ARTICLE ORIGINAL

Prognostic value of Quality of life (QoL) assessment among Tunisian lung cancer patients

Valeur pronostique de l'évaluation de la qualité de vie chez les patients Tunisiens atteints du cancer du poumon

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ABSTRACT

Aim: To investigate the prognostic value of quality of life (QoL) assessment among Tunisian lung cancer patients for survival.

Methods: A prospective cohort study was performed from January 2018 to June 2019. Performance status (PS), QoL questionnaire-core30 (QLQ-C30), QoL questionnaire-Lung Cancer 13 (QLQ-LC13) and European QoL-5 dimensions-3level version questionnaire (EQ-5D-3L) were used to QoL assessment. Patients were divided into 2 groups according to global QLQ-C30 score, a Clinically Significant Deficit (CSD) was considered if the score was ≤50. Cox regression analysis and Stepwise regression analysis were performed to evaluate the prognostic significance of QoL. Overall survival (OS) was calculated using the Kaplan-Meier method. Log-rank test was used to compare survival curves. p value cutoff for statistical significance was 0.05.

Results: One hundred patients were included. Median OS for patients with CSD in QoL was 365 days, compared with 467 days for those without significant difference in QoL (Log-rank test, p=0.036). Similarly, Median progression free survival for patients with CSD in QoL was 122 days compared with 326 days for those who did not report a significant difference in QoL (Log-rank test, p=0.05). Upon multivariable stepwise regression analysis, Global QoL score (QLQ-C30) was a significant predictor of OS (coefficient estimate (CE)=0.336, p=0.005), along with stage IV (CE=-0.193, p=0.033) and tumor progression (CE =-0.238, p=0.047).

Conclusion: QoL was a predictor of survival in our cohort of patients with lung cancer. This should recommend an active intervention for patients with a significant deficit in QoL in Early Palliative Care.

Keywords: Lung Neoplasms; Quality of Life; Prognosis; Survival; Palliative Care.

RÉSUMÉ

Objectif : Etudier la valeur pronostique de l'évaluation de la qualité de vie (QDV) pour la survie chez les patients Tunisiens atteints du CDP.

Méthodes: Une étude prospective de cohorte a été réalisée entre Janvier 2018 et Juin 2019. Le Performance status (PS), QoL questionnaire-core30 (QLQ-C30), QoL questionnaire-Lung Cancer 13 (QLQ-LC13) et European QoL-5 dimensions-3level version questionnaire (EQ-5D-3L) ont été utilisés pour l'évaluation de la QDV. Les patients ont été divisés en 2 groupes selon le score global QLQ-C30, un Déficit Cliniquement Significatif (DCS) a été considéré si le score était ≤50. Les modèles de régression de Cox et Stepwise ont été réalisée pour évaluer la signification pronostique de la QDV. La survie globale (SG) a été calculée à l'aide de la méthode de Kaplan-Meier. Le test du log-rank a été utilisé pour comparer les courbes de survie. Le seuil de valeur de p pour la signification statistique était de 0,05.

Résultats: Cent patients ont été inclus. La médiane de SG des patients avec DCS en qualité de vie était significativement inférieure à celle des patients sans déficit : respectivement 365 jours versus 467 jours, (test du log-rank, p = 0,036). De même pour la médiane de survie sans progression : 122 jours versus 326 jours pour ceux qui n'ont pas signalé de différence significative en QDV (test du log-rank, p = 0,05). L'analyse de régression multivariée stepwise a montré que le score global de QDV (QLQ-C30) était un facteur prédictif significatif de SG (coefficient estimate (CE)= 0.336, p=0.005), ainsi que le stade IV (CE=-0.193, p=0.033) et la progression tumorale (CE =-0.238, p=0.047).

Conclusion: La QDV était un facteur prédictif de survie dans notre cohorte de patients atteints de CDP. Cela devrait recommander une intervention active en soins palliatifs précoces pour les patients présentant un déficit significatif en QDV.

Mots clés: Tumeurs du poumon ; Qualité de vie; Pronostic; Survie; Soins palliatifs.

