EVALUATION OF QUALITY OF LIFE IN LUNG CANCER PATIENTS

Vera Lucia MANNARINO[1]
Gisele Cazale BONIOLI[1]
Emilia Matos do NASCIMENTO[2]
Basilio de Bragança PEREIRA[1]
Fernanda Carvalho de Queiroz MELLO[1]
Marcos Eduardo Machado PASCHOAL[1]

▪ ABSTRACT: There is a growing need to improve end-of-life care in cancer patients and to evaluate it through questionnaires is an important tool to assess its results. The aim of this study was to evaluate the effect of the palliative care in the quality of life, distressing symptoms and functional capacity of patients with primary lung cancer with locally advanced disease and metastatic disease in a university hospital. Thirty patients with lung cancer, previously treated with curative intention and submitted to a palliative treatment, were enrolled for this study. They were divided into three groups. The first group had 10 patients, who lived between 30 and 59 days after admittance, the second, 10 patients who lived between 60 and 89 days and the third, 10 patients who lived 90 days or more. Data collection regarding five stressing symptoms: anorexia, dyspnea, pain, fatigue, hemoptysis, and cough, was performed according to Lung Cancer Symptom Scale and Karnofsky Performance Status Scale. By observational inspection, "Appetite" and "Karnofsky Performance Status Scale", improved; "pain" worsened and "quality of life" improved after palliative care, according to the patients. Physical, psychological, spiritual and social factors influence the symptoms of patients with cancer in later life. Treatment by palliative care can provide comfort for these patients.

▪ *KEYWORDS:* Lung cancer; end-of-life care; quality of life; terminally ill patients; Karnofsky Performance Status Scale.

[1] Universidade Federal do Rio de Janeiro – UFRJ - Faculdade de Medicina; Hospital Universitário Clementino Fraga Filho - HUCFF/UFRJ, CEP: 21941-617, Rio de Janeiro, RJ, Brasil. Email: veramannarino@oi.com.br; giselecazale@oi.com.br; basilio@hucff.ufrj.br ; fcqmello@hucff.ufrj.br; mpaschoal@mac.com
[2] Centro Universitário Estadual da Zona Oeste – UEZO - Escola de Engenharia. CEP: 23070-200, Rio de Janeiro, RJ, Brasil. Email: emiliamatos@yahoo.com

1. Introduction

Lung cancer is the leading cause of cancer death worldwide, with approximately 17% of the total new cancer cases and 23% of the total cancer deaths (JEMAL *et al.*, 2011). Lung cancer also leads cancer deaths in the United States and is the second most common cause of cancer in that country (JEMAL *et al.*, 2010). The number of new cases of lung cancer for Brazil for each year of the 2020-2022 period is estimated to be 17,760 for men and 12,440 for women. These values correspond to an estimated risk of 16.99 new cases for every 100 thousand men and 11.56 for every 100 thousand women. (INCA, 2019).

In most cases, the diagnosis is made in a moment of locally advanced or metastatic disease. At this stage, patients have symptoms related to the tumor (primary symptoms), or related to metastases or paraneoplastic syndromes (secondary symptoms) (KNORST *et al.*, 2003).

When patients are at an advanced stage, it is important that they receive treatment of palliative care to relieve the distressing symptoms and improve quality of life. The World Health Organization considers palliative care (PC) as an approach that improves the quality of life of patients and their families, by prevention and relief of suffering, through early identification, careful assessment and treatment of pain and other physical, psychosocial and spiritual symptoms (JEMAL *et al.*, 2011). Critically ill patients who attend palliative care programs have great chance to have their symptoms relieved (KOVÁCS, 2003).

Palliative care is the ideal option for these patients, although only few countries offer it as a routine standard option.

The aim of this study was to evaluate the influence of palliative care on distressing symptoms, functional capacity and quality of life of patients with primary non-small cell lung cancer, since patients with advanced cancer develop a large number of devastating physical and psychological symptoms, requiring CP, care and attention for their families.

