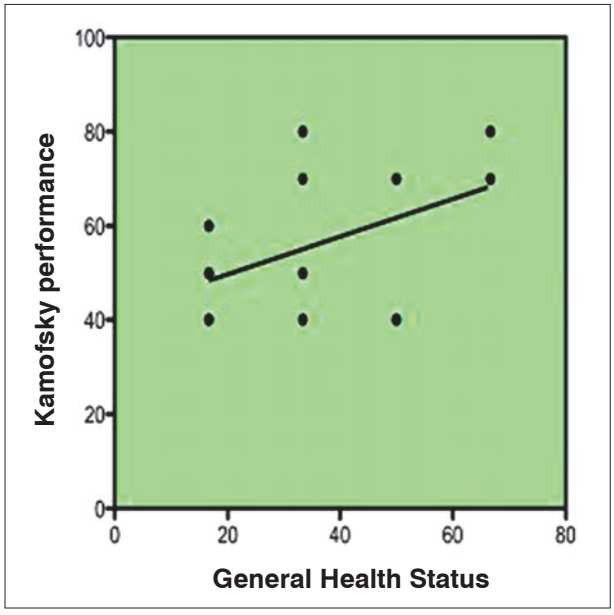

FIGURE 3. Correlation between Karnofsky performance scalesand Global Health Status

and in symptom scales, related both to adverse drug reactions and disease progression. The association of QOL with chemotherapy has been evaluated in several studies. Helsing et al compared platinum based chemotherapy with best supportive care and demonstrated significant survival benefit in the chemotherapy group with significant improvement in dyspnea, pain, insomnia, and social function (38). This study demonstrated the positive aspects of chemotherapy in patients with metastatic lung cancer, as did that of Esbensen et al (39) in which global health status/QLQ showed no significant difference, while emotional function increased and nausea and vomiting decreased.

In contrast, Huinink et al (40) determined that clinical and haematologic toxicity (hair loss, nausea/vomiting, and appetite loss) was more pronounced in patients receiving cisplatin/etoposide compared to single agent gemcitobine. Bozcuk et al assessed the quality of life of patients with advanced disease with an ECOG performance status of ≤ 2. They showed that the patients receiving non-platinum containing, single- agent chemotherapy experienced less fatigue (41).

In our study, all the patients (n= 17) were receiving platinum-based chemotherapy (Table1). From baseline to third chemotherapy, there was a significant increase in treatment-related side effects including sore mouth, dysphagia, peripheral neuropathy, and alopecia (Table 3). At the same time, there was a significant decrease in GHS and Functional Scales including physical functioning, role functioning, emotional functioning, cognitive functions, and social functioning (Table 2). There was also an increase in symptom scales including nausea and vomiting, dyspnea, insomnia, and appetite loss (Table 2). Our data is thus in agreement with previous reports in which patients with metastatic disease and ECOG PS=2 appear to experience more toxicity and treatment- related side effects than patients with PS=1 (42).

When the results of more recent trials are compared to previously published data, the percentage of PS-2 patients in the older trials should be taken into consideration. Comparative trials in advanced disease generally demonstrate only very small superiority of platinum vs non-platinum based therapy ie 4% or 5% gain in survival at two years. This small benefit may be either overestimated or underestimated if populations are not comparable (i.e., same percentage of PS-2 patients). The American Society for Clinical Oncology (ASCO) clinical practice guidelines recommend the use of chemotherapy in selected patients with advanced NSCLC (i.e. PS-0 or -1, and possibly -2). Our data is in agreement with previous reports in which patients with metastatic disease and ECOG PS=2 appear to experience more toxicity and have a shorter duration of survival than patients with PS=1 (43). It could be argued, therefore, that PS-2 patients are generally candidates for systemic treatment in addition to best supportive care, but should be treated with singe agents which have less side effects rather than combination therapy (39). In this regard, single agent regimens such as vinorelbine was found to be active and well tolerated in Stage IV NSCLC patients (44).

Two situations present unique difficulties; firstly if the treatment improves QOL but worsens survival due to drug related toxicity, and secondly, if QOL deteriorates but survival improves. In these cases, the choice of how to manage the disease is usually made jointly with the oncology team and the patient (24). The evidence presented above, suggests that the benefit of chemotherapy over best supportive care is still questionable.