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INTRODUCTION

Lung cancer (LC) is the most commonly diagnosed cancer and the leading cause of oncologic-related death worldwide (18.4% of the total cancer deaths) [1–3] . In the USA, LC resulted in an estimated 25.9% of all cancer deaths in 2017[4]. Regardless of the unceasing efforts made to improve outcome by optimizing multimodality treatment, the impact on survival remains typically limited [5,6].The overall estimated 5-year survival is only 18.1% [7]. In this context, a growing interest for quality of life (QoL) assessment among LC patients was observed worldwide [1,8-10]. Most of the papers from the literature, mainly descriptive, reported that QoL in patients with LC is lower than in healthy population and in several other malignancies [1,11,12]. Moreover, since lengthening survival was considered paramount in cancer management, the clinical implications of the relationship between QoL data and survival could be regarded as very important. Investigators from both clinical oncology and health sciences research have begun demonstrating that QoL in cancer patients could be associated with survival duration. It was believed that QoL data may not only be helpful in evaluating cancer care outcomes but may also like clinical information, be prognostic or predictive of survival duration. [10,13,14].

Given the difference in LC management in developing countries, it was interesting to study this relationship in an Arabic country, particularly Tunisia. As far as we know, it's the first Tunisian and the second Arabic study (after Egypt [15]) to investigate the prognostic value of baseline QoL assessment among LC patients. The primary objective of the present study was to investigate whether baseline QoL assessment among Tunisian LC patients predicted overall survival (OS) and progression free survival (PFS). The secondary objective was to describe characteristics of patients who had a clinically significant deficit (CSD) in QoL versus those who did not.

METHODS

Study design and setting : The present study is a prospective cohort study performed from January 2018 to June 2019 in the department of Pulmonology of «Farhat HACHED» Hospital (Sousse, Tunisia).

Study population : Patients with a histological confirmation of primary LC were included. Non-inclusion criteria were: inability to answer the questionnaire, inability to give an informed consent or refusal to participate. Exclusion criteria were lack of necessary information during follow up e.g.: survival, tumor response...

Data collection : A general questionnaire was used to describe patient and disease-related data. Response Evaluation Criteria in Solid Tumours (RECIST) guidelines version 1.1 were used to evaluate tumor response. Four questionnaires were used including Quality of life questionnaire-core 30 (QLQ-C30), Quality of life questionnaire-Lung Cancer 13 (QLQ-LC13), EQ-5D-3L (European QoL-5 dimensions-3level version questionnaire) and Performance status according to Eastern Cooperative Oncology Group performance scale (ECOG PS). The QLQ-C30 (version 3.0) is a 30-item cancer specific questionnaire that incorporates five functioning scales (physical, psychological, cognitive, social and life roles) and nine symptom scales (fatigue, pain, nausea/vomiting, dyspnea, insomnia, loss of appetite, constipation, diarrhea, financial problems) and a global health status/ QoL scale. The raw scores are linearly transformed to give standard scores in the range of 0 to 100 for each of the functioning and symptom scales. A high score for a functional scale represents a high level of functioning. A high score for the global health status / QoL represents a high QoL but a high score for a symptom scale represents a high level of symptomatology /problems. QLQ-LC13 is a site-specific questionnaire consisting of 13 items on lung cancer symptoms and its treatment side effects. It incorporates one multi-item scale to assess dyspnea and a series of single items assessing pain, coughing, sore mouth, dysphagia, peripheral neuropathy, alopecia and hemoptysis. The scoring approach for the QLQ-LC13 is identical in principle to that for the symptom scales of the QLQ-C30. A high score for the scales represents a high level of symptomatology or problems. The EQ-5D-3 Level version consists of a descriptive system which comprises 5 dimensions: mobility, selfcare, usual activities, pain/discomfort and anxiety/depression. Each dimension has 3 levels: 1 (no problems), 2 (some problems) and 3 (extreme problems). The patient indicates his self-rated health state according to a visual analogue scale from 0 (worst imaginable health state) to 100 (best imaginable health state). Patients were divided into 2 groups according to global QLQ-C30 score: a Clinically Significant Deficit (CSD) if ≤50. To reduce information and selection bias, questionnaires were asked in Arabic dialect in a similar way to all patients. The interviewer was a Pulmonologist who had an experience in thoracic oncology.

