The Impact of Chemotherapy on the EORTC QLQ-C30 and LC-13 Quality of Life Scales in Patients with Lung Cancer

Akciğer Kanserli Hastalarda Kemoterapinin EORTC QLQ-C30 ve LC-13 Yaşam Kalitesi Ölçeklerine Etkisi

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ABSTRACT

Objective: The concept of quality of life (QoL) in lung cancer includes many physical, psychological and social components. We aimed to assess the effect of chemotherapy (CT) on QoL of lung cancer patients using QoL scales.

Methods: Fifty inoperable lung cancer patients who were newly diagnosed and taken into a CT plan were included. Patients were followed in terms of responsiveness and toxicity. Turkish versions of the EORTC QLQ-C30 and LC13 scales were used before every cycles.

Results: The average age was 60.1 years. There was no difference between QoL and age/income levels. The assessment of physical, social and occupational functions and overall health status of the male patients was better than female. Overall health status without comorbidity was better in the first cycle CT. Chemotherapy led to deterioration in social functions and economic status together with increase in neuropathy, constipation and hair loss. Patients with complete or partial response to treatment were observed to have better physical, occupational, emotional, cognitive and social functions, economic status and overall health; less fatigue, pain, shortness of breath, neuropathy and better appetite. Toxicities were found to affect the QLQ C30 and LC13 scales adversely.

Conclusion: Presence of comorbidity, low education levels, socioeconomic status and CT induced hematologic/gastrointestinal toxicities are the major parameters affect QOL in lung cancer. Chemotherapy leads to deterioration in social functions, increase in adverse events as well as worsening in economic status. Radiologic complete or partial response and small cell carcinoma are states in which parameters of QoL are affected positively by chemotherapy.

Keywords: Lung cancer, chemotherapy, EORTC QLQ-C30, LC13, quality of life

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ÖZ

Amaç: Akciğer kanseri hastalarında yaşam kalitesi kavramı; fiziksel, psikolojik ve sosyal olmak üzere pek çok komponenti içermektedir. Bu çalışmada akciğer kanserli hastalarda kemoterapinin yaşam kalitesi üzerine etkisinin yaşam kalitesi ölçekleri kullanılarak belirlenmesi amaçlanmıştır.

Yöntem: Araştırmaya yeni tanı alan ve kemoterapi planlanan 50 inoperabl akciğer kanserli hasta alındı. Hastalar tedaviye yanıt ve toksisite yönünden izleme alındı. EORTC QLQ-C30 ve LC13 ölçeklerinin Türkçe sürümleri her siklus öncesi uygulandı.

Bulgular: Yaş ortalaması 60.1 yıldı. Yaş ve gelir düzeyi ile yaşam kalitesi parametreleri arasında fark bulunmadı. Erkeklerin; fiziksel, sosyal ve uğraş fonksiyonlarının ve genel sağlık durumu değerlendirmesi kadınlara göre daha iyi idi. Komorbiditesi olmayanların, 1. Siklus KT'de genel sağlık durumu değerlendirmesi daha iyi idi. Kemoterapi ile sosyal fonksiyonlarda, ekonomik durumda kötüleşme, nöropati, kabızlık ve saç dökülmesinde artış saptandı. Tedaviye tam veya kısmi yanıt elde edilen hastaların, fiziksel, uğraş, duygusal, kavrama, sosyal fonksiyonlarının, ekonomik durumlarının ve genel durum değerlendirmesinin daha iyi olduğu, yorgunluk, ağrı, nefes darlığı, nöropatinin daha az olduğu ve iştahın daha iyi olduğu belirlendi. Toksisitelerin QLQ C30 ve LC13 ölçeklerini olumsuz yönde etkilediği görüldü.

Sonuç: Akciğer kanserinde komorbidite varlığı, düşük eğitim düzeyi, sosyoekonomik durum ve kemoterapiye bağlı hematolojik/gastrointestinal toksisiteler yaşam kalitesini etkileyen en önemli parametrelerdir. Kemoterapi ile sosyal fonksiyonlar ve ekonomik parametrelerde kötüleşme ile birlikte yan etkilerde artış izlenmiştir. Radyolojik tam veya kısmi yanıt, küçük hücreli karsinom hücre tipi kemoterapi ile yaşam kalitesi parametrelerinin olumlu etkilendiği durumlardır.