2. Material and methods

It was a prospective study conducted at oncopneumology program. The patients were considered beyond therapeutic possibilities of cure, when admitted to this work. According to the criteria, 30 patients with anatomopathologic diagnosis of lung cancer were seen in the oncopneumology program. Those patients were staged according TNM system: III-B and IV, non-small cell lung cancer, previously submitted to oncologic treatment with curative intention.   They were divided into three groups. The first group was composed by ten patients who lived between 30 and 59 days after admittance, the second, by ten patients, who lived between 60 and 89 days and the third, by ten patients who lived 90 days or more. We used a protocol form for data collection of patients: age, gender, histological type and amount of cigarettes. Data collection was performed in the clinic consultation. The data have been individualized for each patient.

The lung cancer symptom scale (LCSS) is a reliable and valid disease- and site-specific quality of life (QOL) instrument. It consists of nine visual analogue scales (0–100mm) assessing QOL in the past 24 h (HOLLEN *et al.*, 1993). The 9-scale mean total represents the overall score, with a lower score corresponding to a better QOL. These

scales focus on physical and functional dimensions only, including six major symptoms of lung cancer: appetite, fatigue, cough, dyspnea, hemoptysis, and pain. The remaining three items include a self-rating of general lung cancer symptoms, how illness affects normal activities of daily living, and overall QOL (HOLLEN *et al.*, 1993).

LCSS questionnaire was applied by the main investigator. The KPS (KARNOFSKY and BURCHENAL, 1949) was performed by the main investigator, too. Patients were seen according their demands, sometimes weekly, but for this study only the monthly assessment (D0, D30, D60, and D90) was considered. The analysis was done on day zero (D0), before the palliative treatment, and at 30th day (D30), for patients in the three groups (total of 30 patients), at the 60th day (D60), for patients who lived 60 days or more (20 patients), and at 90th day (D90), for patients who lived 90 days or more (10 patients).

The statistical analysis was done using the Survival Agreement Plot proposed by Luiz *et al.* (2003), a non-conventional method, to assess the reliability of a quantitative measure. This method implements the Kaplan Meier curves without censored data where the failures occur at the absolute difference between the observer scores. An improved method proposed by Llorca and Delgado-Rodríguez (2005) was also used. This one considers two groups of real score differences instead of the global differences.

Both methods calculate the absolute difference of values regarding the two measures. In the Luiz method, the survival plot shows only if the opinions are similar (small differences) or not. On the other hand, the Llorca method divides the differences into two groups: the first (group A), where the doctor's score is higher, and the second (group B) where the patient's score is higher. These are non-conventional methods of survival curves where the x axis is related to the disagreement level of the observer and patient opinions; and the y axis indicates the probability of a disagreement level over a particular value.

For instance, if a doctor's score is higher, the difference will be in the group A. Otherwise the difference will be in the group B, where the patient score is higher. After evaluating all differences, two curves are plotted: one for group A and another for group B. Then, besides identifying whether the opinions are similar, one can check where the doctor's or the patient's scores are higher.

Graphic demonstration was done by use of box plot, where we utilized the results obtained by the observer and the subjects, divided into groups. The equality of the two survivor functions obtained through the Llorca and Delgado-Rodriguez (2005) method was obtained by using the Tarone-Ware test (TARONE and WARE, 1977), which is a non-parametric weighted rank test.

The star plot (CHAMBERS *et al.*, 1983) a graphical method used to examine multivariate data sets was also performed. It is a technique for analysis of multivariate data through star-shaped figures. Each variable is represented by a radius whose length is proportional to its size, and may take a value from 0 to 1 (a reference unit). The larger the radius, the more favorable the characteristic is.

This method assesses one or more variables in a single graphic. In addition, the first box was implemented to each variable to check the difference between the measure in the observer's and the patient's views. The R software (R CORE TEAM, 2020) was used to implement all the data analysis. Due to ethical considerations, there was no control group. This study was submitted to the Committee for Research Ethics of Hospital Universitário Clementino Fraga Filho, of the Universidade Federal do Rio de Janeiro, receiving assent.

