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Outcomes for patients with lung cancer admitted to intensive care units

Desfecho de pacientes com câncer de pulmão admitidos em unidades de terapia intensiva

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ABSTRACT

Objective: This study aimed to evaluate the outcomes for patients with lung cancer admitted to intensive care units and assess their clinical and demographic profiles.

Methods: Retrospective, analytical, observational study, wherein the outcomes for patients diagnosed with lung cancer admitted to the intensive care unit of university hospital from January 2010 until February 2011 were evaluated.

Results: Thirty-four patients' medical records were included. Twenty-six (76.5%) patients received some type of ventilatory support, of whom 21 (61.8%) used invasive mechanical ventilation and 11 (32.4%) used noninvasive ventilation at some point during their stay at the intensive care

unit. Regarding mortality, 12 (35.3%) patients died during hospitalization at the intensive care unit, totaling 15 (44.1%) deaths during the entire hospitalization period; 19 (55.9%) patients were discharged from the hospital. The analysis of the variables showed that the patients who died had remained on invasive mechanical ventilation for a longer period 5.0 (0.25 to 15.0) days than the survivors (1.0 (0 to 1.0) days) ($p=0.033$) and underwent dialysis during their stay at the intensive care unit ($p=0.014$).

Conclusions: The mortality of patients with lung cancer admitted to the intensive care unit is associated with the time spent on invasive mechanical ventilation and the need for dialysis.

Keywords: Lung neoplasms/mortality; Intensive care unit; Prognosis

This study was conducted at Hospital de Clínicas de Porto Alegre - HCPA - Porto Alegre (RS), Brazil.

Conflicts of interest: None.

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INTRODUCTION

Lung cancer is one of the most frequent types of cancer in both men and women, and it is also one of the most lethal.⁽¹⁾ Advances in the treatment of tumors have occurred in the last years, enabling a greater probability of disease control or cure. However, these new therapies can cause a number of side effects, affecting almost all organ functions. The cancer itself can also cause clinical complications, with immediate risk to life, directly leading to a greater use of beds at the intensive care unit (ICU).⁽²⁻⁴⁾

Patients with the chance of curing or controlling cancer with potentially reversible complications are admitted to the ICU, and the intensive care has been shown to contribute to reducing those patients' mortality rate, even in subjects at higher risk, including patients with sepsis or in need of mechanical ventilation (MV).^(3,5) The ICU support is sometimes necessary for

the immediate relief of symptoms and improved quality of life, even for patients without further therapeutic possibilities of cure.⁽²⁾

Acute respiratory failure is one of the most common complications in patients with lung cancer. It implies a worse prognosis and, in most cases, requires the use of MV. Hypoxemic respiratory failure may be due to infectious pneumonia, invasion of the underlying malignancy, acute lung injury due to chemotherapy, cardiogenic or non-cardiogenic pulmonary edema, or diffuse alveolar hemorrhage. Noninvasive ventilation (NIV) should be offered to patients who are stable from the hemodynamic and hematological standpoint.^(4,6,7)

Considering that some studies have been performed to characterize patients with lung cancer admitted to the ICU, either based on the high morbidity and mortality or the poor prognosis of those subjects, and considering that advanced cancer requires intensive treatment in most cases, this study aimed to evaluate the outcomes for patients with lung cancer admitted to the ICU.

METHODS

A retrospective, analytical, observational study was performed wherein the outcomes for patients diagnosed with lung cancer admitted to the Hospital de Clínicas de Porto Alegre (HCPA) ICU from January 2010 to February 2011 were evaluated. The patients were gathered using the hospital's electronic medical record system. Subsequently, a review of those records was conducted to collect the necessary data.

The patients were evaluated regarding their demographic and clinical profile, the reason for ICU admission, length of stay, whether ventilatory support was used, mortality, complications, prognosis, and treatment (medical and/or surgical), according to the data collected from the evaluation questionnaire for patients with lung cancer admitted to the ICU.

All patients diagnosed with lung cancer and admitted to the adult ICU of HCPA, from January 2010 to February 2011, of both genders, varying age, whether under treatment for cancer or not, were included in the study. Patients who did not meet the inclusion criteria, including patients with other tumors and/or diseases not diagnosed as lung cancer, were excluded.

The study was approved by the Ethics and Research Committee of the HCPA. The Informed Consent Form was waived because it was a retrospective study analyzing medical records.

The modified form of the Brazilian Research in Intensive Care Network (BRICNet),⁽⁸⁾ with demographic and clinical data characteristic of the cancer, cause of ICU admission and reason for the use or non-use of MV, Acute Physiology and Chronic Health Evaluation II (APACHE II) prognostic score, mortality, and treatment, was used for data collection.

Statistical analysis

The data collected were entered into the Microsoft® Excel 2000 database software and were processed and analyzed using the Statistical Package for the Social Sciences (SPSS) software, version 17.0. A descriptive analysis was performed for the study variables. The quantitative data were shown as the mean±standard deviation (SD) and/or as the median and interquartile range (IQR). The frequency data were expressed as the number of subjects (N) and the percentage (%) of cases. The comparison between survivors and non-survivors, regarding the continuous variables, was performed using the Student t test for normally distributed data or the nonparametric Mann-Whitney test for data that are not normally distributed. The chi-square or Fisher's exact (if the expected counts in one group were below 5) tests were used for the two groups with respect to categorical variables. Differences were considered statistically significant at $p < 0.05$.

RESULTS

A total of 34 patients diagnosed with lung cancer were admitted to the ICU of HCPA from January 2010 to February 2011. The patients' demographic and clinical characteristics are shown in table 1. There was a predominance of females and a mean age of 63.3 ± 11.2 years. The histologic type epidermoid cancer prevailed in 13 (38.2%) patients. There were distant metastases in 13 (38.2%) patients and recently diagnosed active cancer in 29 (85.3%) patients. Regarding treatment, 22 (64.7%) patients underwent non-surgical and 12 (35.3%) surgical treatments.