Anahtar kelimeler: Akciğer kanseri, kemoterapi, EORTC QLQ-C30, LC13, yaşam kalitesi

INTRODUCTION

Integrating quality of life (QoL) assessments into the clinical routine in lung cancer patients may provide a subjective measure of symptom severity. It also facilitate patients and their families to participate in medical decisions [1]. Both disease specific and generic instruments are available for QoL of lung cancer patients. The comparison of QoL scores between lung cancer patients and the healthy population may be done by using generic instruments [2]. Recently, QoL becomes a more important outcome measure in assessment of the best standard of care for patients. QoL may be evaluated as a primary endpoint of treatment both in clinical practice and in clinical trials to define meaningful response [3].

Due to serious side effect profiles of treatment models such as chemotherapy (CT) and radiotherapy, serious treatment induced side effects come up and the QoL deteriorates. Besides the success of cancer treatment, response rates and survival time; use of QoL scales has become a significant criterion for doctors in the determination of treatment method and evaluation of the response by measuring the patient's physical, emotional and social functions [4-6].

In patients with advanced lung cancer, clinicians should enhance their ability to notice patients' elevated risk of poor QoL during CT. They should also detect and manage the related physical symptoms and side effects, strengthen patients' social support and control the anxiety and depressive symptoms [7].

The present study aims to to evaluate the effect of the CT on the QoL of lung cancer patients by using the lung cancer specific QoL module.

MATERIAL and METHOD

The study was a prospective, descriptive clinical study and was carried out between 01/08/2014 and 01/06/2015.

Study Population and Sample

The study sample consisted of inoperable (stage IIIA-IIIB-IV) patients who were radiologically and histopathologically diagnosed with lung cancer (small cell and non-small cell carcinoma) (SCLC, NSCLC) and given CT. The fact that the patients had received or would receive palliative treatment was not an obstacle for the study. Patients who were suggested surgical treatment, those followed without treatment, and patients failing to fill in questionnaire forms / having communicational problems were excluded. Patients; accepted to participate, to come for check-ups, were literate and able to read/fill in test forms were included.

In order to conduct the study, permission was taken from the Local Ethics Committee and written informed consent forms were completed by all patients accepted to participate.

Data Collection

Before treatment, demographic data, comorbidity, smoking and alcohol use, performances observed by the doctor, histologically/histopathologically confirmed tumor cell type and the stage of disease were collected. Turkish versions of the EORTC QLQ C30 and LC13 scales were given before the treatment, with face-to-face interviewing technique. Each interview lasted approximately 30 minutes [8].

7th edition tumor-node-metastasis (TNM) staging system were used [7]. Response and ECOG/Karnofsky performance scores assessment was performed after 2nd-4th cycles. The EORTC QLQ-C30 and LC13 scales were applied prior to each cycle with face to face in a vacant and quiet room before examination. Performance was recorded by using ECOG and Karnofsky [9,10]. During four cycle (per three weeks) CT, we used The Response Evaluation Criteria in Solid Tumors (RECIST) and the Common Terminology Criteria for Adverse Events v3.0 (CTCAE) (five categories based on the degree) [11]. Chemotherapy induced adverse effects were recorded following each cycle.

The EORTC-QLQ-30 Scale (European Organization for

Research and Treatment of Cancer QoL Questionnaire)

The questionnaire has 30 questions (Q) and incorporates functional and symptom scales. The functional scale includes six subscales; physical (Q1-5), role (Q6,7), cognitive (Q20,25), emotional (Q21-24), social (Q26,27), global QOL (Q29,30). Symptom scale consists of symptoms of fatigue (Q10,12,18), nausea and vomiting (Q14,15), pain (Q9,19), dyspnea (Q8), insomnia (Q11), loss of appetite (Q13), constipation (Q16), diarrhea (Q17) and perceived financial impact of the disease (Q28). Of the 30 items on the scale, 28 are designed as a 4-point Likert type scale and scored as Not at All: 1, A Little: 2, Quite a Bit: 3, Very Much: 4 points. Q29 asks the patients to rate their health status on a scale rated from 1 to 7 (1: very bad and 7: excellent) and Q30 wants them to assess their global QoL. Q29.30 make up the overall well-being section of the scale, and high scores obtained over this section indicate high QoL while low scores show that QoL decreases. In the functional area and symptoms section, on the other hand, low scores reflect high QoL whereas high scores are indicators of low QoL [12]. The scale was confirmed for validity and reliability for the Turkish society [13].