3. Results

This work consisted of 13 men and 17 women. We obtained the following results as shown below. Figure 1 shows the box plots to assess the difference between the measurements, from view of the observer, considering the variables: "Appetite", "dyspnea", "pain", "fatigue", "hemoptysis", "cough" and "KPS". Through the test of difference of means it was possible to identify the variables that showed statistical significance. For all patients (n = 30), by comparison between D30 and D0, significance was found for the variable "hemoptysis" (p = 0.05), with improvement of this symptom. It is worth noting that the number of patients with this symptom was very small (10% of patients).

Relating to the difference in ratings between D30-D0 of patients who lived between 30 and 59 days (n = 10), we found significant difference for "appetite" (p = 0.06), with symptom improvement and also for the variable "Karnofsky" (p = 0.003), also with improvement. Considering the difference between D60-D0 evaluations of all patients who lived 60 days or more (n = 20), we found a statistically significant difference for the variable "hemoptysis" (p = 0.08), although not graphically identified. Regarding to the difference in ratings between D60-D0, of all patients who lived between 60 and 89 days (n = 10), it was observed that about 75% of patients improved with respect to "dyspnea" and more than 50% with respect to "appetite". Considering the difference in ratings between D90-D0, for patients who lived 90 days or more (n = 10), it was not found any statistical significance.
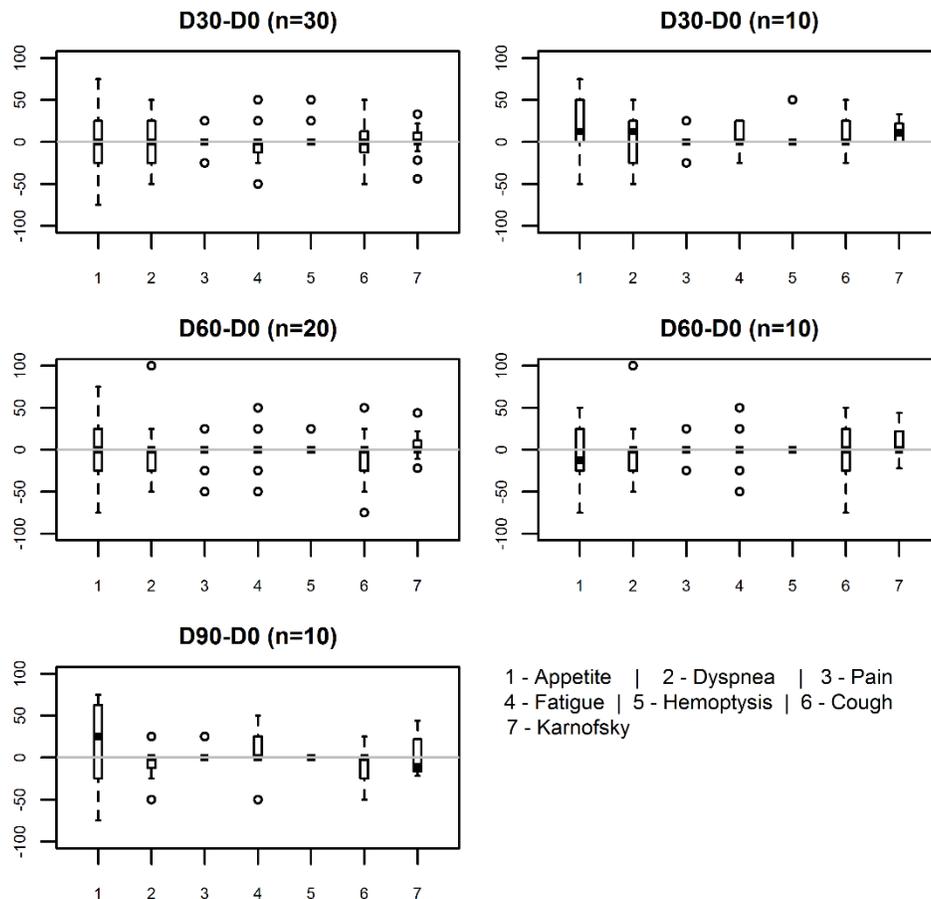
Figure 1 -Evolution of treatment according to the vision of the observer.