Definitions : Overall Survival (OS) was defined as the time interval between the date of first treatment start and the date of death from any cause or the date of last contact /last known to be alive or the date of the end of follow up. Progression Free survival (PFS) was defined as the length of time between the date of first treatment start and the date of the first progression or the date of last contact /last known to be alive or the date of the end of follow up.

A Clinically Significant Deficit in QoL (CSD) was defined by an overall QoL score less than or equal to 50. This cutoff has been validated by a previous study.

Statistical analysis : In our cohort study, at the end of the follow-up (the first of June 2019), two main events were used to measure Overall Survival (OS) and Progression Free Survival (PFS): Patient's death and disease progression . Otherwise, participants were excluded from the study. OS and PFS were calculated to the date of the end of follow up (the first of June 2019). OS was calculated using the Kaplan-Meier method. Log-rank test was used to compare survival curves. T-test was used to compare continuous variables and chi-square test was used to compare categorical variables. Analysis of variance (ANOVA) was used to compare continuous variables. Cox regression analysis was performed to evaluate the prognostic significance of QoL and clinical factors. Multivariable analysis, including Stepwise regression analysis, was used to reduce the effect of confounding factors. Variables were selected for multivariable analysis if they were tested significant among univariable analysis (p<0.05). The effect of QoL parameters on patient survival (the primary objective) was expressed as Hazard Ratios with 95% confidence intervals. The p value cutoff for statistical significance was 0.05. IBM SPSS Statistics version 20 was used.

Ethical considerations : An informed consent was obtained. All patients were assured that refusal to participate would not affect their future care in any way. The study protocol was approved by the ethics committee of the hospital (Reference number 19/2019).

RESULTS

General characteristics of the study population: A total of 100 patients with LC were included in the study. Median follow up was 516 days. Patients' characteristics and disease related information were presented in Table 1. Fifty-six patients reported clinically significant deficit in QoL (the group with QoL score ≤50). Age and gender distribution were similar in both groups (mean age 59 years ±48.9). Patients who reported a clinically significant deficit in QoL were different from those who did not. They were more likely to live in rural areas, to have an unfavorable socioeconomic status, to be current smokers, to have worse performance status (PS ≥2) and to be at advanced stages (IIIB and IV). Moreover, the group with significant deficit in QoL had a higher level of brain metastasis (20% vs 4.5%, p=0.039) and was less treated with curative radiotherapy (3.5% vs 11%, p=0.05).

Table 1. Patient characteristics classified by QoL score (N=100) (Sousse, 2018-2019)

Characteristics	QoL>50 (n=44) N	QoL>50 (n=44) %	QoL ≤50 (n=56) N	QoL ≤50 (n=56) %	Total (N=100) N	Total (N=100) %	P
Gender							
male	40	90.9	50	89.2	90	90	1
Age, years							
<50	7	16	7	13	14		
50 to < 65	26	60	30	54	56		
65 to 80	10	22	19	33	29		0.36
> 80	1	2	0	0	1		
Social security							
NHIF	33						0.21
indigent	11						
Habitat area							
Rural	4	9	13	23	17		**0.05**
Urban	40	91	43	77	83		**0.05**
Socioeconomic status							
Favorable	30	68	29	52	59		0.098
Unfavorable	14	32	27	48	41		0.098
Comorbidities							
Present	12	27.3	16	28.6	28		
COPD	5	11.4	2	3.6	7		
Diabetes	7	16	8	14.3	15		0.88
Hypertension	1	2	8	14.3	9		
Coronaropathy	1	2	0	0	1		
Pulmonary fibrosis	3	6	0	0	3		
Smoker category							
Smoker	40	90.9	50	89	90		
Quitter	27	61.4	24	43	51		0.06
Current	13	29.5	26	46	39		
ECOG performance scale							
0	3	7	4	8	7		
1	37	84	43	77	80		0.390
2	4	9	6	10	10		
3	0	0	3	5	3		
Histological type							
Adenocarcinoma	20	45	29	52	49		
Epidermoid	10	23	17	30	27		0.168
NSCLC	4	9	3	5	7		
SCLC	10	23	7	13	17		
Tumor stage							
IA	2	4.5	0	0	2		
IIA	2	4.5	0	0	2		
IIB	3	7	0	0	3		0.050
IIIA	9	20	7	12	16		
IIIB	7	16	16	29	23		
IV	21	48	33	59	54		
Metastatic							
Brain metastases	2	4.5	11	20	13		0.039
Bone metastases	9		7		16		0.260
Liver metastases	3		5		8		0.930
Adrenal metastases	3		6		9		0.680
Contralateral metastases	8		14		22		0.623
Pleural metastases	7		5		12		0.279
Type of treatment							
Palliative chemotherapy	21	48	32	57	53		**0.600**
Curative chemotherapy	17	39	19	34	36		**0.636**
Neoadj chemotherapy	2	4.5	4	7	6		**0.424**
Adjuvant chemotherapy	6	14	3	5	9		**0.136**
Curative radiotherapy	5	11	2	3.5	7		**0.050**
Surgery	2	4.5	0	0	2		**0.060**

