Effects of Chemotherapy on Quality of Life for Patients with Lung Cancer

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Abstract

Study objectives: The aims of this prospective clinical study were to demonstrate the effects of chemotherapy on quality of life (QOL) lung cancer patients and to compare this effect in non-small cell lung cancer (NSCLC) and small-cell lung cancer (SCLC) patients.

Patients: Twenty-seven small cell cancer patients and 25 non-small cell cancer patients were included in the study.

Measurements: We measured QOL of lung cancer patients using the European Organization for Research and Treatment of Cancer (EORTC) core questionnaire (QLQ C-30) and lung cancer module (LC-13). The questionnaire was given before and after three courses of platinum-containing chemotherapy.

Results: Tumor response status and performance status of our patients was strongly correlated with many fields of QOL. Chemotherapy reduced the requirement for pain control medication. There were only differences in insomnia scores and financial problem scores between NSCLC and SCLC patients initially and also after three courses of chemotherapy. All other domains of QOL were similar between the two histopathologic groups. Symptomatology related to tumor and Global Health Status/QOL scores improved with chemotherapy in both NSCLC and SCLC patients. Scores for emotional and role functions were also improved in SCLC patients. But alopecia, sore mouth, nausea and vomiting scores were also increased with chemotherapy.

Conclusion: Chemotherapy can ameliorate at least some domains of quality of life with palliation of symptoms in both NSCLC and SCLC patients.

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Key words: *quality of life, non-small cell lung cancer, small cell lung cancer, chemotherapy*

Introduction

The quality of life (QOL) of lung cancer patients is affected by several factors related to the patient, stage of disease and treatment characteristics. For small-cell lung cancer (SCLC), the treatment is generally aggressive, primarily based on chemotherapy. Treatment strategy for non-small-cell lung cancer (NSCLC) is strongly dependent on the stage of the disease and ranges from surgery to palliative chemotherapy. Over the last few years, very little progress has been made in terms of survival. Therefore, the effect of treatment on quality of life has become progressively more relevant (1). Health related quality of life is a multifactorial concept and includes effects of disease, side effects of treatment and physical, psychosocial functions (2). Since 1985, the Food and Drug Administration requires that an effect on improvement of quality of life needs to be shown before a new anti-cancer drug is approved for use (3).

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Table 1. Baseline characteristics of the patients

Characteristic	Histopathological Type	
	SCLC	NSCLC
Sex		
Men	25 (92.6%)	25 (100.0%)
Women	2 (7.4%)	0 (0.0%)
Age*		
≤65 yrs	19 (70.4%)	18 (72.0%)
≥65 yrs	8 (29.6%)	7 (28.0%)
Stage+		
A	12 (44.4%)	8 (32.0%)
B	15 (55.6%)	17 (68.0%)
Performance status		
ECOG 0	3 (11.1%)	1 (4.0%)
ECOG 1	18 (66.7%)	16 (64.0%)
ECOG 2	4 (14.8%)	8 (32.0%)
ECOG 3	2 (7.4%)	0.0
ECOG 4	0.0	0.0

* Mean±Standard Deviation for age was 58.63±9.61 yrs in the SCLC group and 55.88±9.32 yrs in the NSCLC group.

+ For SCLC A: localised, B: generalised; and for NSCLC A: unresectable stage III, B: stage IV.

The aims of our study were to demonstrate the effects of chemotherapy on QOL in lung cancer patients and to compare this effect in NSCLC and SCLC patients.

Materials and Methods

There were 52 patients in the series, 27 of which were SCLC and 25 NSCLC cases. The information about QOL of patients was collected using the European Organization for Research and Treatment of Cancer (EORTC) core questionnaire (QLQ C-30 Version 2) and lung cancer module (LC-13), with the permission of EORTC (4). The questionnaire was given before and after three courses of platinum-containing chemotherapies. The patients were not exposed to any intervention other than routine chemotherapy procedures and body weight measurements during this time period. Verbal informed consent was obtained from each patient before the questionnaire was given.