Figure 2 presents the box plots from view of patients, related to "appetite", "dyspnea", "pain", "fatigue", "hemoptysis", "cough", "severity of symptoms (G Symptoms)", "ability to accomplish tasks" (C Conduct) and "quality of life" (QOL), indicator of overall well-being.

Examining the difference between D30-D0 evaluations of all patients (n = 30), significance was found for the variable "pain" (p = 0.02), with worsening of this symptom, and for the variable "hemoptysis" (p = 0.04), with symptom improvement. In relation to the difference between D30-D0, from patients that lived between 30 and 59 days (n = 10), significance was found for the variable "pain" (p = 0.04), with worsening of the symptom, and of variable "quality of life" (value = 0.04), with improvement. The difference between D60-D0, for all patients that lived 60 days or more (n = 20), presented significance for the variable "hemoptysis" (p = 0.08), with symptom improvement. Relatively to the difference between D60-D0, for all patients that lived between 60 and 89

days (n = 10), significance was found for the variable "severity of symptoms" (p = 0.06), assuming a median positive value. Regarding the difference between D90-D0, for patients that lived more than 90 days (n = 10), no statistical significance was found.

1 - Appetite | 2 - Dyspnea | 3 - Pain
4 - Fatigue | 5 - Hemoptysis | 6 - Cough
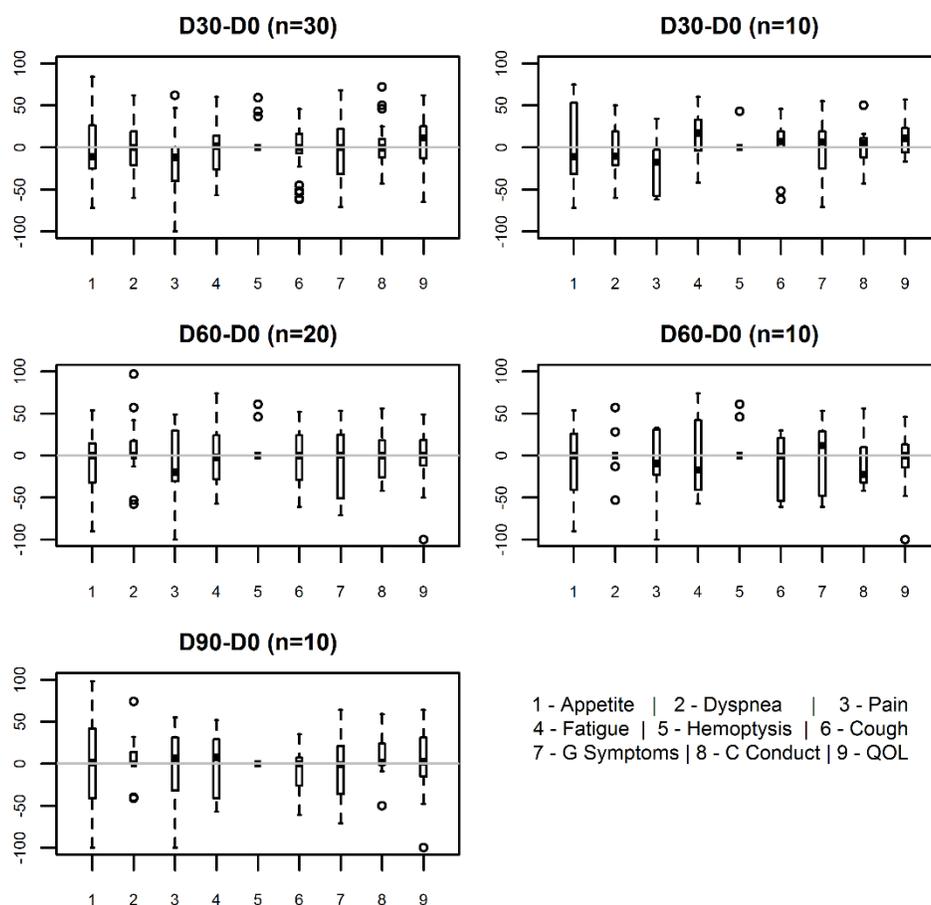7 - G Symptoms | 8 - C Conduct | 9 - QOL

Figure 2 -Evolution of treatment of the patient's vision.