QoL description: According to QLQ-C30, mean global QoL score was 54.13 ± 25.4 for the entire sample. It was significantly lower in the group with CSD in QoL group (35.4±14.3 vs77.8±13.9) p<0.001. Significant difference was observed in physical functioning between two groups (54.97±27.46 vs 72.20± 26.41) p=0.002. Similarly, role functioning and emotional functioning scores were significantly lower in patients with a QoL deficit (p=0.014 and < 0.001 respectively). No statistically significant difference has been found between cognitive functioning and social functioning (p=0.053 and 0.788 respectively). As for symptoms, significant difference has been found between two groups in fatigue score (p<0.001), pain (p=0.002), insomnia (p=0.033) and appetite loss (p=0.002). Regarding nausea/vomiting, dyspnea, constipation, diarrhea and financial difficulties scores no significant difference has been found. According to the QLQ-LC13 supplementary questionnaire, there was a significant difference between the two groups in dysphagia (p=0.004), alopecia (p=0.042), pain in chest (p=0.013) and pain in other parts (p=0.009) but it was not the case for coughing, hemoptysis, dyspnea, sore mouth, peripheral neuropathy and pain in arm or shoulder. According to the visual analogue scale of EQ-5D-3L, mean Health State Score questionnaire was 56.7±26.6. There was a negative correlation between severity of problems and the Health State Score, especially for usual activities and anxiety/depression problems (Pearson correlation = -0.527 and -0.520 respectively).

Survival analysis: Figure 1 compares overall survival (OS) from the first quality of life (QoL) assessment between those who have a clinically significant difference (CSD) in QoL versus those who do not. Median OS for patients with CSD in QoL was 365 days, compared with 467 days for those without significant difference in QoL (p=0.036). Similarly, Kaplan Meier curves for progression free survival by QoL assessment were significantly different between two groups. Median PFS for patients with CSD in QoL was 122 days compared with 326 days for those who reported a non CSD in QoL (p=0.05) (Figure 2). Data related to the association of OS with clinical parameters and QoL dimensions upon univariable analysis were presented in Tables 2 and 3. The following clinical parameters were independent predictors of a lower overall survival: gender (female) (p=0.001), tumor stage IV (p=0.018), liver metastases (p=0.04), advanced PS (p=0.001), palliative chemotherapy (p=0.018), tumor progression (p<0.001). Favorable economic status (vs unfavorable) (p=0.030), tumor stability (p=0.013) were predictors of a longer overall survival (Table 2). As for QoL dimensions, according to QLQ-C30, global QoL score (p=0.005), physical functioning (p=0.001), role functioning (p<0.001), emotional functioning (p=0.015), fatigue (p<0.001), insomnia (p=0.003) and appetite loss (p=0.002) were independent predictors of overall survival. According
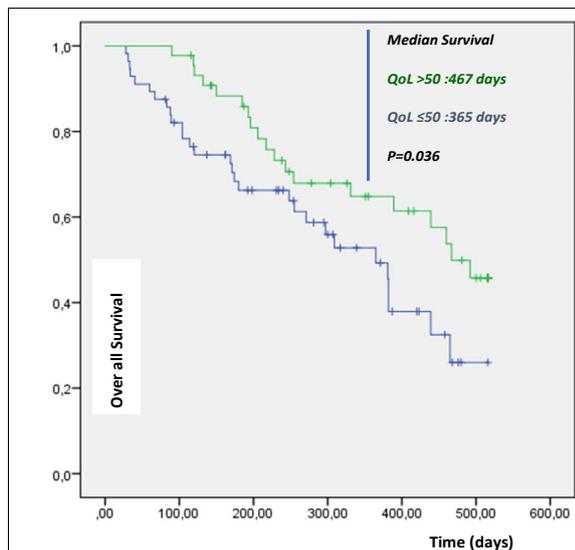