Newly diagnosed Stage IIIb and IV for NSCLC or SCLC patients younger than 75 years of age, who had normal liver, renal and bone marrow functions, who had not received any anticancer treatment prior to the study but for whom chemotherapy was considered as the treatment of choice, whose expected survival was longer than 3 months and whose ECOG performance status was between 0 and 2 were included in the study. Exclusion criteria consisted of cooperation problems related to hearing, language or brain metastases.

Table 2. Distribution of tumor response according to histopathologic types

Tumour response	SCLC		NSCLC		All Cases	
	n	%	n	%	n	%
Complete response	4	14.8	1	4	5	9.6
Partial response	14	51.8	10	40	24	46.2
No change	5	18.6	10	40	15	28.8
Progression	4	14.8	4	16	8	15.4
Total	27	100	25	100	52	100

All SCLC patients and 12 NSCLC patients received cisplatin 25 mg/m^2 and etoposide 100mg/m^2 administered on days 1, 2 and 3, and repeated at three week intervals. Vinorelbine 25 mg/m^2 on day 1 and 8, cisplatin 100 mg/m^2 on day 1 were administered to 6 of the NSCLC patients and 4 NSCLC patients received gemcitabin 1000 mg/m^2 on days 1, 8 and 15, cisplatin 100 mg/m^2 on day 15. This regimen was repeated following an interval of 28 days. Paclitaxel 200 mg/m^2 and carboplatin 6xAUC were administered with an interval of three weeks to 3 NSCLC patients.

Tumor response to treatment was evaluated by WHO criteria. Accordingly, responses were categorized as a complete response when all known disease disappears, and as a partial response when a 50% or greater reduction occurs in the largest and perpendicular diameter of the lesion and this reduction in size lasts for more than 4 weeks (5).

We used the scoring procedures described in EORTC QLQ C30 Scoring Manual (6). A high scale score represents a higher response level. Thus a high score for a functional scale represents a high level of functioning, a high score for global health status/QOL represents a high QOL, but a high score for a symptom scale or item represents a high level of symptomatology.

According to specifications of data, statistical inferences were made with Wilcoxon signed rank test, Mann Whitney U test, and Spearman correlation test with Statistical Package for Social Sciences (SPSS) software. The usage of nonparametric statistics in analysis of quality of life data has also been recommended in the study by Hopwood *et al* (7). Median and interquartile range values were used to describe distribution of variables due to very skewed distributions of QOL of life scores. Two sided $p<0.05$ was accepted as statistically significant.

Results

Age distributions of SCLC and NSCLC patients were similar. Only 2 of the 52 cases were women. Baseline characteristics of patients are shown in Table 1. Tumor responses to chemotherapy are presented in Table 2. Tumor

Table 3. Variables showing statistically significant correlations with one another			
Variable pairs		**Spearman rho (r_s)**	**p value of correlation coefficient**
ECOG performance status with	Presence of metastasis	0.341	0.0130
ECOG performance status with	Post-chemotherapy ECOG	0.552	0.0001
ECOG performance status with	Tumor response	- 0.374	0.0060
	QLQ C-30 and LC-13 scales/items (before chemotherapy)		
ECOG performance status with	Emotional function	- 0.304	0.0280
ECOG performance status with	Role function	- 0.477	0.0001
ECOG performance status with	Physical function	- 0.525	0.0001
ECOG performance status with	Global Health Status /QOL	- 0.630	0.0001
ECOG performance status with	Dyspnea	0.319	0.0210
ECOG performance status with	Fatigue	0.519	0.0001
ECOG performance status with	Pain	0.532	0.0001
ECOG performance status with	Financial problems	0.296	0.0330
ECOG performance status with	LC haemoptysis	0.323	0.0190
ECOG performance status with	LC Dyspnea	0.529	0.0001
ECOG performance status with	LC Coughing	0.315	0.0230
After chemotherapy LC alopecia with	Tumor response	- 0.334	0.0150
After chemotherapy LC pain in arm with	Tumor response	- 0.277	0.0470

response rates were not significantly different in the two histological subtypes.