The EORTC QLQ-LC13 Scale

It measures treatment symptoms and consists of 13 items. The questions assess dyspnea (Q3,4,5), coughing (Q1), haemoptysis (Q2), sore mouth (Q6), dysphagia (Q7), peripheral neuropathy (Q8), alopecia (Q9), chest pain (Q10), pain in arms and shoulders (Q11), other types of pain (Q12) and any medication taken for pain (Q13) [14].

Data Analysis and Assessment Techniques

The data obtained from the study were analyzed using SPSS 18 (Statistical Package For Social Sciences). Mean, standard deviation, median, minimum and maximum values pertaining to the continuous variables were presented. These variables and their subgroups were analyzed for normal distribution. Considering the graphical research and normality tests and the sample size, it was concluded that not all the variables met the conditions required for normal distribution. Thus, non-parametric test methods were employed for the comparisons of these variables.

Independent groups were compared using Mann Whitney test; while the comparisons of the variables obtained from repeated measures were carried out employing Friedman and Wilcoxon tests. The relations between variables were analyzed with the non-parametric correlation method.

Frequency tables were created for class variables and the equality of the distribution between groups was tested using chi-square tests. Class variables were measured repeatedly and the change was studied with Mc-Nemar test method. In all statistical comparison tests, margin of type 1 error was accepted as α:0,05 and was tested as two-way.

RESULTS

General characteristics are presented in Table 1. 60% had equal income and expenses, 34% had lower income than their expenses and 6% had higher income than their expenses. No difference was observed in the ECOG and KPS at diagnosis, following two cycles and at the end of the treatment (p>0.05).

44 (88%) of the patients had completed four cycles of treatment, one (2%) died after the 1st cycle, two (4%) died after the 2nd. Due to low performance, CT was not given to two (4%) after the 2nd cycle and to one (2%) after the 3rd cycle. Response assessments following two cycles of CT showed partial response in 15 (30%), progression in 16 (32%), stable response in 17 (34%) and complete response in one (2%). In the response assessments following four cycles, six failed to complete four cycles due to varying reasons. Fifteen (30%) had partial response, eight (16%) had progression, 19 (38%) had stable response and two (4%) had complete response.

No correlation was found between age and QoL (p>0.05). Men had better physical and occupational

functions in the 1st and 2nd cycle CT, and social functions and global health status of men were better than women in the 1st cycle (p<0.05). No difference was found in other parameters. Patients completed primary and further education had better social functions in the 1st cycle (p=0.024), better physical

functions in the 3rd cycle (p=0.040) and better occupational functions in the 3rd (p=0.022) and 4th cycles (p=0.023). No difference was found for other scores according to number of cycles in emotional function, cognitive function and global health status evaluations (p>0.05).

QoL did not vary by income status (p>0.05). Global health status evaluation with no comorbidity was better in the 1st cycle in comparison with those having comorbidities (p<0.05), whereas no significant difference was found in the other functions (p>0.05).

According to QLQ-C30 scale; social functions deteriorated (p=0.000) while constipation (p=0.000) and financial distress (p=0.000) increased with CT, and LC13 scale showed that hair loss (p=0.000) and neuropathy (p=0.000) increased together with CT. Other parameters of both scales did not differ (p>0.05).

In the cell type-based analysis, occupational function in the 1st cycle was better in NSCLC than SCLC (p=0.028). In SCLC, physical functions (p=0.030 and p=0.015), occupational functions (p=0.042 and p=0.023) and global health status (p=0,018 and p=0.006) evaluation were better in the 3rd and 4th cycles; and that fatigue (p=0.025 and p=0.005), pain (p=0.020 and p=0.028) and loss of appetite (p=0.041 and p=0.079) symptoms were better in the 3rd and 4th cycles. Other parameters of both scales did not differ (p>0.05). With the LC13 scale, neuropathy (p=0.000) was experienced more severely in the 3rd and 4th cycles, alopecia (p=0.042) in the 1st cycle and pain in arms and shoulders (p=0.028) in the 3rd cycle in NSCLC. Other parameters were similar between tumor cell types (p>0.05).

In complete/partial response group, physical functions in cycles 2,3,4; occupational functions in cycles 3 and 4; emotional functions in cycle 3, cognitive functions in cycles 3 and 4, financial status and social functions in cycle 1; and global status evaluations were better than stable/progressive. Complete/partial group had less pain in cycle 4, experienced less

Table 1. General characteristics of the patients with lung cancer.

