Artigo de Revisão

Brief fatigue inventory as a fatigue identification scale in lung cancer patients under immunotherapy – A real-life study

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ABSTRACT

Introduction: Lung cancer (LC) is one of the most frequent oncological diseases in the world, and the use of immunotherapy is a substantial progress regarding new therapeutic options. Fatigue is the most frequently reported adverse effect in patients starting immunotherapy treatment, but it remains underdiagnosed. The purpose of this study was to identify whether the assessment of fatigue, recorded by the clinical team in the pulmonology consultation, agrees with that reported by patients with Non-Small Cell Lung Cancer (NSCLC), when answering the *Brief Fatigue Inventory* (BFI) questionnaire during treatment with immunotherapy alone or in combination with chemotherapy.
Methods: A prospective observational study was conducted over 8 months. The research took place through the collection of medical records from the clinical files of the patients and the application of the BFI questionnaire, before each of 4 treatment cycles. **Results:** The sample consisted of 31 patients with 26 males and 5 females, with a mean age of 68.5 years. The mean value of the BFI score before the 1st treatment, as well as in the following 3 evaluations, was higher for the participants who presented symptoms of asthenia/tiredness/fatigue recorded in the clinical files at the consultation and lower for those who did not. However, the differences were not statistically significant (pre 1st treatment- *p=0.299,* pre 2nd treatment- *p=0.125,* pre 3rd treatment- *p=0.103* and pre 4th treatment- *p=0.954).* By comparing the BFI questionnaire score with the medical records, we found that fatigue remained underreported in the consultation at the different evaluation moments (75.9% of the sample participants were not identified with fatigue at the 1st moment of evaluation; 75% at the pre-2nd treatment consultation; 81.2% at the pre-3rd treatment consultation and 88.9% at the pre-4th treatment consultation).
Conclusions: The benefit of applying the BFI questionnaire was relevant. This tool allowed the identification and stratification of fatigue, demonstrating greater sensitivity when compared only with the medical records of the consultation. The fact that the study sample was small was a limitation and made it difficult to obtain more robust results. Therefore, it is desirable to carry out more prospective, long-term studies in this area, to consolidate the results found in the present investigation.

Key words: non-small cell lung cancer; immunotherapy; adverse effects; fatigue; medical records; *brief fatigue inventory*

INTRODUCTION

LC is currently considered one of the most frequent oncological diseases in the world, diagnosed mainly after 65 years, with a median age close to 70 years. This cancer, composed of a considerable histological and molecular diversity, is divided into two main groups, Non-Small Cell Lung Cancer (NSCLC), constituting approximately 85% of cases and Small Cell Lung Cancer (SCLC) with a representativeness of about 15%[1]

The treatment of PC has undergone remarkable progress in recent decades, regarding the development of new therapies aimed at this pathology.[2] In patients with stage IV NSCLC, the therapeutic option is based on systemic therapy, equated according to the histological result, tumor genetics, expression of Programmed Cell Death Ligand 1 (PD L1), comorbidities, age, and patient preference.[3]

Immunotherapy has a prominent place as therapeutic option in patients with LC. Nevertheless, this treatment may develop adverse effects of which fatigue stands out.[4] This symptom, which has an extremely significant impact on patients' quality of life, is often undervalued and underdiagnosed despite being one of the most prevalent adverse effects related to LC and its treatment.[5] The use of symptom auto assessment instruments is extremely important to systematize and standardize procedures, to clarify the communication between the health professional and the patient, promoting an improvement in the quality of health care.[6] The fatigue assessment scale, BFI, is an instrument for assessing this symptom that presents a high reliability and internal consistency, consisting of 9 questions on a scale from 0 to 10. It assesses the severity of fatigue and its effects on patients' ability to perform their activities of daily living in the last 24 hours. It is a short questionnaire and assesses fatigue in a one-dimensional way. The overall score can be obtained through the average of all responses to the questionnaire, ranging from 0 to 10. Thus, absent fatigue is considered if the score is 0, mild fatigue between 1-3.99, moderate between 4-6.99 and severe 7-10. [7,8]

The purpose of this study is to evaluate whether fatigue is properly identified by clinicians in LC consultations, comparing the fatigue reported by patients by filling out the BFI questionnaire periodically, with the evaluation made by the physician in the consultation, through the records in the clinical files of the patients, during the period of treatment with immunotherapy.

METHODS

Study population

An observational study with a prospective design was conducted between March 4, 2022, and November 30, 2022. The study participants were selected in the multidisciplinary consultation of thoracic tumors of the Department of Pulmonology of the Portuguese Institute of Oncology of Lisbon, Francisco Gentil (IPO). All patients with NSCLC stage II or IV proposed for treatment with immunotherapy in monotherapy in 1st or 2nd line or treatment of 1st line in combined regimen with chemotherapy were included.

Al patients that were invited to participate signed an informed consentient. Study was approved by the local ethical board.

Methodology of data collection

Sociodemographic data, characterization of the disease, comorbidities and factors associated with fatigue and analytical results were collected through consultations of the participants' clinical processes. Patients completed the BFI questionnaires.

