Reliability of the Brazilian version of the Functional Assessment of Cancer Therapy-Lung (FACT-L) and the FACT-Lung Symptom Index (FLSI)

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OBJECTIVES: The purpose of this study was to assess the reliability of the Brazilian version of the Functional Assessment of Cancer Therapy-Lung (FACT-L) with the FACT-Lung Symptom Index (FLSI) questionnaire.

INTRODUCTION: The assessment of quality of life in patients with lung cancer has become an important evaluative endpoint in current clinical trials. For lung cancer patients, one of the most common quality of life tools available is the FACT-L. Despite the amount of data available regarding this questionnaire, there are no data on its performance in Brazilian lung cancer patients.

METHODS: The FACT-L with the FLSI questionnaire was prospectively administered to 30 consecutive, stable, lung cancer outpatients at baseline and at 2 weeks.

RESULTS: The intraclass correlation coefficient between test and retest for the FACT-L ranged from 0.79 to 0.96 and for the FLSI was 0.87. There was no correlation between these questionnaire dimensions and clinical or functional parameters.

CONCLUSIONS: The Brazilian version of the FACT-L with FLSI questionnaire is reliable and is quick and simple to apply. This instrument can now be used to properly evaluate the quality of life of Brazilian lung cancer patients.

KEYWORDS: Quality of life; Lung cancer; Questionnaires; Reproducibility of results; Validation studies.

INTRODUCTION

Lung cancer has become a disease of great global impact and remains the leading cause of death from cancer in the world.1 As smoking and environmental pollution cannot be controlled in the short term, the incidence of lung cancer continues to increase, especially in females.2,3 In Brazil, the estimate for 2010 is approximately 18 new cases per 100 000 men and 10 per 100 000 women, corresponding to 17 800 and 9 930 new cases of lung cancer among men and women respectively.4

Advances in lung cancer therapy have been improving survival rates, although the prognosis remains poor. The 5-year survival rate is around 15% in developed countries1 and 10% in Brazil.4 Therefore, the impact of both disease and treatment on the health and psychosocial functioning of these patients should be considered.5 In this context, quality of life assessment and the analysis of the main symptoms that lead to functional capacity limitation have become issues of utmost importance in the evaluation of lung cancer patients. However, in Brazil, there are few studies that evaluate this aspect of the disease, mainly because of the lack of specific tools adapted to and reproducible for the Brazilian Portuguese language.

Several instruments are currently used to evaluate the quality of life in patients with lung cancer. The Functional Assessment of Cancer Therapy-Lung (FACT-L) was generated by the Functional Assessment of Chronic Illness Therapy (FACIT) group. It is a specific, multidimensional questionnaire widely used in clinical studies.6-9 Moreover, the FACT-Lung Symptom Index (FLSI), which is a brief measure involving five common symptoms in lung cancer patients, can be applied in combination with the FACT-L or alone. Although the FACT-L is currently used in Brazil, mainly in international multicenter trials, there is no study assessing the reliability of this questionnaire in the Brazilian Portuguese language. Therefore, the purpose of this study was to evaluate the reproducibility of the FACT-L and the FLSI for Brazilian lung cancer patients.

METHODS

A convenience sample comprising 30 patients with lung cancer was recruited from the outpatient lung cancer clinic.
of the São Paulo Hospital - Federal University of São Paulo. This study was approved by the Institutional Review Board of our center, and a Term of Informed Consent was signed by all patients.

The following inclusion criteria were used: histologically proven lung cancer; 18 years of age or older; a minimum score of 21 on the Mini Mental State Examination (MMSE),\textsuperscript{10,11} out of chemotherapy/radiotherapy treatment; and clinical stability during the study and at least 10 days before the beginning of the evaluations. Clinical stability was defined as the absence of change in cough, sputum, and dyspnea, assessed by a structured form filled out during outpatient follow-up, and no hospitalizations or modifications in the therapeutic regimen. An exclusion criterion was the refusal to answer any questionnaire.

The sample size was based on previous reliability studies of other quality of life questionnaires related to respiratory diseases in Brazil.\textsuperscript{12–15} Clinical evaluation and physical examination were performed by a team of physicians, based on a structured form. All patients met the stability criteria. The drug regimen used by the patients remained unchanged during the 15-day interval between questionnaire applications.