TABLE 4. ECOG and KFS performance scale at the four assessments

Performance scale	Baseline	1st Chemotherapy	2nd Chemotherapy	3rd Chemotherapy
ECOG*	2.05 ± 0.1	2.23 ± 0.1	2.52 ± 0.1	2.58 ± 0.1
KARNOFSKY**	60 ± 4	55.88 ± 3	50 ± 3	45.29 ± 2

* ECOG, score range from 0 to 4, with a lower score representing a higher level of performance.
** KFS, score range from 0 to 100, with a higher score representing a higher level of performance.
Filled boxes indicate significant changes from baseline values or between chemotherapy cycles ($p < 0.05$).

Other factors that might affect QOL in this patient group

Matsumoto et al (45) analyzed factors that affect quality of life, and noted an increase of the QOL in patients over 65 years. Mohan et al (46) however, demonstrated that QOL did not correlate with age, a finding consistent with our study. Further research including a large sample in each age group may be needed to confirm the findings from these studies.

Montazeri at al (29) also evaluated the impact of gender on quality of life in 129 lung cancer patients and there was not a significant difference. Tanrikol et al (47) assessed the factors that affect QOL in Turkish lung cancer patients, and showed that men have significantly higher quality of life scores than women. These results have been confirmed in a study conducted in the United States. (48). We did not evaluate the effect of gender on quality of life because there were only 3 women in the study group.

Analyses using statistical modeling techniques show a tight association between national mortality rates and smoking (49). The risk of lung cancer among cigarette smokers increases with the duration of smoking and the number of cigarettes smoked per/year. In some studies, it was found that patients who continue smoking after diagnosis have a poor QOL score (50, 51). In our study, no relation was observed between duration of smoking in terms of packet years, and QOL scores. This result is similar to the findings of an earlier study conducted by Sarna et al (49).

Relationship between QOL and performance status

Schaafsma and Osoba (52) reported that QOL was a much broader concept than that reflected by KPS, and they observed only a weak correlation between the two in lung cancer patients. However, in our study, there was a strong significant negative correlation between ECOG performance and all domains of the EORTC QLQ-C30, and a strong significant positive correlation between KPS and all domains of the EORTC QLQ-C30 (see Fig 2 and 3), which is consistent with the findings of Mohan et al (46). Compromised performance status leads to decreased performance of activities of daily living, and infringes on the independent functioning of the patient. Thus, although performance status is not a true measure for QOL, it should be seen as an important predictor of QOL of the patient and should be routinely assessed by the oncological team.

CONCLUSION

Our research indicates that patients with advanced disease do not benefit from platinum-based chemotherapy in terms of QOL. Routine QOL assessment may encourage the development of treatment programs which minimize chemotherapy side-effects, while maximizing patients' well being.

Our research did not show any significant relationship between age or smoking history and QOL. However, larger multi-center studies may help in providing a more comprehensive evaluation of the effect of various demographic and clinical variables on QOL in this setting.

Although performance status is not a true measure for QOL, it should be seen as an important prognostic factor and predictor of QOL, and should therefore be routinely assessed by physicians. (27). Our study confirms the prognostic value of performance status in patients with advanced lung cancer.

Platin içeren kemoterapi alan metastatik akciğer kanserli hastaların yaşam kalitesinin değerlendirilmesi

ÖZET

AMAÇ: Bu çalışmanın amacı, kemoterapi sırasında yaşam kalitesinde olması muhtemel değişiklikler, yaşam kalitesini etkileyen faktörler ve performans durumuyla yaşam kalitesi arasındaki ilişkiyi incelemektir.

MATERYAL ve Metotlar: Bu çalışma Dr. Lütfü Kırdar Kartal Eğitim ve Artaştırma Hastanesi onkoloji kliniklerinde yürütülmüştür. İleri düzeyde küçük hücreli akciğer kanseri ve faz IV(metastatik) küçük hücreli olmayan akciğer kanseri teşhisi alan hastalar çalışma kapsamına alınmıştır. Hastalara platin içeren kemoterapi uygulanmıştır. Hastaların yaşam kalitesini ölçen QOL (Quality of Life) EORTC QLQ-C30 (European Organization for Research and Treatment of Cancer Quality of Life Questionnaire/Avrupa Kanser Araştırmaları ve Tedavi Organizasyonu Yaşam Kalitesi Anketi) (versiyon 3.0) ve akciğer kanseri modülü QLQ-LC13 (Quality of Life Questionanaire Lung Cancer) dört kez yürütülmüştür. Hastaların klinik ve performans durum {Karnofsky Performance Status Scale (KPS) ve Eastern Cooperative Oncology Group/Doğu Kooperatif Onkoloji Grubu (ECOG)} verileri çalışma süresince kaydedilmiştir.