Statistical analysis

Descriptive statistics were used to describe the characteristics of the study population. The variables measured in Likert scale were analyzed through the categories presented with description of some relevant statistics such as the mean, the standard deviation, the coefficient of variation and the minimum and maximum values observed. To evaluate the relationship of two qualitative variables, Fisher's test and Student's t parametric test were used *to* study quantitative variables and a dichotomous variable. To study the relationship between quantitative variables and a qualitative variable, the ANOVA parametric test was used and the degree of correlation between two quantitative variables was measured using Pearson's correction coefficient. Finally, the t-test for paired samples was used to evaluate the differences in a variable measured at two moments for the same elements of the sample. Statistical analysis and graphical representations were performed using IBM® SPSS® Statistics software version 27, considering a 95% confidence interval.

RESULTS

The sample consisted of 31 patients, 26 males (84%) and 5 females (16%). The mean age was 68.5 years with a standard deviation of 8.7 years. Regarding smoking habits, 7% were non-smokers, 30% smokers and 63.3% former smokers. In this study, 13 patients received pembrolizumab therapy, 5 patients received nivolumab therapy and 13 patients received IQT therapy. Regarding treatment lines, 83.9% were 1st line of treatment and 16.1% the 2nd line of treatment. Regarding number of treatments, 6 underwent only 1 treatment cycle (interruption due to disease progression), 2 patients underwent 3 treatment cycles, 1 patient underwent 2 cycles and 2 patients underwent 3 treatment cycles. A total of 20 patients underwent the 4 proposed treatment cycles. The mean value of the BFI score before the 1st treatment, as well as in the following 3 evaluations, was higher for the participants who presented symptoms of asthenia/tiredness/fatigue recorded in the clinical files at the consultation and lower for those who did not. However, the differences were not statistically significant (pre 1st *treatment- p=0.299- table 1, pre 2nd treatment- p=0.125, table 2, pre 3rd treatment- p=0.103- table 3 and pre 4th treatment-*

Table 1. Baseline assessment – Pre 1st treatment

	Asthenia/Tiredness/Fatigue				t	p
	No (N=29)		Yes (N=2)			
	M	SD	M	SD		
BFI baseline score	3,23	2,93	5,50	2,91	-1,058	0,299

Table 2. Pre 2nd treatment evaluation

	Asthenia/Tiredness/Fatigue				t	p
	No (N=20)		Yes (N=5)			
	M	SD	M	SD		
BFI pre 2nd treatment score	3,00	2,14	4,71	2,20	-1,591	0,125

Table 3. Pre 3nd treatment evaluation

	Asthenia/Tiredness/Fatigue				t	p
	No (N=16)		Yes (N=8)			
	M	SD	M	SD		
BFI pre 3rd treatment score	3,82	2,56	5,76	2,82	-1,699	0,103

Table 4. Pre 4nd treatment evaluation

	Asthenia/Tiredness/Fatigue				t	p
	No (N=9)		Yes (N=11)			
	M	SD	M	SD		
Yes (N=11)	5,88	2,63	6,00	3,14	-0,059	0,954

p=0.954- table 4). By comparing the BFI questionnaire score with the medical records, it was found that fatigue remained underreported in the consultation at the different evaluation moments (75.9% of the sample participants were not identified with fatigue at the 1st moment of evaluation; 75% at the pre-2nd treatment consultation; 81.2% at the pre-3rd treatment consultation and 88.9% at the pre-4th treatment consultation).

DISCUSSION

The purpose of this study was to optimize the monitoring of fatigue caused by immunotherapy, reported by the patient, to contribute to the improvement in the quality of life of cancer patients. As for the main objective, the assessment of fatigue identified by the physician in the consultation compared with the evaluation of each BFI questionnaire, deserves an individualized interpretation in the different treatment cycles. Regarding this correspondence, *the p* values in the statistical tests used differed, but it was not possible to obtain statistically significant results. Regarding the survey used, it is important to note that this proved to be an instrument capable of identifying different stages of fatigue, and it is particularly important to highlight the easy access in its completion.

Thus, it is possible to admit that the selected scale was adequate as an instrument to measure fatigue in this sample. Analyzing the 4 moments of pre-treatment evaluation, it was possible to verify that fatigue always remained underreported by the doctor in the consultation in a percentage greater than or equal to 75%. Thus, a congruent evolution of the mean BFI *score* was identified in relation to the evidence in terms of the expected time for the development of fatigue during the treatment cycles of patients with NSCLC, reaching a higher mean value in the pre-4th treatment evaluation, which corresponds approximately to the 12th week after the beginning of the therapeutic cycles with IO or IQT. The results also suggest that this tool is sensitive in the identification of fatigue not reported in the consultation, as well as in the stratification of different degrees of severity, namely in moderate and severe cases. The main limitations of this study were the small sample size, 31 patients. Some of the participants died before the end of the study, which contributed to the increased complexity of the statistical analysis of the results.

In conclusion, fatigue is a multifactorial symptom that should be carefully monitored to improve the patient's quality of life and consequently maintain compliance with NSCLC treatment.

With regard to future research, it is desirable to conduct a greater number of long-term prospective studies to assess fatigue, preferably with different fatigue measurement instruments, with a larger number of participants, in order to consolidate the results found in this research.

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