Feature	N	%
Age, years	60.1±8,1	
Cigarette smoking, package years	41±24	
Gender		
Men	40	80
Women	10	20
Education		
Primary	39	78
Secondary	7	14
High school	2	4
College or higher levels	2	4
Histopathology		
Small cell	14	28
Squamous cell	4	8
Adeno carcinoma	10	20
Non-small cell (subtype not identified)	22	44
Performance Status		
ECOG 0	10	20
ECOG I	23	46
ECOG II	14	28
ECOG III	3	6
Karnofsky, >80%	40	80
Comorbidity[†]		
Yes	34	68
No	16	32
Stage at Diagnosis		
Stage 3A	8	16
Stage 3B	8	16
Stage 4	20	40
Metastatic *	10	20
Limited *	4	8
Total	**50**	

*Small cell lung carcinoma
†Diabetes mellitus, hypertension, chronic heart disease, chronic obstructive lung disease

Table 2. QLQ-C30 and toxicity correlation in the 2nd cycle.

		Anemia	Leucopenia	Neutropenia	Thrombocytopenia	Weight loss	Nausea	Vomiting
Physical Function (Total)	CorrelationCoefficient	0,217	0,240	0,197	,327(*)	,535(**)	,422(**)	,431(**)
	Sig. (2-tailed)	0,134	0,097	0,176	0,022	0,000	0,003	0,002
	N	49	49	49	49	49	49	49
Occupational Function (Total)	CorrelationCoefficient	0,231	0,176	0,244	,337(*)	,379(**)	0,261	,341(*)
	Sig. (2-tailed)	0,110	0,227	0,092	0,018	0,007	0,070	0,017
	N	49	49	49	49	49	49	49
Emotional Function (Total)	CorrelationCoefficient	,303(*)	0,205	0,155	0,279	,392(**)	,323(*)	,385(**)
	Sig. (2-tailed)	0,034	0,158	0,289	0,052	0,005	0,024	0,006
	N	49	49	49	49	49	49	49
Cognitive Function (Total)	CorrelationCoefficient	0,047	0,199	0,204	-0,074	0,233	,287(*)	0,182
	Sig. (2-tailed)	0,749	0,171	0,161	0,612	0,106	0,045	0,211
	N	49	49	49	49	49	49	49
Social Function (Total)	CorrelationCoefficient	0,277	0,205	0,204	0,242	,482(**)	0,248	,327(*)
	Sig. (2-tailed)	0,054	0,158	0,160	0,094	0,000	0,085	0,022
	N	49	49	49	49	49	49	49
Fatigue (Total)	CorrelationCoefficient	0,185	,286(*)	,298(*)	,301(*)	,556(**)	,498(**)	,431(**)
	Sig. (2-tailed)	0,203	0,046	0,038	0,036	0,000	0,000	0,002
	N	49	49	49	49	49	49	49
Pain (Total)	CorrelationCoefficient	0,088	0,181	0,255	,292(*)	,308(*)	,408(**)	,559(**)
	Sig. (2-tailed)	0,550	0,214	0,077	0,042	0,031	0,004	0,000
	N	49	49	49	49	49	49	49
Nausea/Vomiting (Total)	CorrelationCoefficient	,291(*)	,311(*)	,298(*)	0,260	,583(**)	,872(**)	,719(**)
	Sig. (2-tailed)	0,043	0,030	0,038	0,071	0,000	0,000	0,000
	N	49	49	49	49	49	49	49
Dyspnea	CorrelationCoefficient	0,132	0,158	0,229	0,234	,312(*)	,386(**)	,381(**)
	Sig. (2-tailed)	0,368	0,278	0,113	0,105	0,029	0,006	0,007
	N	49	49	49	49	49	49	49
Insomnia	CorrelationCoefficient	0,054	0,120	0,124	0,222	,521(**)	,436(**)	,325(*)
	Sig. (2-tailed)	0,714	0,410	0,394	0,125	0,000	0,002	0,023
	N	49	49	49	49	49	49	49
Loss of appetite	CorrelationCoefficient	0,226	0,159	0,135	0,161	,496(**)	,495(**)	,439(**)
	Sig. (2-tailed)	0,118	0,275	0,354	0,270	0,000	0,000	0,002
	N	49	49	49	49	49	49	49
Constipation	CorrelationCoefficient	-0,026	0,199	0,127	0,051	0,101	0,106	0,099
	Sig. (2-tailed)	0,862	0,169	0,383	0,726	0,491	0,470	0,501
	N	49	49	49	49	49	49	49
Diarrhea	CorrelationCoefficient	0,056	-0,083	-0,205	-0,188	0,180	-0,052	-0,101
	Sig. (2-tailed)	0,702	0,570	0,157	0,196	0,217	0,722	0,491
	N	49	49	49	49	49	49	49
Global health status evaluation	CorrelationCoefficient	-0,214	-0,148	-0,142	-0,117	-,383(**)	-,385(**)	-,380(**)
	Sig. (2-tailed)	0,141	0,309	0,332	0,425	0,007	0,006	0,007
	N	49	49	49	49	49	49	49

*p<0.05, **p<0.01

Table 3. LC13 and toxicity correlation in the 2nd cycle.