BULGULAR: Tedaviyle birlikte, kemoterapiye bağlı yan etkiler ile advers ilaç reaksiyonları ve hastalığın ilerlemesiyle ilgili semptomlarda anlamlı artışlar kaydedilmiştir. Hem ECOG performans ile EORTC QLQ-C30 tüm alanlarında ($r=-0.74$, $p<0.05$), hem de KPS ve EORTC QLQ-C30 arasındaki ($r= -0.71$, $p<0.05$), güçlü, anlamlı ve nagatif korelasyon gözlenmiştir.

SONUÇLAR: Bu çalışma metastatik akciğer kanserinde platin içeren kemoterapi alan hastalarda yaşam kalitesi açısından fayda göremedikleri gözlenmiştir. Bu hasta popülasyonunda yaşam kalitesi rutin olarak değerlendirildiği takdirde, kemoterapi yan etkilerini en aza indirilmiş tedavi programlarının geliştirilmesi ve hastaların iyi halinin maksimum düzeye çıkarılması konusunda teşvik edilebilir.

ANAHTAR KELİMELER: Küçük hücreli akciğer kanseri, Küçük hücreli olmayan akciğer kanseri, Yaşam kalitesi, Karkofsky Performans Durum Ölçeği, Kemoterapi

APPENDIX 1. Lung cancer symptoms according to tumor invasion (15)

Primary tumor	Intrathoracic spread	Extrathoracic spread
Cough	Chest wall invasion	Bone pain
Dyspnea	Esophageal symptoms	Confusion, personality change
Chest discomfort	Horner syndrome	Elevated alkaline phosphate level
Hemoptysis	Pleural effusion	Focal neurological defects
	Laryngeal nerve paralysis	Headache
	Superior vena cava syndrome	Nausea, vomiting

APPENDIX 2: Stage IV nsclc common treatment (21)

Regimen	Dose	Common Side Effects
Docetaxel	75 mg / m^2	nausea and vomiting, nephrotoxicity, ototoxicity, peripheral neuropathy
Cisplatin	75 mg / m^2	
Cisplatin	100 mg/ m^2 iv	nausea and vomiting, nephrotoxicity, ototoxicity, peripheral neuropathy, hydration
Gemcitabine	1,000 mg/ m^2 iv	
Paclitaxel	225 mg m^2 iv	neutropenia, myelopsuppresion, hyperensitivity, sensory neuropathy, nausea and vomiting
Carboplatin	AUC 6 iv	
Cisplatin	60-100 mg /m^2 iv	cytotoxicity, nausea and vomiting, peripheral neuropathy
Etopozide	0-120 mg/ m^2 iv	

APPENDIX 3: EORTC QLQ C-30 questionnaire (English)

PORTEC-3 Quality of life questionnaire PORTEC-3 trial number: |__|__|__|

EORTC QLQ-C30 (version 3)

We are interested in some things about you and your health. Please answer all of the questions yourself by circling the number that best applies to you. There are no "right" or "wrong" answers. The information that you provide will remain strictly confidential.

Please fill in your first initial: |___|
Your birth date (Day, Month, Year): |__|__||__|__||__|__|__|__|
Today's date (Day, Month, Year): |__|__||__|__||__|__|__|__|

	Not at All	A Little	Quite a Bit	Very Much
1. Do you have any trouble doing strenuous activities, like carrying a heavy shopping bag or a suitcase?	1	2	3	4
2. Do you have any trouble taking a long walk?	1	2	3	4
3. Do you have any trouble taking a short walk outside of the house?	1	2	3	4
4. Do you need to stay in bed or a chair during the day?	1	2	3	4
5. Do you need help with eating, dressing, washing yourself or using the toilet?	1	2	3	4