Figure 1. Kaplan Meier Overall survival curves for 100 patients with lung cancer by overall quality of life (QoL) categorization into clinically meaningful deficit versus no deficit (Log Rank test) **(Sousse, 2018-2019)**
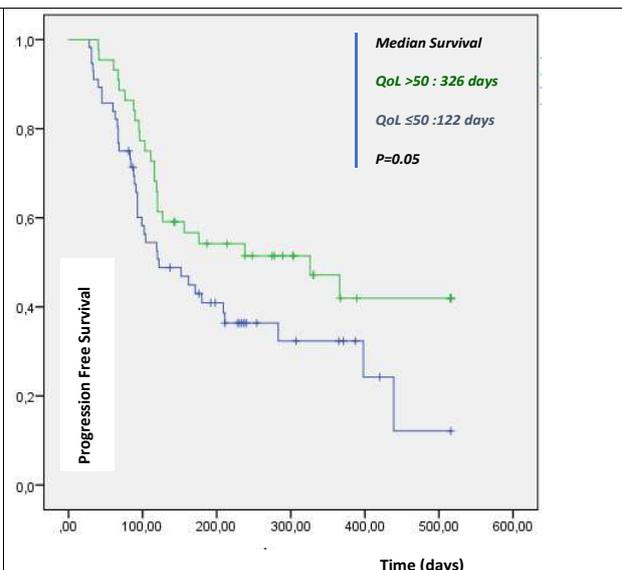
Figure 2. Kaplan Meier Progression Free Survival curves by overall quality of life (QoL) categorization into clinically meaningful deficit versus no deficit (Log Rank test) **(Sousse, 2018-2019)**

to QLQ-LC13, only pain in arm or shoulder was found to be a predictor for OS (p=0.049). As for EQ-5D-3L, mobility (p=0.004), usual activities (p=0.003), pain/discomfort (p=0.006), anxiety/depression (p=0.047) as well as health state (0.017) were predictors for OS (Table 3). Clearly, many of these variables were related to one another. When these variables were input into a stepwise logistic regression procedure, Global QoL score (according to QLQ-C30), stage IV and tumor progression were significant predictors on OS via the modeling process. One thing to be noted was that Global QoL score had the highest absolute value of coefficient estimate (0.336) meaning that this variable had the stronger effect on the independent variable (Overall survival). This model had R2 of 30.3% indicating that that OS was influenced but not completely explained by those variables (Table 4).

Table 2. Univariable Cox regression with clinical parameters associated with overall survival (Sousse, 2018-2019)

Variables	HR	95% CI	P-value
Gender (female vs male)	**3.404**	**1.630 - 7.108**	**0.001**
Age	1.001	0.968 - 1.035	0.962
Socioeconomic status (favorable vs unfavorable)	**0.532**	**0.302 - 0.939**	**0.030**
Habitat area (urban vs rural)	0.783	0.348 - 1.757	0.552
Comorbidities	1.350	0.740 - 2.463	0.328
Smoker category (current vs quitter)	0.831	0.450 - 1.533	0.553
ECOG PS	**2.114**	**1.349 - 3.313**	**0.001**
BMI	1.013	0.933 - 1.099	0.766
Diagnostic delay	0.996	0.986 - 1.006	0.447
Stage IV	**2.047**	**1.128 - 3.751**	**0.018**
Adenocarcinoma	1.030	0.584 - 1.816	0.918
Epidermoid	1.007	0.532 -1.908	0.982
NSCLC	1.064	0.330 - 3.425	0.917
SCLC	1.071	0.501 - 2.289	0.859
Liver metastasis	**2.672**	**1.048 - 6.809**	**0.040**
Cerebral M.	1.723	0.804 - 3.693	0.162
Pleural M.	1.274	0.540 - 3.004	0.580
Contralateral M.	1.668	0.864 - 3.219	0.127
Adrenal M.	0.466	0.113 - 1.922	0.291
Palliative chemo.	**2.058**	**1.129 - 3.749**	**0.018**
Curative Radio.	0.278	0.065 - 1.182	0.083
Tumor progression	**4.488**	**2.168 - 9.292**	**<0.001**
Stability	**0.272**	**0.097 - 0.760**	**0.013**
Partial response	0.479	0.189 - 1.212	0.120
Complete response	0.045	0.000 - 8.200	0.242

chemo, chemotherapy; M, metastasis ; NSCLC, non-small cell lung cancer; radio, radiotherapy ; SCLC, small cell lung cancer