There were statistically significant correlations between tumor response status and Global Health Status/QOL before (r_s=0.348, p=0.012) and after three courses (r_s=0.296 p=0.033) of chemotherapy. We found that previous performance status of the patients strongly correlated with many fields of QOL. Some improvement was observed in the performance status of the patients with chemotherapy, but the differences were not statistically significant. Other variables that were found to show statistically significant correlations are presented in Table 3.

Before chemotherapy, 35 patients (67.3%) complained of pain. Pain scores were lower after chemotherapy (p=0.033). Following chemotherapy the requirement for pain control medication was reduced.

Body weight was 5.19±7.59 kg lower after chemotherapy in the total group (p=0.0001), but no differences in extent of weight loss were noted between patients with small and non-small cell lung cancer. The majority of the patients did not reach their basal weight again.

Evaluation of QOL before chemotherapy showed that insomnia scores were higher in SCLC and financial problem scores were higher in NSCLC patients. Other domains of QOL questionnaire showed no statistical significant differences between NSCLC and SCLC patients. A re-evaluation of QOL after 3 courses of platinum-containing chemotherapy showed that both insomnia and financial problem scores were higher in the NSCLC patients. Scores for other domains of QOL were similar in the two histopathologic groups.

After chemotherapy Global Health Status/QOL scores improved in both NSCLC and SCLC patients. Also general pain, pains in chest and arm, haemoptysis, dyspnea, and lung cancer module (LC) coughing scores were lower in both NSCLC and SCLC patients due to improved symptomatology. Fatigue scores were lower only in NSCLC and insomnia scores were lower only in SCLC patients.

LC alopecia, sore mouth, nausea and vomiting scores increased after chemotherapy. Additionally LC peripheral neuropathy scores were higher in SCLC patients. Emotional and role functions scores increased in SCLC patients (Table 4).

Discussion

We achieved complete and partial responses with platinum-containing chemotherapy in 14.8% and 51.8% of SCLC patients respectively. These percentages were 4%, 40% in the NSCLC patients. Tumor responses to treatment were better in the SCLC group but the difference was not statistically significant. This may be due to the small sample size of our study.

There were statistically significant correlations in our patients between tumor response status and Global Health Status/QOL before and after three courses of chemotherapy.