		Anemia	Leucopenia	Neutropenia	Thrombocytopenia	Weight loss	Nausea	Vomiting
Coughing 2	CorrelationCoefficient	-0,003	0,000	-0,058	-0,062	,453(**)	,371(**)	0,264
	Sig. (2-tailed)	0,982	0,998	0,692	0,671	0,001	0,009	0,067
	N	49	49	49	49	49	49	49
Haemoptysis 2	CorrelationCoefficient	0,105	,310(*)	,364(*)	,287(*)	,501(**)	,463(**)	,421(**)
	Sig. (2-tailed)	0,471	0,030	0,010	0,045	0,000	0,001	0,003
	N	49	49	49	49	49	49	49
Dyspnea (ort) 2	CorrelationCoefficient	0,212	0,225	0,231	,300(*)	,546(**)	,552(**)	,446(**)
	Sig. (2-tailed)	0,144	0,121	0,110	0,037	0,000	0,000	0,001
	N	49	49	49	49	49	49	49
Sore mouth 2	CorrelationCoefficient	-0,064	0,271	,321(*)	0,243	,302(*)	,287(*)	,295(*)
	Sig. (2-tailed)	0,664	0,060	0,025	0,093	0,035	0,046	0,039
	N	49	49	49	49	49	49	49
Dysphagia2	CorrelationCoefficient	-0,038	0,197	0,233	0,259	,298(*)	,451(**)	,549(**)
	Sig. (2-tailed)	0,797	0,176	0,107	0,073	0,038	0,001	0,000
	N	49	49	49	49	49	49	49
Neuropathy 2	CorrelationCoefficient	0,038	,285(*)	0,279	0,248	,367(**)	,350(*)	0,231
	Sig. (2-tailed)	0,793	0,047	0,052	0,086	0,010	0,014	0,111
	N	49	49	49	49	49	49	49
Alopecia 2	CorrelationCoefficient	-0,077	-0,115	-0,102	0,137	0,113	-0,071	-0,129
	Sig. (2-tailed)	0,598	0,432	0,487	0,348	0,438	0,629	0,377
	N	49	49	49	49	49	49	49
Chest pain 2	CorrelationCoefficient	0,157	0,227	,289(*)	0,237	,282(*)	0,279	,328(*)
	Sig. (2-tailed)	0,280	0,117	0,044	0,102	0,050	0,052	0,021
	N	49	49	49	49	49	49	49
Pain in arms and shoulders2	CorrelationCoefficient	0,012	0,073	0,127	0,122	0,264	,283(*)	,329(*)
	Sig. (2-tailed)	0,933	0,620	0,383	0,402	0,066	0,049	0,021
	N	49	49	49	49	49	49	49

*$p<0.05$, **$p<0.01$

dyspnea and fatigue in cycles 3 and 4, had better appetite in cycles 3 and 4, less neuropathy in cycles 2,3 and 4 and less pain in arms and shoulders in cycle 3 ($p<0.05$).

In 2nd cycle, strong positive correlations were found between deterioration in physical functions and weight loss, nausea and vomiting; between deterioration in occupational functions and weight loss; between deterioration in emotional functions and weight loss/vomiting; and between deterioration in social functions and weight loss. Strong positive correlations were found between fatigue and nausea, vomiting and weight loss; between insomnia and

Table 4. QLQ-C30 and toxicity correlation in the 4ᵗʰ cycle.