Table 3. Univariable Cox regression with QoL scores associated with overall survival (Sousse, 2018-2019)

	HR	95% CI	p
QLQ-C30			
Global QoL	**0.984**	**0.973 - 0.995**	**0.005**
Physical functioning	**0.984**	**0.974 - 0.994**	**0.001**
Role functioning	**0.984**	**0.976 - 0.992**	**<0.001**
Emotional functioning	**0.987**	**0.978 - 0.998**	**0.015**
Cognitive functioning	0.992	0.982 - 1.002	0.113
Social functioning	0.996	0.999 - 1.004	0.359
Fatigue	**1.017**	**1.008 - 1.026**	**<0.001**
Nausea/Vomiting	1.003	0.989 - 1.017	0.698
Pain	1.006	0.996 - 1.017	0.240
Dyspnea	1.011	1 - 1.023	0.058
Insomnia	**1.015**	**1.005 - 1.024**	**0.003**
Appetite loss	**1.012**	**1.004 - 1.020**	**0.002**
Constipation	1.010	0.998 - 1.023	0.117
Diarrhea	1.009	0.992 - 1.027	0.299
Financial difficulties	1.004	0.995 - 1.014	0.361
QLQ-LC13			
Pain in arm/shoulder	**1,014**	**1.000 - 1.029**	**0.049**
EQ-5D-3L			
Mobility	**2.902**	**1.393 - 6.045**	**0.004**
Usual activities	**2.312**	**1.335 - 4.006**	**0.003**
Pain/discomfort	**0.006**	**1.231 - 3.433**	**0.006**
Anxiety/depression	**1.585**	**1.006 - 2.500**	**0.047**
Health state	**0.987**	**0.977 - 0.998**	**0.017**

for QLQ-LC13 and EQ-5D-3L, only significant parameters associated with OS were presented

Table 4. Univariable and Multivariable Regression Model Results: clinical and QoL dimensions associated with overall survival (Sousse, 2018-2019)

Variables	Univariable Analysis		Multivariable analysis (Stepwise logistic)	
	HR (95% CI)	p value	Coefficient estimate	p
Gender (female)	3.404 (1.630-7.108)	0.001	-0.076	0.406
PS	2.114 (1.349-3.313)	0.001	-0.156	0.162
Stage IV	2.047(1.128-3.751)	0.018	**-0.193**	**0.033**
Liver metastases	2.672(1.048-6.809)	0.040	-0.500	0.643
Progression	4.488(2.168-9.292)	<0.001	**-0.238**	**0.047**
Stability	0.272(0.097-0.760)	0.013	0.077	0.514
Global QoL score (QLQ-C30)	0.984(0.973-0.995)	0.005	**0.336**	**0.005**
Physical functioning	0.984(0.974-0.994)	0.001	-0.082	0.627
Role functioning	0.984(0.976-0.992)	<0.001	0.012	0.935
Fatigue	1.017(1.008-1.026)	<0.001	0.029	0.873
Insomnia	1.015(1.005-1.024)	0.003	-0.019	0.868
Appetite loss	1.012(1.004-1.020)	0.002	-0.024	0.855

DISCUSSION

The present study aimed mainly at investigating the prognostic value of QoL assessment among Tunisian lung cancer patients for survival. Median overall survival (OS) and progression free survival for patients with CSD in QoL were significantly lower. The following parameters were significant predictors for OS among univariable analysis: gender, tumor stage, liver metastases, PS, palliative chemotherapy, tumor response, socioeconomic status, global QoL score, physical functioning, role functioning, emotional functioning, fatigue, insomnia and appetite loss (QLQ-C30), pain in arm or shoulder (QLQ-LC13) and mobility, usual activities, pain/discomfort, anxiety/depression, health state (EQ-5D-3L). Upon final analysis, Global QoL score (QLQ-C30) was a significant predictor of OS, along with stage IV and progression.