The analysis of concordance between the physicians and patients' scores was assessed graphically using methods of Luiz *et al.* (2003) and Llorca and Delgado-Rodríguez (2005). Figure 3 shows the results of this analysis, which took into account the following variables: "appetite", "dyspnea", "pain", "fatigue" and "cough". The variable "hemoptysis" was excluded from the analysis, given the small number of patients with this manifestation. The Tarone-Ware test (TARONE and WARE, 1977) was used to evaluate equality of survival curves obtained by the method of Llorca and Delgado-Rodríguez (2005).

For the variable "appetite", there was no difference between the survival curves (p = 0.355), suggesting concordance between observer ratings and patient. There is also agreement among the opinions related to the variable "fatigue" (p = 0.796). However, the same was not observed for the variable "dyspnea", which showed a significant difference between assessments (p = 0.0124). Related to the variables "pain" and "cough", significant differences were also observed (p < 0.01) and (p < 0.01), respectively.
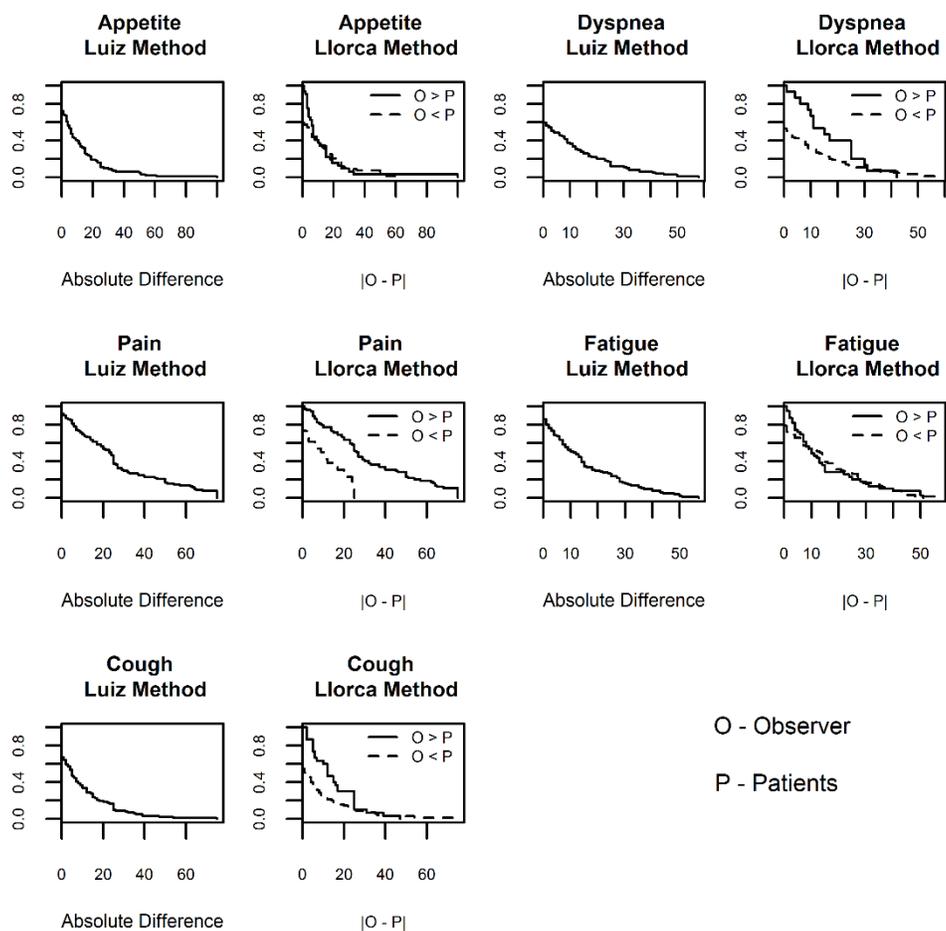

Figure 3 - Concordance analysis of symptoms between the observer and the patients' view: Luiz Method and Llorca Method.