Table 4. Comparisons of QLQ-C30 and LC-13 scores cases before and after chemotherapy						
	SCLC			NSCLC		
Domain	**Before ***	**After ***	**p**	**Before ***	**After ***	**p**
Global Health Status						
Global Health Status /QOL	58.3 (33.3)	75.0 (25.0)	**0.004**	50.0 (29.2)	83.3 (25.0)	**0.001**
Functional scales						
Emotional function	75.0 (33.3)	91.7 (16.7)	**0.001**	58.3 (47.9)	83.3 (33.3)	0.051
Role function	66.7 (66.7)	91.7 (50.0)	**0.030**	66.7 (66.7)	83.3 (41.7)	0.054
Cognitive function	100.0 (0.0)	100.0 (0.0)	0.414	100.0 (0.0)	100.0 (0.0)	1.000
Social function	83.3 (50.0)	66.7 (66.7)	0.089	83.3 (50.0)	66.7 (58.3)	0.270
Physical function	180.0 (20.0)	180.0 (40.0)	0.072	170.0 (50.0)	180.0 (30.0)	0.334
Symptom scales/items						
Dyspnea	33.3 (66.7)	0.0 (33.3)	**0.002**	33.3 (66.7)	0.0 (33.3)	**0.001**
Fatigue	44.4 (55.6)	22.2 (44.4)	0.052	50.0 (44.4)	33.3 (33.3)	**0.022**
Nausea/vomiting	0.0	58.3 (83.3)	**0.000**	0.0	50.0 (91.7)	**0.001**
Pain	33.3 (66.7)	16.7 (33.3)	**0.002**	50.0 (50.0)	16.7 (50.0)	**0.004**
Insomnia	33.3 (33.3)	0.0	**0.001**	0.0	0.0	0.351
Appetite loss	33.3 (66.7)	66.7 (100.0)	0.417	33.3 (66.7)	33.3 (66.7)	0.535
Constipation	0.0	0.0 (33.3)	0.813	0.0 (25.0)	0.0 (16.7)	0.903
Diarrhoea	0.0	0.0	0.603	0.0+	0.0+	**0.046**
Financial problems	0.0 (33.3)	0.0 (66.7)	0.271	66.7 (100.0)	66.7 (100.0)	0.739
Lung Cancer module						
LC Dyspnea	33.3 (33.3)	11.1 (33.3)	**0.005**	22.2 (55.6)	11.1 (27.8)	**0.004**
LC Coughing	33.3 (41.7)	16.7 (33.3)	**0.005**	33.3 (33.3)	0.0 (33.3)	**0.001**
LC Haemoptysis	33.3 (33.3)	0.0	**0.008**	0.0 (33.3)	0.0	**0.014**
LC Sore mouth	0.0	0.0 (33.3)	**0.004**	0.0	0.0 (33.3)	**0.015**
LC Dysphagia	0.0	0.00 (8.3)	0.216	0.0	0.0	1.000
LC Peripheral neuropathy	0.0	0.0 (33.3)	**0.012**	0.0	0.0	0.792
LC Alopecia	0.0	100.0 (33.3)	**0.000**	0.0	66.7 (66.7)	**0.000**
LC Pain in chest	33.3 (66.7)	0.0 (33.3)	**0.005**	33.3 (66.7)	0.0 (33.3)	**0.001**
LC Pain in arm	33.3 (66.7)	0.0 (33.3)	**0.016**	33.3 (50.0)	0.0 (50.0)	**0.007**
LC Pain other	0.0 (33.3)	0.0	0.248	0.0 (66.7)	0.0 (33.3)	0.116
Variables for which statistically significant differences were found between NSCLC and SCLC						
Insomnia (before chemotherapy)	33.33 (33.33)			0.00 (0.00)		**0.048**
Insomnia (after chemotherapy)**		0.00 (0.00)			0.00 (0.00)	**0.032**
Financial problems		0.00 (66.7)			66.7 (100.00)	**0.031**

* Median (interquartile range), +Patients with diarrhoea increased from 1 to 5 after chemotherapy in the NSCLC group. **: In the NSCLC 4 patients complained from insomnia; there were no patients with insomnia in the SCLC group.

This finding was in agreement with the results of the study reported by Wolf *et al* which showed that QOL was significantly correlated with tumor response in 195 of 312 SCLC patients. (8). Bergman and colleagues also reported time related differences in EORTC QLQ-C36 scores significantly correlated with tumor response and performance status (9). Improvement in the performance status was also observed in our cases with chemotherapy, but the difference was not found statistically significant. It is also reported that tumor response is well correlated with performance status. However, this was not a uniform finding, performance status of patients deteriorated after chemotherapy in some studies and improved in other studies (10-14). Although some studies report only a weak correlation between Karnofsky performance score and QOL measured by EORTC QLQ-C30 (15), there are many studies showing that performance status is correlated with QOL (16,17). Osoba and colleagues detected a strong correlation between ECOG performance

status and EORTC QLQ-C30 scores (18). Also in our study previous performance status of our patients was strongly correlated with many aspects of QOL.

Weight loss of patients continued during chemotherapy in both NSCLC and SCLC patients in our study. There are controversies about the effect of chemotherapy on the nutritional state. Weight gain after chemotherapy is reported in some studies while the reverse is reported in other studies (13,19).