A CSD was defined as an overall QoL score (according to QLQ-C30) inferior or equal to 50. This cutoff was chosen in collinearity with the study of Sloan et al. [16] which used overall QoL according to Lung Cancer Symptom Scale. Given that in both questionnaires, overall QoL was a continuous variable, taking integer values from 0 to 100. A score below 50 was indicative of a need for immediate exploration and intervention for the QoL deficit. This cutoff has been validated independently by previous studies. This was different from other studies which interpreted results according to QLQ-C30 reference values. This may be explained by the fact that they were mainly descriptive while the primary aim of the present study was to analyze the impact of QoL on survival [17].

The major findings of the present paper were in line with several studies. This included Kaplan Meier curves for overall survival [15,16, 18] and QoL score as a significant predictor of survival.

Fiteni et al. demonstrated that Global health GH status dimension score at baseline was associated with favorable OS even when adjusted for clinical, functional and histological factors (HR:0.986, 95% CI:0.980-0.992) [18].

According to Efficace et al, a 10-point shift worse in the scale measuring pain and dysphagia translated into an 11% and 12% increase in the likelihood of death respectively [15]. Montazeri et al reported that pre-diagnosis global QoL was the most significant predictor of the length of survival even after adjusting for known prognostic factors (age, p<0.04; extent of disease, p<0.03; global QoL, p<0.02) [10]. According to Braun et al, global QoL as well as physical function, gender, stage of disease and prior treatment history were significant prognostic factors [19].

The present study had four major strengths: First, it was a prospective cohort study with a prognostic aim. Second, the questionnaires were most frequently used in oncology. Third, analysis methods were in line with the literature. Fourth, description of patients' characteristics was also comparative between the two groups based on presence of a clinically meaningful deficit. This was in line with the study of Sloan et al [16]. It ensured first a better description of patients with altered QoL and second an analysis of clinical and demographic factors associated with altered QoL.

The major limitation was results comparison between the questionnaires used as they were differently calculated. Robert wood et al , for instance, showed that patients reported lower EQ-5D-3L utility index, EQ-VAS and QLQ-C30 global health status and greater work and activity impairment with worsening ECOG-PS (all p < 0.05) [20]. However, it was difficult to interpret the exact linearity between QLQ-C30 results and EQ-5D-3L as scores were differently calculated. Therefore, more studies comparing HR-QL questionnaires must be developed [21].

Developing palliative care centers must be considered as a primary aim. Action plans must include facilitating access to health care, early diagnosis strategies, smoking cessation program and developing therapeutic modalities (implementation of targeted therapy). The lack of radiotherapy centers is, for instance, a major public health concern in Tunisia. Specific measures must be applied to patients with a CSD in QoL: cancer rehabilitation, management of psychological problems, motivating social support, alleviating symptoms (Box 1)…Research in this field is in progress. Several studies have confirmed that increased physical activity may improve cluster symptoms and fatigue in patients with LC even without a precise schema for the application of this technique [22-24]. Carnio et al recommended developing a customized screening and treatment for cancer-related fatigue in patients with LC [22]. Further research in this field is needed.

Conclusion : The present study showed that Median OS and PFS for patients who had a significant deficit in QoL were significantly lower than for those who didn't. In the final analysis, Global QoL score (according to QLQ-C30), stage IV and tumor progression were significant predictors of OS. This should recommend considering an early QoL evaluation as a priority and implementing an active intervention for patients with a significant deficit in QoL in early palliative care.

What is already know on this topic

- Regardless of the unceasing efforts made to optimize multimodality treatment among LC patients, the impact on survival remains typically limited.

- QoL in patients with LC is lower than in healthy population and in several other malignancies.

Box1: Key messages, what this study adds

- Survival among Tunisian LC patients who had a deficit in QoL was significantly lower than for those who didn't.

- Global QoL score, stage IV and tumor progression were significant predictors of OS. Global QoL score (according to QLQ-C30) had a higher impact on OS than other factors.

- Early QoL evaluation is crucial. Specific palliative care for patients with a significant deficit in QoL must include cancer rehabilitation, management of psychological problems, motivating social support, alleviating symptoms.

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