The choice of the type of graphical presentation by scales of intensity and variation of symptoms collected is a crucial task. In our case, we decided to use signals, to build diagrams with a global view of symptom variation, obtaining good results. Patients were numbered according to their order of admittance, 0 to 30. Four of them, herein represented by their numbers, were chosen to show the evolution of symptoms in the chart.

In order to illustrate the intrapersonal variation of some patients, was used the method "Star Plot" shown below. Figure 4 shows the "star plot" for the four patients who stood out among the 30 evaluated, ("Patient 10", "Patient 13", "Patient 22" and "Patient 24"), where each axis represents a symptom assessed according to patients' vision.

"Patient 10" appeared at the first consultation (D0) in an important clinical situation of loss, with improvement in the assessments of 15, 30 and 45 days and worsening from day 60th onwards.

"Patient 13" arrived in the first consultation (D0), also in an important clinical situation of loss, with improvement in some variables until the 60th day, when he returned to worsen.

"Patient 22" appeared at the D0 greatly compromised, with improvement in other outpatient visits, reaching maximum improvement in the 45th day of evaluation.

"Patient 24" has evolved with many losses until the 45th day and then started to improve, performing well in all variables. Note that the variable "hemoptysis" never appeared in the diagram for "patient 24", who had not this symptom.
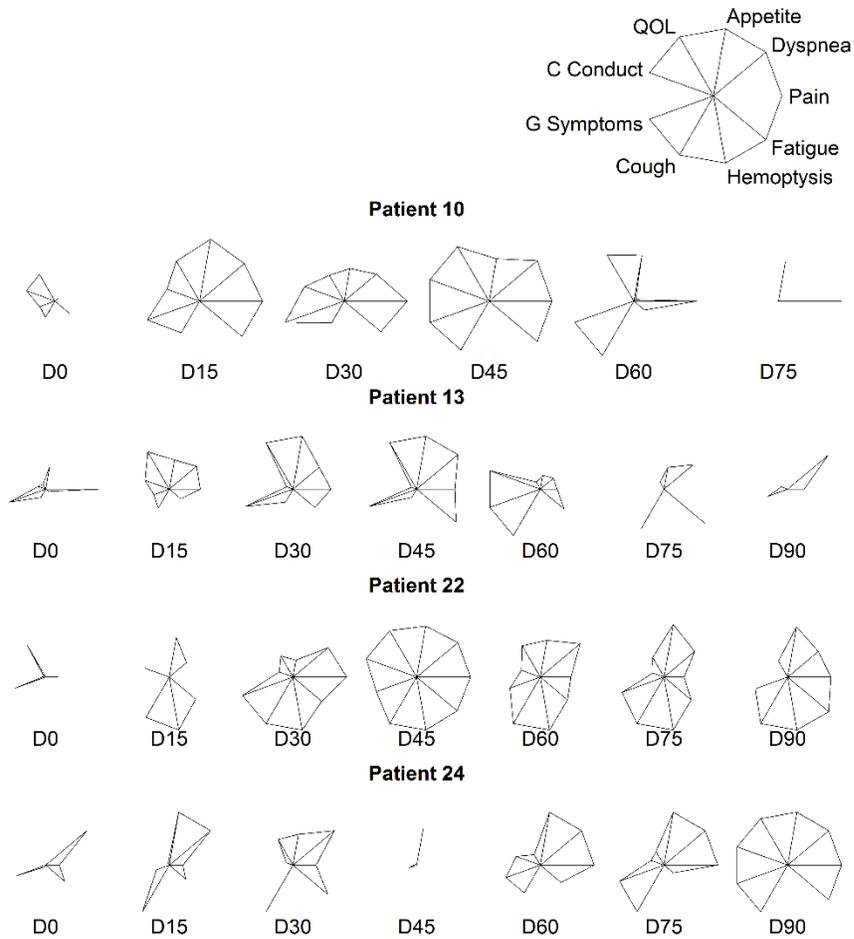
Figure 4 - Star plots.

4. Discussion

The present research evaluated the impact of palliative care over the distressing symptoms and functional capacity of the patients with lung cancer in final stage of life with symptoms and limitations inherent of this phase of the disease, as described hereinafter.