		Anemia	Leucopenia	Neutropenia	Thrombocytopenia	Weight loss	Nausea	Vomiting
Physical Function (Total) 4	CorrelationCoefficient	0,113	-0,125	-0,125	0,107	,428(**)	,432(**)	,410(**)
	Sig. (2-tailed)	0,465	0,417	0,417	0,489	0,004	0,003	0,006
	N	44	44	44	44	44	44	44
Occupational Function (Total) 4	CorrelationCoefficient	0,235	0,003	0,003	0,201	,510(**)	,379(*)	,317(*)
	Sig. (2-tailed)	0,125	0,984	0,984	0,191	0,000	0,011	0,036
	N	44	44	44	44	44	44	44
Emotional Function (Total) 4	CorrelationCoefficient	0,080	-0,164	-0,164	0,104	,363(*)	,479(**)	,323(*)
	Sig. (2-tailed)	0,604	0,287	0,287	0,501	0,015	0,001	0,032
	N	44	44	44	44	44	44	44
Cognitive Function (Total) 4	CorrelationCoefficient	0,104	0,050	0,050	0,257	0,253	,432(**)	,301(*)
	Sig. (2-tailed)	0,501	0,747	0,747	0,092	0,097	0,003	0,047
	N	44	44	44	44	44	44	44
Social Function (Total) 4	CorrelationCoefficient	0,074	-0,106	-0,106	0,081	,380(*)	,489(**)	,401(**)
	Sig. (2-tailed)	0,634	0,495	0,495	0,600	0,011	0,001	0,007
	N	44	44	44	44	44	44	44
Fatigue (Total) 4	CorrelationCoefficient	0,141	-0,101	-0,101	0,073	,486(**)	,464(**)	,424(**)
	Sig. (2-tailed)	0,363	0,513	0,513	0,636	0,001	0,002	0,004
	N	44	44	44	44	44	44	44
Pain (Total) 4	CorrelationCoefficient	0,120	0,060	0,060	0,114	,396(**)	,304(*)	,462(**)
	Sig. (2-tailed)	0,436	0,698	0,698	0,462	0,008	0,045	0,002
	N	44	44	44	44	44	44	44
Dyspnea 4	CorrelationCoefficient	-0,115	-,298(*)	-,298(*)	-0,019	0,269	,406(**)	,305(*)
	Sig. (2-tailed)	0,459	0,049	0,049	0,905	0,078	0,006	0,044
	N	44	44	44	44	44	44	44
Insomnia 4	CorrelationCoefficient	-0,077	-0,254	-0,254	0,010	,367(*)	,390(**)	0,200
	Sig. (2-tailed)	0,620	0,096	0,096	0,948	0,014	0,009	0,193
	N	44	44	44	44	44	44	44
Loss of Appetite 4	CorrelationCoefficient	0,223	0,054	0,054	0,186	,566(**)	,612(**)	,463(**)
	Sig. (2-tailed)	0,146	0,725	0,725	0,226	0,000	0,000	0,002
	N	44	44	44	44	44	44	44
Constipation 4	CorrelationCoefficient	-0,028	0,207	0,207	0,101	0,275	,356(*)	,336(*)
	Sig. (2-tailed)	0,855	0,178	0,178	0,512	0,070	0,018	0,026
	N	44	44	44	44	44	44	44
Diarrhea 4	CorrelationCoefficient	0,142	-0,137	-0,137	0,269	,555(**)	0,173	0,087
	Sig. (2-tailed)	0,356	0,376	0,376	0,078	0,000	0,262	0,575
	N	44	44	44	44	44	44	44
Financial distress4	CorrelationCoefficient	0,136	-0,074	-0,074	-0,024	0,281	,322(*)	0,158
	Sig. (2-tailed)	0,378	0,635	0,635	0,877	0,064	0,033	0,306
	N	44	44	44	44	44	44	44
Global health status evaluation (Total) 4	CorrelationCoefficient	-0,011	0,092	0,092	-0,039	-,441(**)	-,336(*)	-0,270
	Sig. (2-tailed)	0,942	0,553	0,553	0,803	0,003	0,026	0,077
	N	44	44	44	44	44	44	44

*p<0.05, **p<0.01

Table 5. LC13 and toxicity correlation in the 4th cycle.