The frequency of pain as a symptom in early stages, during chemotherapy and in the late stage of lung cancer is given as 20-50%, 33% and 75-90% respectively (20). Untreated pain effects activity, motivation, mood, and global QOL of patients. In our study chemotherapy reduced the requirement for pain control medication. There are many studies reporting that chemotherapy ameliorates pain severity or requirement of the pain control medication (19,21).

There were differences in insomnia scores and financial problem scores between NSCLC and SCLC patients at the beginning of chemotherapy and after three courses of chemotherapy, but all other domains of QOL were similar between the two histopathologic groups. After chemotherapy Global Health Status/QOL scores improved in both NSCLC and SCLC patients. Three courses of chemotherapy effectively decreased symptomatology related to tumor (pain, haemoptysis, dyspnea and coughing) in both NSCLC and SCLC patients. Fatigue scores were lower only in NSCLC and insomnia scores were lower only in SCLC patients. Unfortunately, alopecia, sore mouth, nausea and vomiting scores were higher due to the toxicity of chemotherapy. Additionally LC peripheral neuropathy scores were higher in SCLC patients. Nevertheless many studies indicate that QOL of patients improved despite these adverse effects of chemotherapy (22-24).

Early studies evaluating the effects of chemotherapy on QOL of NSCLC patients reported a deterioration in the general status (10,25). On the other hand, many recent studies demonstrate improvement in QOL of patients with chemotherapy. QOL of 31 NSCLC patients increased by 75% after high dose combination chemotherapy in the study of Fernandez *et al* (19). In the study by Buccheri, physical status was found to improve with chemotherapy and compliance to treatment was found to be better in the group who received supportive care (14). Recently Paesmans reviewed randomized trials using QOL as an endpoint, also comparing best supportive care with or without chemotherapy. This review concluded that most of the selected trials showed an improvemed QOL with chemotherapy (26).

Anxiety and depression are frequently encountered in lung cancer patient (27). Sarna and colleagues reported that risk factors for poorer QOL are strongly linked to distressed mood (28). Scores for emotional and role functions increased after chemotherapy in SCLC patients in our study. This improvement may be related to a lessening of disturbing symptoms, to a belief that chemotherapy will be successful, or acceptance of faith. Consequently, chemotherapy can ameliorate at least some domains of QOL with palliation of symptoms in both NSCLC and SCLC patients.