Ninety-six percent (n=29) of patients in this study have anorexia at some time of our follow-up on CP. Literature data show its presence in 65-85% (INCA, 2001) and 89-90% in anorexia-cachexia syndrome of patients with advanced cancer (NERVI, 2004). Many of our patients had oral candidiasis, nausea, and fecal impaction, the last one due to the use of opioids. All this contributed to anorexia. We were able to intervene on these factors, for example, treating oral candidiasis, adapting diet, with concomitant treatment of pain with

tricyclic antidepressants. There was a statistically significant improvement, from the viewpoint of the observer, of the variable "appetite" (p value = 0.06) in the difference in the evaluation of D30-D0 (n = 10).

Dyspnea was present in 80% of patients. These data are in accordance to the literature (SKAUG *et al.*, 2007; FORNELLS, 2004). Eighty percent of our patients (n = 24) had been smokers, and many of them had chronic obstructive pulmonary disease (COPD). Some had cardiovascular disease and other had pleural effusion, lymphangitis carcinomatosis, anemia, fever due to respiratory infection or due to tumor, superior vena cava syndrome, and, with rare exceptions, had cachexia in later life. Ventilatory support measures and medications for symptom relief were adopted for these patients, however there was no modification of the symptom, most likely because it is a subjective symptom that depends on various physical and psychological factors, as related above. There was no statistically significant change of variable "dyspnea" in several comparative measurements made by the box plots. There was no statistically significant change of the variable "dyspnea" in the various comparative measures.

A hundred percent (n = 30) of the patients had pain at some time of our follow-up on CP. Pain tends to increase in the final stages of the patient's life. The literature shows that pain assessment is a complex process and currently there are three value dimensions in pain: the sensory-discriminative, motivational-affective and the cognitive-evaluative. Besides the approaching death, with all aspects, insecurity, uncertainty, separation, may negatively influence this variable in the variable "pain", we must take into account the extent of disease, interference by the patient's life, the social and emotional aspects. This patients are in the final stages of life, with limitations inherent to this stage and should be considered, besides the problems related to the injury itself, the prospect of approaching death, with all questions, insecurity, uncertainty, separation, among other factors that may negatively influence this variable.

This variable suffers influence of the extent of disease, personal life, and the social and emotional aspects (ANGELOTTI and SARDÁ, 2005). It is important to say that two thirds (n = 20) of our patients were in stage IV of diagnosis, a decisive factor, considering that patients with metastatic cancer are more likely to feel pain (LARUE *et al.*, 1995). It is also important to mention that economic and social problems can interfere negatively with pain (ELLIOTT *et al.*, 1999; BERGMAN *et al.*, 2001; LASCH, 2002). Our patients had limited financial resources that influence pain negatively.

It is interesting that there were differences between the assessments of patients an observer about pain during the consultation. Often patients reported having a very intense pain, but not presented, e.g., fascia or pain behavior. We intervened with analgesics, treatment of emotional factors, among others. Despite these interventions, many of these patients were still complaining of pain. Perhaps this assessment tool, in this particular situation of palliative care, was not been able to assess pain in all its dimensions.

A hundred percent (n = 30) of the patients had fatigue at some time of our follow-up on CP. According to the literature, fatigue is an almost universal symptom in patients with advanced cancer (WAGNER and CELLA, 2004). We observed similar changes in our work. We know that as time goes by, there is a progressive deterioration of general condition, often with anemia and other debilitating symptoms, worsening levels of anorexia, and episodes of dyspnea and pain. All this, combined with great sadness, anxiety or depression, related to perception of a radical change, which is death

approaching, negatively contributes to fatigue. There was no statistically significant change of variable "fatigue" in several comparative measurements made by the box plots. This is in agreement with the literature that describes this symptom as one with less responsive of effective interventions (INCA, 2001).

Hemoptysis was a sporadic event in our sample (three patients), short term and in small quantities (less than 100 ml). In general, this symptom was reversed after treatment of infection and administration of cough sedative, as suggested in the literature (INCA, 2001).