In the first visit, the following independent variables were collected: gender (male and female proportion), age (in years), history of tobacco use (yes or no) and consumption (pack–years), histologic subtypes (adenocarcinoma, squamous cell, small cell lung cancer and others),\textsuperscript{16} staging according to the 1997 TNM classification for non-small cell lung cancer (NSCLC) patients (stratified from IA to IIIA and from IIIB to IV),\textsuperscript{17} Karnofsky Performance Status (KPS),\textsuperscript{18} spirometry (forced expiratory volume in the first second (FEV\textsubscript{1}) and forced vital capacity (FVC) percentage of predicted and FEV\textsubscript{1}/FVC percentage),\textsuperscript{19} MMSE, and FACT-L and FLSI scores.\textsuperscript{5}

The Portuguese version of the FACT-L and FLSI was released for use by the FACIT group (the developer of the questionnaire). The translation into Brazilian Portuguese, back translation and review by an expert committee to access the semantic, conceptual, idiomatic, cultural and metabolic equivalences were previously done by that group.\textsuperscript{20,21}

The FACT-L, version 4, is a combination of the 27-item FACT-General (FACT-G) and the 9-item Lung Cancer Subscale (LCS).

A total FACT-G score is calculated by summing the physical well-being (PWB), social/family well-being (SWB), emotional well-being (EWB), and functional well-being (FWB) subscale scores, with a score ranging from 0 to 108. A total FACT-L score is obtained by summing the FACT-G score with the LCS (two of the nine items are not scored). The FACT-L score ranges from 0 to 136.\textsuperscript{6}

The FACT-L Trial Outcome Index (FACT-L TOI) is, a priori, an index that sums the PWB, FWB, and LCS into a 21-item scale. Its score ranges from 0 to 84.\textsuperscript{8}

The FLSI is a symptom index with six questions regarding the five most frequent symptoms reported by lung cancer patients, especially in the advanced stages: dyspnea, fatigue, pain, weight loss, and coughing. Its score ranges from 0 to 24.

Higher scores generated by the FACT-L and FLSI correspond to better quality of life.

The score on each aspect of the FACT-L and FLSI is obtained according to the option chosen by the patient. The available options were: ‘not at all’, ‘a little bit’, ‘some-what’, ‘quite a bit’, or ‘very much’. The higher the score obtained by each patient in question, the greater the final score of the subscale and the better the quality of life. However, these scores have a non-linear behavior.

Patients answered the questionnaire after being read each question, all by the same interviewer. The process took place in a calm environment with no interruptions allowed. The questionnaires were reviewed at the end of the interview to avoid any missed questions. The response time was timed in the two visits.

All doubts expressed by patients during the questionnaire were documented. Patients were also asked not only about what they felt in terms of question content, but also about the length of the questionnaire.

The test–retest design was adopted for the reliability study. The questionnaire was administered by the same researcher twice with a 15-day interval.

The scores obtained on different scales and subscales of FACT-G were compared with reference values established by the FACTIT group.\textsuperscript{22} For this comparison, we used the minimal clinically significant difference, determined by the same group.\textsuperscript{5}

**Statistical analysis**

Variables were expressed as mean and standard deviation. The intraclass correlation coefficient (ICC) and Kappa reliability coefficient were calculated to assess the reliability of the questionnaire and questions respectively. To compare the two groups, we used the chi-square test for categorical variables, t test for parametric continuous variables, and Mann–Whitney test for nonparametric continuous variables. For the correlations between spirometry and questionnaire scores, the Spearman’s correlation coefficient was used. Statistical analysis was performed with SPSS\textsuperscript{®} software version 13.0. All tests were two-tailed, and the level of significance was 5%.

**RESULTS**

The main characteristics of the 30 patients who completed the study are shown in Table 1. Some 63.3% of the patients were over 60 years of age.

There was no statistically significant difference between genders regarding age, KPS, spirometry, staging, and histological type. Among patients who never smoked, only one had a history of passive smoking. There was a prevalence of smoking habits in males ($p = 0.04$), with a higher tobacco smoke load for men than for women, consuming a mean of 53.2 pack–years (SD = 31.6) and 29.6 pack–years (SD = 25.5) respectively ($p = 0.02$).

Eight patients (26.7%) were diagnosed with chronic obstructive pulmonary disease (COPD), according to the GOLD guideline.\textsuperscript{23}

The mean values for each scale of the FACT-L and FLSI are illustrated in Table 2. The intraclass correlation coefficient values for the different scales of the FACT-L and FLSI showed excellent correlations (Table 2).