		Anemia	Leucopenia	Neutropenia	Thrombocytopenia	Weight loss	Nausea	Vomiting
Coughing 4	CorrelationCoefficient	-0,124	0,000	0,000	0,043	0,165	,413(**)	,312(*)
	Sig. (2-tailed)	0,423	1,000	1,000	0,780	0,285	0,005	0,039
	N	44	44	44	44	44	44	44
Haemoptysis 4	CorrelationCoefficient	-0,058	0,111	0,111	0,065	,311(*)	,370(*)	,386(**)
	Sig. (2-tailed)	0,708	0,473	0,473	0,677	0,040	0,014	0,010
	N	44	44	44	44	44	44	44
Dyspnea (ort) 4	CorrelationCoefficient	-0,174	-0,209	-0,209	0,076	,341(*)	0,207	0,079
	Sig. (2-tailed)	0,259	0,172	0,172	0,623	0,023	0,177	0,612
	N	44	44	44	44	44	44	44
Sore mouth 4	CorrelationCoefficient	0,166	0,028	0,028	,379(*)	,422(**)	,358(*)	0,172
	Sig. (2-tailed)	0,282	0,859	0,859	0,011	0,004	0,017	0,266
	N	44	44	44	44	44	44	44
Dysphagia4	CorrelationCoefficient	0,225	0,068	0,068	0,242	,519(**)	,364(*)	,411(**)
	Sig. (2-tailed)	0,142	0,663	0,663	0,114	0,000	0,015	0,006
	N	44	44	44	44	44	44	44
Neuropathy 4	CorrelationCoefficient	0,150	-0,020	-0,020	0,118	0,214	0,089	0,177
	Sig. (2-tailed)	0,331	0,896	0,896	0,446	0,162	0,564	0,250
	N	44	44	44	44	44	44	44
Alopecia 4	CorrelationCoefficient	-0,027	-,327(*)	-,327(*)	-0,211	0,188	-0,024	-0,149
	Sig. (2-tailed)	0,860	0,030	0,030	0,170	0,221	0,877	0,334
	N	44	44	44	44	44	44	44
Chest pain 4	CorrelationCoefficient	0,184	0,231	0,231	0,152	0,247	0,223	,342(*)
	Sig. (2-tailed)	0,232	0,132	0,132	0,325	0,106	0,145	0,023
	N	44	44	44	44	44	44	44
Pain in arms and shoulders 4	CorrelationCoefficient	0,066	-0,069	-0,069	-0,053	,377(*)	0,025	0,145
	Sig. (2-tailed)	0,673	0,656	0,656	0,733	0,012	0,871	0,348
	N	44	44	44	44	44	44	44

*p<0.05, **p<0.01

vomiting; and between loss of appetite and nausea, vomiting and weight loss. Global health status evaluation was strongly correlated with weight loss, nausea and vomiting in a negative direction (Table 2).

In the evaluation of the relation of LC13 with toxicity in cycle 2, strong positive correlations were found between coughing and weight loss and nausea; between haemoptysis and weight loss, nausea and

vomiting; between dyspnea and weight loss, nausea and vomiting. Similarly, strong positive correlations were observed between dysphagia and nausea/vomiting and between neuropathy and weight loss (Table 3).

The relation between the QLQ-C30 and toxicity in the 4th cycle showed that deterioration in physical function scale was strongly positively correlated with weight loss, nausea and vomiting; deterioration in occupational functions with weight loss; deterioration in emotional functions with nausea; deterioration in cognitive functions with nausea; and deterioration in social functions with nausea and vomiting. Also, fatigue was strongly positively correlated with weight loss, nausea-vomiting; pain scale with weight loss/vomiting; dyspnea with nausea and vomiting; insomnia with nausea; and loss of appetite with weight loss, nausea and vomiting. Global health status evaluation was strongly correlated with weight loss and weakly correlated with nausea in a negative direction (Table 4).

As a result of the examinations on LC13 and toxicity relation in cycle 4, strong positive correlations were determined between sore mouth and dysphagia; nausea and coughing; and coughing and dysphagia scales (Table 5).

DISCUSSION

Quality of life in lung cancer is how a patient's physical, emotional and social well-being is affected by the disease and the treatment process depending on the state of the disease and its treatment [15,16]. Besides the effectiveness of standard cancer treatment, response rates and survival time; QoL has become a significant criterion to determine how the patient's physical, emotional and social functions are affected by the disease itself and to plan the following treatment [4,5]. No significant difference was found in the comparisons of QoL parameters in patients over and under 60 years of age in this study. QoL is adversely affected by age in studies on healthy individuals whereas those conducted on cancer patients report

that elderly individuals accept cancer more easily than the young, which make the former better than the latter in emotional and social aspects [6,17].

Men had better physical and social functions in 1st-2nd CT, and that men's social functions and global health status evaluation were better than women in 1st CT. Similar with general cancer patients, women are reported to experience cancer more intensely and have higher anxiety [6,17,18].

Education and income are factors affect QoL positively [19,20]. In this study, patients who completed primary or further education were observed to have better social functions in 1st CT, better physical functions in 3rd CT and occupational functions in 3rd, 4th CT. Income statue did not correlate with QoL. Global health status of the patients without comorbidities was better than comorbid patients in first CT. Comorbidities increased with age. In NSCLC, although age is not an independent factor affecting survival, presence of comorbidities was correlated with increased mortality. In an observational study with 20.000 patients aged >65 years, age was considered more than comorbid diseases and treatment response rates were lower in elderly patients with less comorbidity in comparison to younger with more comorbid diseases [21].