In our sample, cough was present in 96% (n = 29) of patients at some point in their evolution. According to the literature, cough has a prevalence of 47% - 86% of patients with lung cancer (CHAN *et al.*, 2004).

There are many causes of cough in patients with lung cancer, for instance, endobronchial lesions, tracheoesophageal fistula, lymphangiticcarcinomatosis, fibrosis induced by radiotherapy and chemotherapy, carcinomatous lymphangitis, pleural and pericardial effusion, pneumonia, asthma, or pulmonary parenchymal infiltration (CHAN *et al.*, 2004).

We prescribed all specific treatments and, when appropriate, administered sedative drugs such as codeine. There was no statistically significant change of variable "cough" in several comparative measurements made by box plots.

The variable severity of symptoms was measured only by patients, following the protocol of the LCSS. Statistical significance (p = 0.06) of the difference was obtained in evaluations between D60-D0 (n = 10), in the vision of patients, where the median is at a positive value on the box plots, indicating that we should interfere with distressing symptoms, seeking improvement in their severity. However, the variable was difficult to understand by patients, even following a routine clarification. In our observation, the patient felt that the progression of the disease was directly related to worsening of symptoms, even when this did not occur. Also, following the protocol of LCSS, this assessment was made only in the scale of the patient. We have improved KPS, by interfering in distressing symptoms and general quality of life. Patients could perform tasks and acquire a skill level better than before, which was detected in some ratings. There was no statistically significant change of variable "ability to perform tasks", in several comparative measurements made by box plots. In this variable, by our observation, patient was, in general, compared to the activities performed before falling ill, making the interpretation often difficult. Many patients recovered temporarily their capacity for self-care and some other activities of daily living. Only one of our patients could return to a previous level of ability.

Following the same protocol of LCSS, the evaluation of the variable "quality of life" was made only by patients. In the box plots showing the difference in ratings between D30-D0 (n = 10), there was improvement (p = 0.04). This confirms the feeling that, in patients with advanced cancer, quality of life is strongly influenced by the presence of distressing symptoms (McMILLAN and SMALL, 2002) for example, improving appetite and food intake, even on a temporary basis, positively affect quality of life of patients.

Palliative care provides comfort to patients who are in the final stages of life. Efforts should be made to implement this kind of therapy, even in countries with limited resources, because it is relatively inexpensive and presents quite convincing results.

Acknowledgements

- RESUMO: Há uma necessidade crescente de melhorar o cuidado ao final da vida em pacientes com câncer e avaliá-lo por meio de questionários é uma ferramenta importante para avaliar seus resultados. O objetivo deste estudo foi avaliar o efeito dos cuidados paliativos na qualidade de vida, sintomas angustiantes e capacidade funcional de pacientes com câncer primário de pulmão com doença localmente avançada e doença metastática em um hospital universitário. Foram incluídos neste estudo 30 pacientes com câncer de pulmão, previamente tratados com intenção curativa e submetidos a tratamento paliativo. Eles foram divididos em três grupos. O primeiro grupo era composto de 10 pacientes, que viveram entre 30 e 59 dias após a admissão, o segundo, 10 pacientes que viveram entre 60 e 89 dias e o terceiro, 10 pacientes que viveram 90 dias ou mais. A coleta de dados referente a cinco sintomas estressantes: anorexia, dispneia, dor, fadiga, hemoptise e tosse, foi realizada de acordo com a Escala de Sintomas de Câncer Pulmonar e Escala de Status de Desempenho de Karnofsky. Por inspeção observacional, o "apetite" e a "Escala de Status de Desempenho de Karnofsky" melhoraram; a "dor" piorou e a "qualidade de vida" melhorou após os cuidados paliativos, segundo os pacientes. Fatores físicos, psicológicos, espirituais e sociais influenciam os sintomas de pacientes com câncer no final na vida. O tratamento por cuidados paliativos pode proporcionar conforto a esses pacientes.

- *PALAVRAS-CHAVE:* Câncer de pulmão; cuidados de fim de vida; qualidade de vida; pacientes em estado terminal; Escala de Status de Desempenho de Karnofsky.

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