The kappa coefficient was used to test question reliability, which was less than 0.4 on questions GP1, GP5 (PWB), GS3, GS4, GS5 (SWB), GF1, GF2, GF3, GF5, GF6 (FWB), and LCL4 (LCS). The remaining questions had a moderate agreement. As for the FLSI, the kappa coefficient was moderate on
Table 1 - Subject characteristics of 30 lung cancer patients.

| Variables                  | Values                  |
|----------------------------|-------------------------|
| Age (years) mean ± SD      | 62.0 ± 10.4             |
| Male n (%)                 | 23 (73.7)               |
| Smoking history            |                         |
| Former smokers n (%)       | 27 (90)                 |
| Never smokers n (%)        | 3 (10)                  |
| Pack-year mean ± SD        | 52.5 ± 33.4             |
| Spirometry mean ± DP       |                        |
| FEV1 % prev                | 75.0 ± 19.1             |
| FVC % prev                 | 86.7 ± 13.1             |
| FEV1 / FVC %               | 71.9 ± 12.2             |
| Histological types n (%)   |                        |
| Adenocarcinoma             | 14 (46.7)               |
| Squamous cells             | 9 (30)                  |
| SCLC                       | 2 (6.7)                 |
| Others                     | 5 (16.7)                |
| KPS mean ± SD              | 93.2 ± 9.9              |
| Staging status n (%)       |                        |
| I and II                   | 14 (46.7)               |
| III                        | 13 (43.3)               |
| IV                         | 3 (10)                  |
| Mini Mental mean ± SD      | 27.9 ± 1.9              |

SD, standard deviation; FEV1, forced expiratory volume in the first second; FVC, forced vital capacity; SCLC, small cell lung cancer; KPS, Karnofsky Performance Status.

Table 2 - Mean for the two visits (15-day interval) and intraclass correlation coefficient (ICC) for FACT-L scales and FLSI.

| Scales                      | 1st visit | 2nd visit | ICC    |
|-----------------------------|-----------|-----------|--------|
| Physical well-being         | 22.9      | 22.7      | 0.90   |
| Social/family well-being    | 19.5      | 18.6      | 0.78   |
| Emotional well-being        | 18.4      | 19.0      | 0.92   |
| Functional well-being       | 18.1      | 17.0      | 0.89   |
| FACT-G                      | 78.9      | 76.3      | 0.93   |
| LCS                         | 20.0      | 19.8      | 0.94   |
| FACT-L                      | 98.9      | 97.1      | 0.95   |
| FACT-L TOI                  | 61.0      | 59.6      | 0.96   |
| FLSI                        | 19.0      | 18.1      | 0.87   |

FACT-G, Functional Assessment of Cancer Therapy-General; LCS, Lung Cancer Scale; FACT-L, Functional Assessment of Cancer Therapy-Lung; FACT-L TOI, Functional Assessment of Cancer Therapy-Lung Trial Outcome Index; FLSI, Functional Assessment of Cancer Therapy-Lung Symptom Index.

There was no correlation between spirometry and any of the questionnaire scales.

Table 3 - Mean values for the FACT-L scales in different reliability and validity trials with cancer patients.

| Source                        | PWB | S/FWB | EWB  | FWB  | FACT-G | LCS   | FACT-L | FACT-L TOI |
|-------------------------------|-----|-------|------|------|--------|-------|--------|------------|
| Current study                 | 21.7| 19.8  | 18.4 | 16.6 | 76.5   | 19.3  | 95.8   | 57.6       |
| Brucker et al 2005            | 21.3| 22.1  | 18.7 | 18.9 | 80.9   | –     | –      | –          |
| Browning et al 2009           | 16.5| 20.4  | 14.2 | 13.8 | –      | 16.2  | 81.1   | 46.3       |
| Wan et al 2007                | 18.3| 18.2  | 16.3 | 12.2 | 65.9   | 16.7  | 82.9   | 47.2       |
| Saitoh et al 2007             | –   | –     | –    | –    | –      | 17.8  | –      | –          |
| Yoo et al 2006                | 20.7| 23.2  | 15.5 | 17.4 | 84.1   | 20.5  | –      | 59.0       |
| Cella et al 2003              | 20.2| 22.7  | 16.4 | 16.1 | 73.7   | 18.9  | 94.6   | 33.4       |
| Dapueto et al 2003            | 15.7| 18.6  | 13.5 | 16.0 | 63.7   | –     | –      | –          |
| Cella et al 1995              | 20.7| 23.2  | 15.5 | 17.4 | 84.1   | 20.3  | –      | 59.0       |

PWB, physical well-being; S/FWB, social/family well-being; EWB, emotional well-being; FWB, functional well-being; FACT-G, Functional Assessment of Cancer Therapy-General; LCS, Lung Cancer Scale; FACT-L, Functional Assessment of Cancer Therapy-Lung; FACT-L TOI, Functional Assessment of Cancer Therapy-Lung Trial Outcome Index.

Table 4 - Response time of the FACT-L and FLSI and p value of the comparison between the two visits (Student’s t test).

|                  | Mean | Median | SD  | Range | p    |
|------------------|------|--------|-----|-------|------|
| 1st FACT-L + FLSI| 9.6  | 8      | 3.8 | 5–20  | 0.001|
| 2nd FACT-L + FLSI| 9.0  | 9      | 2.9 | 4–15  |      |

FACT-G, Functional Assessment of Cancer Therapy-Lung; FLSI, Functional Assessment of Cancer Therapy-Lung Symptom Index.