EORTC-C30, during the follow-up period, reveal an overall deterioration in functional scales, correlated with physical, emotional and cognitive functions. Symptom scale showed deterioration in fatigue, nausea-vomiting and insomnia scales. In stage III-IV NSCLC, improvement was found in emotional function on the functional scale and in insomnia, constipation and pain on the symptom scale [22]. Decrease was reported in the QLQ-C30 functional areas and the global health status as well as increases in alopecia, constipation and sore mouth [23]. In the evaluation of the QLQ-C30 during four cycles of CT, social functions deteriorated while constipation and financial distress increased with CT. As LC13 over four cycles was studied, alopecia and neuropathy increased together with CT.

Small cell lung cancer is a progressive tumor that responds to CT more rapidly and at higher rates. Improvements were observed in global health status, emotional and role functions with CT in patients with SCLC whereas only global health status improved in NSCLC [24]. Similarly, when NSCLC was compared to SCLC during four cycles of CT, we found occupational function to be better in the first cycle in NSCLC. Physical/occupational functions and global health status were better as well as symptoms of fatigue, pain and appetite in 3rd-4th cycles in SCLC. LC13 revealed that neuropathy was experienced more severely in 3rd-4th cycles, alopecia in 1st cycle and pain in arms/shoulders in 3rd cycle in NSCLC.

The physical/cognitive/occupational functions in 2nd-4th cycles; emotional functions in 3rd; financial status and social functions in 1st and global status evaluation in 2nd-4th cycles were better in the complete/partial response group. Less fatigue and dyspnea were experienced and appetite was better in 3rd–4th; patients had less pain in cycle 4; neuropathy was less frequent in cycles 2nd-4th; and less pain was felt in arms and shoulders in cycle 3 in the complete/partial response group.

Local progression or progression with distant metastases of the disease was likely to affect QoL with the newly occurring symptoms and findings. The fact that pain becomes more severe and restricting, performance scores fall, such symptoms as asthenia and weight loss increase due to the new symptoms may have an impact on the patient's physical and emotional status which in turn could limit social activities. These symptoms may increase anxiety and depression in patients. The most common and significant toxicities are hematologic and gastrointestinal [25,26]. In this study, the most frequent toxicity types were same. Anemia and neutropenia as well as fever, nausea-vomiting and cachexia were generally found to be at grade 1-2. Life threatening or mortal, grade 4th-5th level toxicities occurred very rarely. As the level of toxicity increased, QoL parameters deteriorated in a reverse correlation.

Lung cancer symptom scale revealed significant correlations between fatigue, haemoptysis, daily activities and QoL in first follow-up, dyspnea in 2nd, and between fatigue and hemoglobin/hematocrit values in 3rd. Nausea and/or vomiting may develop in 70-80% receiving CT and affect the patient's diet, performance and QoL [26,27,28]. We similarly observed nausea and vomiting to deteriorate QoL significantly. Being aware of the adverse effects of CT is just as important as the effectiveness of the treatment. During patient check-ups, the primary concern is following the disease and assessing treatment response. It is known that questioning the treatment induced adverse effects and QoL is disregarded [29].

As one can assume, presence of comorbidities turned out to be one of the most critical factors affecting both the decision and method for treatment and QOL parameters. Patients were observed to have deteriorated social functions, increased constipation, alopecia and neuropathy and deteriorated economic parameters together with CT. Since SCLC is a tumor that responds rapidly/well to CT, QoL were observed to improve better in these patients in comparison to NSCLC. QoL of patients with complete/partial response to CT were affected positively when compared to patients accepted as stable/progressive. A significant relation was found between toxicity and deterioration in QoL.

As a limitation the study lacks of an analysis with control group

CONCLUSION

While planning the treatment, clinicians should provide treatment and care with a multidisciplinary teamwork understanding and "holistic treatment and care" approach in order to improve the patients' QoL. Social and psychological support should be planned besides to medical treatment.

In the treatment of advanced stage lung cancer today, it is still among the main purposes to improve QoL or not to disturb it further as well as extending

lifetime. In patients receiving chemotherapy, accompanying comorbidities, low educational level, socioeconomic status and treatment oriented hematologic and gastrointestinal toxicities are the most significant parameters affecting QoL.

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