Letter to the Editor

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Assessing the Quality of Life of Metastatic Non-Small Cell Lung Cancer Patients after Chemotherapy: An Assessment Which Tells What's Next

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Dear Editor

Clinical, biological, pathological, or cytogenetic markers have already been described as predictors of the prognosis of non-small cell lung cancer (NSCLC). However, the correlation between different quality of life indicators in stage IV lung cancer patients with the mean overall survival has not been studied.

A first publication was made to discuss the correlation between the different dimensions of quality of life, sleep quality, and psychological distress in NSCLC patients (1). The same cohort, still consenting, was followed to get prognostic parameters: progression-free survival (PFS) and overall survival (OS).

This second analysis detailed below aims to assess the correlation between quality of life indicators with the prognosis of the disease.

This was a single-arm prospective descriptive cohort study conducted in the pulmonology department Pavilion 4 in Ariana Hospital, Tunisia.

We included all NSCLC patients in stage IV of the disease according to the 8th edition of TNM classification, during an inclusion period from January to December 2019.

Clinical data were collected at the end of the last chemotherapy course. Then, questionnaires offered to our patients assessed the quality of life and the quality of sleep (respectively QLQ C-30 and Pittsburgh sleep quality index (PSQI) questionnaires in an Arabic Tunisian version). A subsequent follow-up of the disease was consistent with international recommendations for metastatic lung cancer (2). Patients were followed until death or until the point date of 31-12-2020.

The statistical study was conducted then, to assess the correlation between the quality of life indicators, regimen of antitumor treatment, and the prognosis of metastatic NSCLC.

The study protocol was first, discussed in the hospital ethics committee. Then, the study was submitted to the Pan African Clinical Trial Registry (PACTR): Study number PACTR202104725647601

We enrolled 120 patients during the study. Exclusion criteria were decisive in 49 cases. We kept 71 cases in the datacollecting step. The mean age of our patients was 62.17 years.

The most common histological type was adenocarcinoma (58%). Sixty percent of patients received at least three cycles of palliative chemotherapy.

Twenty-six patients had a response after 1st line treatment (37% of patients). Their average progression-free survival (PFS) was 194 days. The mean overall survival (OS) was 317 ± 20 days (95% confidence interval = 292 - 377) with extremes of 1.6 months to 21 months. The one-year survival rate was 44%.

1. QLQ-C30 Questionnaire Analysis

Differences in mean scores of QOL among the three subgroups of patients receiving different regimens of chemotherapy were minor and non-significant. The regimen of chemotherapy did not interfere so, with the QOL in metastatic NSCLC patients (Table 1).

Table 1. Comparison of Qol scores among subgroups of patients receiving the regimen of chemotherapy

Regimen of treatment	Coeff. of symptoms	Coeff. of performances	Coefficient of global life
Cisplat/Vinorelbin	33.4	66.1	26.9
Cisplat/Gemcitabin	37.7	62.8	25.3
Carboplatin/Paclitaxel	40.1	64.8	26.4

2- Sleep Quality Questionnaire: Analysis of the PSQI score

Analysis of the PSQI score at the end of chemotherapy showed that 55% of patients had a score \leq 5 (good sleep quality). Insomnia was the most reported sleep disorder (85% of patients). Excessive daily sleepiness was noted in 52% of patients. There was no significant difference between the three subgroups of patients receiving different regimens of chemotherapy (Table 1).

3- Analysis of factors correlated with OS:

3.1. Prognostic impact of epidemiological and clinical features:

OS was longer for patients with a preserved PS when chemotherapy started (Table 2), whatever the chemotherapy regimen used to treat the NSCLC (Table 3).