The mean score of the FACT-G scales was similar to the reference values for all scales that have these values established.22 Table 3 shows the mean values for the scales of FACT-G and FACT-L described in several studies of reliability and cultural adaptation into other languages.

The time spent by patients in answering the questionnaire was measured at both visits (Table 4). The response time on the second application was significantly lower (p = 0.001).

DISCUSSION

The focus of this study was to analyze the reliability of the FACT-L and the FLSI, a specific instrument for assessing the quality of life of lung cancer patients in the Brazilian population. It was observed that the Brazilian version shows excellent reliability for this population.

The FACT-L is an instrument that has been widely used in phase I, II, and III clinical trials. It has been translated and adapted into several languages and cultures.2,3,7,22–27 A feature of this instrument is the nonlinearity of the scores of its scales, a factor that complicates the interpretation of isolated study data. To facilitate the explanation of the results, the authors of the general questionnaire (FACT-G) have developed normative values from two reference groups, one from normal adults and another from adults with cancer in general.22 However, these normative values are only for the general questionnaire (FACT-G) and its scales. When comparing the results obtained in our study with the reference values, we observe that the score was similar in all scales and for the total value. A possible explanation for the fact that our patients have quality of life similar to patients with other cancer types is that, in the study for the establishment of benchmarks, besides including patients with various types of cancer, such as breast cancer, colon and rectum cancer, and cancer of the head and neck, they also included patients with lung cancer. Furthermore, 76.7% of the sample comprised patients treated and in remission from the underlying disease and,
therefore, with better quality of life. When our FACT-L results are compared with those from other studies using the same questionnaire, we find that there is great variability between countries and different cultures, which may be due to differing perceptions of the questions according to each culture and also differences in patient characteristics, such as staging, age, socioeconomic status, among others.

The FLSI is an index designed to identify the presence of the major symptoms related to lung cancer, including dyspnea, pain, fatigue, cough, and weight loss. These symptoms can negatively influence quality of life. In this study, in addition to the medical evaluation, FLSI was also used to assess the patient’s clinical stability.

The reliability for all scores of the FACT-L showed ICC values greater than 0.75, ranging from 0.78 (SWB) to 0.96 (FACT-L TOI). These values show excellent reliability and are similar to those found in other studies. In the validation study of the Korean version of the FACT-L, the ICC ranged from 0.52 to 0.84. The Chinese version varied from 0.76 to 0.82. In the reliability study of the original version, the ICC ranged from 0.56 (SWB) to 0.89 (FACT-L TOI). The FLSI also showed high reliability, which confirms the stability of the sample. Most of the FACT-L questions showed adequate reliability, analyzed by the kappa coefficient.

In this study, the reliability analyses were conducted with a convenience sample similar to other studies evaluating the reliability and cultural adaptation of other questionnaires to the Portuguese language. In our sample, males predominated, in agreement with the worldwide prevalence of lung cancer. The mean age was 61.3 years, which is consistent with most studies that include patients with lung cancer. Regarding histological type, adenocarcinoma was the most prevalent, consistent with several epidemiological studies in developed countries. Unfortunately, regarding staging, there was a predominance of stage III and IV, stages with less chance of survival after treatment. The mean FEV$_1$ (% predicted) and FEV$_1$/FVC ratio in our study were similar to the results reported by Young et al., who observed a FEV$_1$ (% predicted) mean of 73% and FEV$_1$/FVC mean of 64% in smokers with lung cancer. In our study, there was no correlation between the questionnaire and the analyzed lung function parameters, consistent with other studies that found no significant correlation when investigating the effects of altered pulmonary function on the quality of life of cancer patients.

The process of translating the FACT-L questionnaire and FLSI into the Portuguese language (Brazil) was performed by the FACIT group. Only a few doubts were reported by the patients, which warrants its use in the current form. Few patients had difficulty in interpreting the word “muitíssimo”; however, many of the patients interviewed understood the meaning of the term not because it is a familiar word, but because they realized that it was a scale with a progressive score in which the numerical value assigned to the word “muitíssimo” yielded the highest score. The suggested changes were sent to the FACIT group. Alterations to this tool were proposed only for question Q1 “Independentemente do seu nível a(dunder e a)atividade sexual, favor de responder à pergunta a seguir. Se preferir não responder, assine o quadriculo [x] e passe para a próxima seção”. Despite not raising doubts, the words “atual” and “atividade” do not require the letter “(c)”, and there is no need to use the preposition “de” after the word “favor”, both grammatical constructions used in the Portuguese language in previous studies.

We conclude that the Brazilian version of the FACT-L questionnaire and FLSI is reproducible, fast, and of simple application, and that they are capable of measuring the quality of life in lung cancer patients in Brazil.

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