During the past week:	Not at All	A Little	Quite a Bit	Very Much
6. Were you limited in doing either your work or other daily activities?	1	2	3	4
7. Were you limited in pursuing your hobbies or other leisure time activities?	1	2	3	4
8. Were you short of breath?	1	2	3	4
9. Have you had pain?	1	2	3	4
10. Did you need to rest?	1	2	3	4
11. Have you had trouble sleeping?	1	2	3	4
12. Have you felt weak?	1	2	3	4
13. Have you lacked appetite?	1	2	3	4
14. Have you felt nauseated?	1	2	3	4
15. Have you vomited?	1	2	3	4

Please go on to the next page

APPENDIX 3: EORTC QLQ C-30 questionnaire (English)

PORTEC-3 Quality of life questionnaire PORTEC-3 trial number: |__|__|__|

During the past week:	Not at All	A Little	Quite a Bit	Very Much
16. Have you been constipated?	1	2	3	4
17. Have you had diarrhea?	1	2	3	4
18. Were you tired?	1	2	3	4
19. Did pain interfere with your daily activities?	1	2	3	4
20. Have you had difficulty in concentrating on things, like reading a newspaper or watching television?	1	2	3	4
21. Did you feel tense?	1	2	3	4
22. Did you worry?	1	2	3	4
23. Did you feel irritable?	1	2	3	4
24. Did you feel depressed?	1	2	3	4
25. Have you had difficulty remembering things?	1	2	3	4
26. Has your physical condition or medical treatment interfered with your family life?	1	2	3	4
27. Has your physical condition or medical treatment interfered with your social activities?	1	2	3	4
28. Has your physical condition or medical treatment caused you financial difficulties?	1	2	3	4

For the following questions please circle the number between 1 and 7 that best applies to you:

29. How would you rate your overall health during the past week?

1	2	3	4	5	6	7
Very poor						Excellent

30. How would you rate your overall quality of life during the past week?

1	2	3	4	5	6	7
Very poor						Excellent

APPENDIX 4: EORTC QLQ LC-13 questionnaire (English)

ENGLISH

EORTC QLQ - LC13

Patients sometimes report that they have the following symptoms or problems. Please indicate the extent to which you have experienced these symptoms or problems during the past week. Please answer by circling the number that best applies to you.

During the past week :		Not at All	A Little	Quite a Bit	Very Much
31.	How much did you cough?	1	2	3	4
32.	Did you cough up blood?	1	2	3	4
33.	Were you short of breath when you rested?	1	2	3	4
34.	Were you short of breath when you walked?	1	2	3	4
35.	Were you short of breath when you climbed stairs?	1	2	3	4
36.	Have you had a sore mouth or tongue?	1	2	3	4
37.	Have you had trouble swallowing?	1	2	3	4
38.	Have you had tingling hands or feet?	1	2	3	4
39.	Have you had hair loss?	1	2	3	4
40.	Have you had pain in your chest?	1	2	3	4
41.	Have you had pain in your arm or shoulder?	1	2	3	4
42.	Have you had pain in other parts of your body?	1	2	3	4
	If yes, where _____				
43.	Did you take any medicine for pain?				
	1 No 2 Yes				
	If yes, how much did it help?	1	2	3	4

APPENDIX 5. Karnofsky performance scale

Grade	Description
100%	No symptoms.
90%	Able to carry on normal activity; minor signs or symptoms of disease.
80%	Able to carry on normal activity with effort; some signs or symptoms of disease.
70%	Cares for self, unable to carry on normal activity or do active work.
60%	Requires occasional assistance but is able to care for most of own needs.
50%	Requires considerable assistance and frequent medical care.
40%	Disabled; requires special care and assistance.
30%	Severely disabled; hospitalization indicated, although death not imminent.
20%	Very ill; hospitalization necessary; active supportive treatment required.
10%	Moribund, fatal processes progressing rapidly.
0 %	Patient expired.

APPENDIX 6. Eastern Cooperative Oncology Group (ECOG) performance status

Grade	Description
0	Fully active, able to carry on all pre-disease performance without restriction
1	Restricted in physically strenuous activity but ambulatory (can walk) and able to carry out work of a light or sedentary (sitting) nature, e.g., light house work, office work
2	Ambulatory and capable of all self-care but unable to carry out any work activities. Up and about more than 50% of waking hours
3	Capable of only limited self care, confined to bed or chair more than 50% of waking hours
4	Completely disabled. Cannot carry on any self-care. Totally confined to bed or chair