References

1. Gridelli C, Perrone F, Nelli F et al. Quality of life in lung cancer patients. Ann Oncol 2001;12 Suppl 3:S21-5.
2. Cooley ME. Quality of life in persons with non-small cell lung cancer: A concept analysis. Cancer Nurs. 1998;21:151-61.
3. Johnson JR, Temple R. Food and Drug Administration requirements for approval of new anticancer drugs. Cancer Treat Rep. 1985; 69:1155-7.
4. Aaronson NK, Ahmedzai S, Bergman B et al. The European Organisation 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.
5. WHO Handbook for Reporting the Results of Cancer Treatment. Geneva: WHO, 1979.
6. Fayers PM, Aaronson NK, Bjordal K et al. on behalf of the EORTC Quality of Life Study Group. The EORTC QLQ-C30 Scoring Manual, 2nd Ed. EORTC, Brussels 1999.
7. Hopwood P, Stephens RJ, Machin D. Approaches to the analysis of quality of life data: Experiences gained from a Medical Research Council Lung Cancer Working Party palliative chemotherapy trial. Qual Life Res 1994;3:339-52.
8. Wolf M, Pristsch M, Drings P, et al. Cyclic-alternating versus response oriented chemotherapy in small-cell lung cancer: a multicentre randomised trial of 321 patients. J Clin Oncol. 1991; 9: 614-24.
9. Bergman B, Sullivan M, Sörenson S. Quality of life during chemotherapy for small cell lung cancer: II a longitudinal study of the EORTC core quality of life questionnaire and comparison with the sickness impact profile. Acta Oncol. 1992; 31: 19-28.
10. Bakker W, Vanoosterom AT, Aaronson NK, et al. vindesine, cisplatin and bleomycin combination chemotherapy in non-small cell lung cancer: survival and quality of life. Eur J Cancer Clin Oncol. 1986; 22: 963-70.
11. Coats A, Abraham S, Kaye S, et al. On the receiving end-patient perception of the side effects of cancer chemotherapy. Eur J Cancer Clin Oncol. 1983; 19: 203-8.
12. Splinter TAW. Chemotherapy in advanced non-small cell lung cancer. Eur J Cancer. 1990; 26: 1093-9.
13. Bleehen NM, Girling DJ, Machin D, et al. A randomised trial of three or six courses of etoposide cyclophosphamide methotrexate and vincristine or six courses of etoposide and ifosfamide in small cell lung cancer (SCLC) II: quality of life. Br J Cancer. 1993; 68: 1157-66.
14. Buccheri GF, Ferrigo D, Curcio A, et al. Continuation of chemotherapy versus supportive care alone in patients withinoperable non-small cell lung cancer and stable disease after two or three cycles of MACC. Cancer. 1989; 63; 428-32.
15. Montazeri A, Gilis RC, McEven J. Quality of life in patients with lung cancer. Chest. 1998; 113: 467-81.
16. Nou E, Aberg T. Quality of survival in patients with surgically treated bronchial carcinoma. Thorax. 1980; 35:255-63.
17. Hopwood P, Stephens RJ. Symptoms at presentation for treatment in patients with lung cancer: implications for the evaluation of palliative treatment. Br J Cancer. 1995; 71:633-6.
18. Osoba D, Murray N, Gelman R, et al. Quality of life, appetite and weight change in patients receiving dose intensive chemotherapy. Oncology. 1994; 8:61-5.
19. Fernandez C, Rossel R, Abad-Esteve A, et al. Quality of life during chemotherapy in non-small cell lung cancer patients. Acta Oncol 1989; 28:29-33.

20. Grossman S. Pain control in patients with cancer. In: Klasteisky J, Schimpff SC, Senn HJ. (Eds). Handbook of Supportive Care in Cancer. New York: Marcel Dekker Inc., 1995: 207-20.
21. Bergman B, Aaronson NK, Ahmedzai S, et al. The EORTC QLQ-LC13: a modular supplement to the EORTC core quality of life questionnaire (QLQ-C30) for use in lung cancer 1994; 30A:635-42.
22. Bleehen NM, Fayers PM, Girling DJ, et al. Survival, adverse reactions and quality of life during combination chemotherapy compared with selective palliative treatment for small-cell lung cancer. Resp Med. 1989; 83: 51-8.
23. Bleehen NM, Fayers PM, Girling DJ, et al. Controlled trial of 12 versus six courses of chemotherapy in the treatment of small-cell lung cancer. Br J cancer. 1989; 59: 584-90.
24. Fayers PM, Bleehen NM, Girling DJ, et al. Assessment of quality of life in small-cell lung cancer using a Daily Diary Card developed by the Medical Research Council Lung Cancer Working Party. Br J Cancer 1991; 64: 299-306.
25. Ganz PA, Figlin RA, Haskel CM, et al. Supportive care versus supportive care and combination chemotherapy in metastatic non-small cell lung cancer: does chemotherapy make a difference? Cancer 1989; 63: 1271-8.
26. Paesmans M. Benefits of chemotherapy for quality of life in patients with advanced nonsmall-cell lung cancer. Curr Opin Oncol 2002;14:389-93.
27. Razovi D, Stiefel F. Psychiatric and emotional problems of lung cancer patients. In: Klasteisky J, Schimpff SC, Senn HJ. (Eds). Handbook of Supportive Care in Cancer. New York: Marcel Dekker Inc., 1995: 221-43.
28. Sarna L, Padilla G, Holmes C et al. Quality of life of long-term survivors of non-small-cell lung cancer. J Clin Oncol 2002;20:2920-9.