Table 2.	Correlation between	clinical features and	d overall surviva	l in stage V	I CBNPC patients
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Clinical featu	ure	Overall survival (days)	One-year survival rate	Р
Age	Age < 60 y	355	46%	0.14
	Age ≥ 60 y	292	41.8%	0.14
	PS = 0	424	63.4%	0.002
PS	PS = 1	371	50%	
	PS = 2	252	27.9%	
Chest pain		Overall survival (days)		р
No (n = 51)		322		0,072
Yes (n = 20)		313		
Dyspnea		Overall survival (days)		р
No (n = 34)		342		0,195
Yes (n = 37)		293		
Hemoptysis		Overall survival (days)		Р
No (n = 53)		305		0,27
Yes (n = 18)		352		
Weight loss		Overall survival (days)		Р
No (n = 54)		347		0,044
Yes (n = 17)		228		
Stage of the	disease	Overall survival (days)	One-year survival rate	Р
M1a		364	47%	0.56
M1b		354	44%	
M1c		300	34%	
Response to	chemotherapy	Overall survival (days)	One-year survival rate	Р
Partial regres	sion (n= 7)	551	85%	0.0001
Stability (n= 1	19)	430	61%	
Progression ((n= 42)	265	28%	

Table 3. Correlation between overall survival and chemotherapy molecules

Regimen of treatment	Overall survival (days)	One-year survival rate	Р
Cisplat/Vinorelbin	344	45.7%	
Cisplat/Gemcitabin	354	45%	0.22
Carboplatin/Paclitaxel	311	39.5%	

Mean OS was closely correlated with tumor response after 1st line chemotherapy. In patients who had objective partial tumor response, OS was 551 days and the one-year survival rate was 85%. For patients who had tumor progression, OS was 265 days with a one-year survival rate of 28% (p=0.0001).

3.2. Correlation between OS and quality of life:

OS was correlated and proportional with the coefficient of global life and the coefficient of performances, which means a poor prognosis related to the degradation of quality of life, as perceived by the patient after chemotherapy (Table 4).

Considering the nine dimensions of symptoms separately, there was a significant inverse proportional correlation between OS and the dimensions of "Fatigue",

Table 4. Correlations between mean scores of quality of life

Mean scores	Coeff. of symptoms	Coeff. of performances	PSQI	Overall survival
Coefficient of global life	0,699	-0,757	-0,678	0,547
	0,0001	0,0001	0,013	0,0001
Coefficient of Performance	-0,723		-0,480	0,617
	0,0001		0,011	0,0001
Coefficient of symptoms		-0,723	0,608	-0,538
		0,0001	0,003	0,0001

3.3. Correlation between OS and sleep quality:

Mean OS in patients with $PSQI \le 5$ scores was better than in patients with PSQI scores > 5. The difference was significant (Figure 1; Log Rank test revealed an OS in good and poor sleepers equal to 441 days VS 219 days, respectively; p 0.001).



Figure 1. Kaplan-Meier curves displaying the estimated survival probability for good and poor sleepers (Log Rank test)

The prognostic impact of an early introduction of palliative treatment for cancer patients was a hypothesis to be verified. Palliative management is typically provided by a trained doctor and nurse, but almost systematically involves the intervention of the psychologist, nutritionist, and physiotherapist at the slightest subjective degradation felt. Paradoxically, the correlation of this personalized intervention with the average survival of patients with advanced cancers was not significant. On the other hand, palliative treatment prescribed "on-demand" significantly improved prognosis according to the multicenter study of the Early Palliative Care Italian Study Group (3).

A wide range of publications including NSCLC patients at various stages suggested a statistically significant close link between quality of life and overall survival. These studies reported degradation of overall survival to be correlated with scores of "Fatigue", "Nausea/Vomiting", "Insomnia" and "Diarrhea" dimensions assessed by QLQ-C30. At the end of the chemotherapy course, a pejorative prognostic impact of the dimension "Fatigue" was still significant. The authors therefore recommended conducting studies dedicated to the search for therapeutics that promote quality of life, especially in the absence of curative treatment.

In our study, we found a statistically significant correlation between overall survival on the one hand and indicators of quality of life and sleep quality on the other, which would give value to the various palliative treatments designed to promote quality of life. Many studies have discussed which factors promote quality of life among cancer survivors, increasingly investigated since the publication of the EORTC multicenter study (4). Opinions concerning the role of alternative medicine remain controversial. These studies often include patients with neoplasms of good prognosis, after a good response to anti-tumoral treatment. There is still a lack of specific studies for patients with advanced NSCLC.

The study was submitted to the Pan African Clinical Trial Registry (PACTR): Study number PACTR202104725647601 Open access HTML and verified link of the registration number: https://pactr.samrc.ac.za/Search.aspx

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