REFERENCES

1. Spiro SG, Porter JC. Lung cancer-Where are we today? Current advances in staging and nonsurgical treatment. Am J Respir Crit Care Med 2002; 166:1166-96.
2. Parkin GM, Pisani P, Ferlay J. Global cancer statistics. CA Cancer J Clin 1999; 49:33-64.
3. Ries LAG, Eisner MP, Kosary CL (eds.) Year relative survival rates based on follow up of patients through 2004. Cancer statistics review, 1975–2002. National Cancer Institute, Bethesda, MD 2005.
4. Ries LAG, Kosary CL, Hankey BF (eds.) Lung and bronchus cancer. SEER Cancer Statistics Review 1973-2003. National Cancer Institute, Bethesda, MD 2006.
5. Ferlay J, Bray F, Parkin DM, Pisani P (eds.) Globocan 2000: Cancer Incidence and Mortality Worldwide (IARC Cancer Bases No. 5), IARCPress, Lyon 2001.
6. Ries LA, Kosary CL, Hankey BF (eds.) Lung and bronchus cancer. SEER Cancer Statistics Review 1973-1996. National Cancer Institute, Bethesda, MD 1999.
7. Halilcolar H, Tatar D, Ertuğrul E. Epidemijoloji. In: Akciğer Kanseri, Multidisipliner Yaklaşım. Editors: Akkoclu A, Oztürk C, Bilimsel Tıp Yayınevi, Ankara, 1999 pp. 17- 22.
8. T.C. Sağlık Bakanlığı Kanser Savaş Daire Başkanlığı. Kanser bildirimlerinin değerlendirilmesi 1993-1994. Ankara, Yayın no: 582. 1997.
9. Arınç S, Özvaran MK, Güngör N, Çelik O, Soğukpınar Ö, Çolak F, Baran R. Hastanemizde tanı alan akciğer kanserli olguların epidemiyolojik ve histolojik özellikleri. Akciğer Ars 2005; 6:149-52.
10. Hong WK, Tsao AS. Lung Cancer. Last full review/revision in March 2008 (accessed in 17/09/2012) http://www.merckmanuals.com/home/sec04/ch053/ch053a.html?qt=lungcarcinoma&alt=sh#v728252
11. Cooley ME. Symptoms in adults with lung cancer: a systematic research review. J Pain Symptom Manage 2000; 19:137-53.
12. Beckles MA, Spiro SG, Colice GL, Rudd RM. Initial evaluation of the patient with lung cancer: symptoms, signs, laboratory tests, and paraneoplastic syndromes. Chest 2003; 123:97-104.
13. Fuller RW, Jackson DM. Physiology and treatment of cough. Thorax 1990; 45:425-30.
14. Jennings AL, Davies AN, Higgins JP, Gibbs JS, Broadley KE. A systematic review of the use of opioids in the management of dyspnoea. Thorax 2002; 57:939-44.
15. Kelly K, Bunn Jr. PA. Is it time to reevaluate our approach to the treatment of brain metastases in patients with non-small cell lung cancer? Lung Cancer 1998; 20:85-91.
16. Tanvetyanon T, Robinson LA, Schell MJ, Strong VE, Kapoor R, Coit DG, Bepler G. Outcomes of adrenalectomy for isolated synchronous versus metachronous adrenal metastases in non-small-cell lung cancer: a systematic review and pooled analysis. J Clin Oncol 2008; 26: 1142-7.
17. Carlsen K, Jensen AB, Jacobsen E, Krasnik M, Johansen C. Psychosocial aspects of lung cancer. Lung Cancer 2005; 47:293-300.
18. Stewart AF. Hypercalcemia associated with cancer. New Engl J Med 2005; 352:373-9.
19. List AF, Hainsworth JD, Davis BW, Hande KR, Greco FA, Johnson DH. The syndrome of inappropriate secretion of antidiuretic hormone (SIADH) in small-cell lung cancer. J Clin Oncol 1986; 4:1191-8.
20. Shepherd FA, Laskey J, Evans WK, Goss PE, Johansen E, Khamsi F. Cushing's syndrome associated with ectopic corticotropin production and small-cell lung cancer. J Clin Oncol 1992; 10:21-7.
21. Manegold C. Chemotharpy for advanced non-small cell lung cancer. Sem Oncol Suppl 7 2001; 28:1-6.
22. Shepherd FA. Chemotherapy for advanced non-small cell lung cancer: Modest progress, many choices. J Clin Oncol Suppl 21 2000; 18:35-8.
23. Roila F, Cortesi E. Quality of life as a primary end point in oncology. Ann Oncol 2001; 12: (Suppl 3):3-6.
24. Cella DF, Bonomi AE, Lloyd SR, Tulsky DS, Kaplan E, Bonomi P. Reliability and validity of the functional assessment of cancer therapy-lung (FACT-L) quality of life instrument. Lung Cancer 1995; 12:199-220.
25. Cella D, Eton DT, Fairclough DL, Bonomi P, Heyes AE, Silberman C, Wolf MK, Johnson DH. What is a clinically meaningful change on the functional assessment of cancer therapy-lung (FACT-L) questionnaire? Results from Eastern Cooperative Oncology group (ECOG) Study 5592. J Clin Epidemiol 2002; 55:285-95.

26. Aaronson NK, Ahmedzai S, Bergman B, Bullinger M, Cull A, Duez NJ, Filiberti A, Flechtner H, Fleishman SB, de Haes JCJM, Kaasa S, Klee M, Osoba D, Razavi D, Rofe PB, Schraub S, Sneeuw K, Sullivan M, Takeda F. The European Organization for Research and Treatment of Cancer QLQ-C30: a quality of life instrument for use in international clinical trials in oncology. J Natl Cancer Inst 1993; 85:365-76.

27. Bergman B, Aaronson NK, Ahmedzai S, Kaasa S, Sullivan M. The EORTC QLQ-LC13: a modular supplement to the EORTC core quality of life questionnaire (QLQ-C30) for use in lung cancer clinical trials. EORTC Study Group on Quality of Life. Eur J Cancer 1994; 30:635-42.

28. Crinò L, Scagliotti GV, Ricci S, De Marinis F, Rinaldi M, Gridelli C, Ceribelli A, Bianco R, Marangolo M, Di Costanzo F, Sassi M, Barni S, Ravaioli A, Adamo V, Portalone L, Cruciani G, Masotti A, Ferrara G, Gozzelino F, Tonato M. Gemcitabine and cisplatin versus mitomycin, ifosfamide, and cisplatin in advanced non-small cell lung cancer. A randomized phase III study of the Italian lung cancer project. J Clin Oncol 1999; 17:3522-30.

29. Montazeri A, Milroy R, Hole D, McEwen J, Gillis CR. Quality of life in lung cancer patients: as an important prognostic factor. Lung Cancer 2001; 31:233-40.

30. Altıparmak S, Fadıloğlu Ç, Gürsoy ST, Altıparmak O. Kemoterapi tedavisi alan akciğer kanserli hastalarda öz bakım gücü ve yaşam kalitesi ilişkisi. Ege Tıp Dergisi 2011; 50:95-102.

31. http:// www.toraks.org.tr / SunuMerkezi / ?s= 5A37225E3B575C232C (accessed 04/02/2013)

32. Aras M, Ünsal Delialioğlu S, Atalay N, Taflan Selçuk S. Kanser Hastalarının Rehabilitasyon Gereksinimi. Türk Fiz Tıp Rehab Derg 2009; 55:25-9.

33. Şeker M, Mengi A, Bilici A, Ustaalioğlu BB, Kefeli U, Özşeker NI, Mayadağlı A, Salepci T, Gümüş M. Hodgkin lenfoma olgularının retrospektif değerlendirilmesi ve prognostic faktörlerin saptanması. TJ Oncol 2011; 26: 108-114.

34. Hollen PJ, Gralla RJ, Kris MG, Cox C. Quality of life during clinical trials: conceptual model for the Lung Cancer Symptom Scale (LCSS). Support Care Cancer 1994; 2:213-22.

35. FFrasci G, Lorusso V, Panza N, Comella P, Nicolella G, Bianco A, De Cataldis G,Iannelli A, Bilancia D, Belli M, Massidda B, Piantedosi F, Comella G, De Lena M. Gemcitabine plus vinorelbine versus vinorelbine alone in elderly patients with advanced non-small cell lung cancer. J Clin Oncol 2000; 18:2529-36.

36. Hollen PJ, Gralla RJ, Kris MG, Eberly SW, Cox C. Normative data and trends in quality of life from the Lung Cancer Symptom Scale (LCSS). Support Care Cancer 1999; 7:140-8.

37. Klastersky J, Paesmans M. Response to chemotherapy, quality of life benefits and survival in advanced non-small cell lung cancer: review of literature results. Lung Cancer 2001; 34:95-101.

38. Helsing M, Bergman B, Thaning L, Hero U. Quality of life and survival in patients with advanced non-small cell lung cancer receiving supportive care plus chemotherapy with carboplatin and etoposide or supportive care only. A multicentre randomized phase III trial. Joint Lung Cancer Study Group. Eur J Cancer 1998; 34:1036-44.

39. Esbensen BA, Osterlind K, Roer O, Hallberg IR. Quality of life of elderly persons with newly diagnosed cancer. Eur J Cancer Care 2004; 13:443-53.

40. Hten Bokkel Huinink WW, Bergman B, Chemaissani A, Dornoff W, Drings P, Kellokumpu-Lehtinen PL, Liippo K, Mattson K, von Pawel J, Ricci S, Sederholm C, Stahel RA, Wagenius G, Walree NV, Manegold C. Single agent gemcitabine: an active and better tolerated alternative to standard cisplatin-based chemotherapy in local advanced or metastatic lung cancer. Lung Cancer 1999; 26: 85-94.

41. Bozcuk H, Dalmis B, Samur M, Ozdogan M, Artac M, Savas B. Quality of Life in Patients With Advanced Non-Small Cell Lung Cancer. Cancer Nur 2006; 29:104-110.

42. Aaronson NK, Cull A, Kaasa S, Sprangers M. The EORTC modular approach to Quality of Life assessment in Oncology. Int J Ment Health 1994; 23:75-96.

43. Anthony J, Alberg D, Rex C, Jonathan M. Epidemiology pof lung cancer. In: Murray and Nadel's Textbook of Respiratory Medicine. Editors: Mason J, Murray JF, Broaddus VC. Elsevier Saunders Inc, Philadelphia 2005, pp.1328-54.

44. Gridelli C, Gallo C, Shepherd FA, Illiano A, Piantedosi F, Robbiati SF, Manzione L, Barbera S, Frontini L, Veltri E, Findlay B, Cigolari S, Myers R, Ianniello GP, Gebbia V, Gasparini G, Fava S, Hirsh V, Bezjak A, Seymour L, Perrone F. Gemcitabine plus vinorelbine compared with cisplatin plus vinorelbine or cisplatin plus gemcitabine for advanced non-small-cell lung cancer: a phase III trial of the Italian GEMVIN Investigators and the National Cancer Institute of Canada Clinical Trials Group. J Clin Oncol 2003;21:3025-34.

45. MMatsumoto T, Ohashi Y, Morita S, Kobayashi K, Shibuya M, Yamaji Y, Eguchi K,Fukuoka M, Nagao K, Nishiwaki Y, Niitani H; CPT-11 Lung Cancer Study Groups West and East. The quality of life questionnaire for cancer patients treated with anticancer drugs (QoL-ACD): validity and eliability in Japanese patients with advanced non-small cell lung cancer. Qual Life Res 2002; 11:483-93.

46. Anant M, Guleria R, Pathak AK, Bhutani M, Pal H, Charu M, Kochupillai V. Quality of life measures in lung cancer. Indian J Cancer 2005; 42:125-32.

47. Tanrıkol G, Kaya P, Çolak D, Alkış N, Özyılkan E. Onkolojik Hastalarda Yaşam Kalitesinin Değerlendirilmesi. MN-Klinik Bilimler&Doktor 2005; 11:122-6.

48. Thomas L, Doyle LA, Edelman MJ. Lung cancer in women: emerging differences in epidemiology, biology, and therapy. Chest 2005; 128:370-81.

49. Sarna L. Women with lung cancer: Impact on quality of life. Qual Life Res 1993; 2:13-22.

50. Tillman M, Silcock JA. Comparison of smokers and ex smokers health-related quality of life. J Public Health Med 1997; 19:268-73.

51. Wilson D, Parsons J, Wakefield M. The health-related quality of life of never smokers, ex-smokers and light, moderate and heavy smokers. Prev Med 1999; 29:139-44.

52. Osoba D, Murray N, Gelmon K, Karsai H, Knowling M, Shah A, McLaughlin M, Fetherstonhaugh E, Page R, Bowman CA**.** Quality of life, appetite, and weight change in patients receiving dose-intensive chemotherapy. Oncology (Williston Park) 1994; 8: 61-5.