Twenty-nine (85.3%) of the 34 patients were admitted to the clinical ICU and only 5 (14.7%) to the elective surgical ICU. Seventeen (50%) came from the infirmary, 5 (14.7%) from the emergency room, 8 (23.5%) from the surgical center, 3 (8.8%) from the recovery room, and only 1 (2.9%) from the outpatient clinic.

The main reasons for admission to the ICU were respiratory failure in 16 patients (47.1%), sepsis in 6 (17.6%), and postoperative monitoring in 5 (14.7%). During the ICU stay, 21 (61.8%) patients had some

type of infection, and pneumonia was the most prevalent, occurring in 16 (47%) patients, followed by sepsis in 8 (23.5%). Fifteen patients (44.1%) used vasoactive drugs, and only 3 (8.8%) required dialysis. Only 1 (2.9%) patient was treated with chemotherapy at the ICU.

Twenty-six (76.5%) of the 34 patients received some form of ventilatory support: 21 (61.8%) used IMV, and 11 (32.4%) used NIV at some point during the ICU stay. Two (5.9) of these had NIV failure, and 3 (8.8%) had difficulty weaning from the IMV (Table 1).

Concerning the patient mortality, 12 (35.3%) patients died during the period of the ICU stay, with a total of 15 (44.1%) deaths during hospitalization (ICU and infirmary), and 19 (55.9%) were discharged from the hospital. The decision of therapeutic obstinacy occurred in 11 (32.4%) patients. Twelve (35.3%) patients did not receive any physical therapy.

Univariate analyses of quantitative variables, associated with the primary outcome, which is mortality, were performed. The results of the univariate analyses are shown

Table 1 - Demographic and clinical characteristics of patients with lung cancer

Variables	Results N=34
Age (years)	63.3±11.2
Gender	
Male	15 (44.1)
Female	19 (55.9)
Histological type	
NSCLC	
Epidermoid	13 (38.2)
Adenocarcinoma	10 (29.4)
Large-cell	1 (2.9)
SCLC	1 (2.9)
Other subtypes	3 (8.8)
NSCLC without classification	5 (5.4)
Staging	
Limited-stage	12 (35.3)
Locally advanced	8 (23.5)
Distant metastases	13 (38.2)
Grade cannot be assessed	1 (2.9)
Cancer status	
Under control/remission	2 (5.9)
Active/recent diagnosis	29 (85.3)
Active/progression	3 (8.8)
Treatment	
None	21 (61.7)
Surgery	12 (35.3)
Radiation therapy/Chemotherapy	1 (2.9)

NSCLC - non-small cell lung cancer; SCLC - small cell lung cancer. Results expressed as the mean±standard deviation or number of subjects (n) and percentage (%).

in tables 2 and 3. The analysis of variables showed that the patients who died remained on IMV for a longer period than the survivors ($p=0.033$) and underwent dialysis during the ICU stay ($p=0.014$). The other variables, including gender, treatment, infection, use of vasoactive drugs, NIV and performing physical therapy were not statistically significant regarding mortality.

The Mann-Whitney test could not be performed regarding the duration of dialysis because only three patients underwent dialysis, and all died; therefore, no patient remained in the group of survivors, and the test could not be performed using an empty group.

Table 2 - Univariate analysis of quantitative variables associated with mortality

Variables	N (%)	ICU mortality N (%)	Odds ratio (95%CI)	p value
Gender				
Female	19 (55.9)	7 (58.3)	0.86(0.21-3.55)	0.832
Male	15 (44.1)	5 (41.7)		
Treatment				
Surgical	12 (35.3)	3 (25)	2.08(0.44-9.87)	0.354
Non-surgical	22 (64.7)	9 (75)		
Infection				
Yes	21 (61.8)	9 (75)	2.50(0.53-11.81)	0.241
No	13 (38.2)	3 (25)		
Vasoactive drugs				
Yes	15 (44.1)	7 (58.3)	2.45(0.58-10.33)	0.218
No	19 (55.9)	5 (41.7)		
Dialysis				
Yes	3 (8.8)	3 (25)	1.33(0.96-1.85)	0.014
No	31 (91.2)	9 (75)		
IMV				
Yes	21 (61.8)	9 (75)	2.50(0.53-11.81)	0.241
No	13 (38.2)	3 (25)		
NIV				
Yes	11 (32.4)	3 (25)	0.58(0.12-2.80)	0.498
No	23 (67.6)	9 (75)		

ICU - intensive care unit, 95% CI - 95% confidence interval; IMV - invasive mechanical ventilation, NIV - noninvasive ventilation. Variables analyzed using the chi-square test.

Table 3 - Univariate analysis of quantitative variables associated with mortality

Variables (days)	Survivors	Non-survivors	p value
Vasoactive drugs	2.0 (1.0-5.25)	5.0 (2.0-9.0)	0.189
Dialysis	0	9.0 (0-4)	-
Ventilatory support	1.0 (0-3.0)	3.50 (0.63-9.0)	0.152
IMV	1 (0-1.0)	5.0 (0.25-15.50)	0.033
NIV	0 (0-1.0)	0 (0-0.25)	0.492
ICU	3.0 (2.0-6.0)	5.0 (2.0-14.75)	0.657
Hospitalization	26.50 (15.75-47.25)	23.0 (9.25-31.75)	0.157
APACHE II	12 (0-19.75)	15.50 (0-24.75)	0.511

IMV - invasive mechanical ventilation, NIV - noninvasive ventilation, ICU - intensive care unit; APACHE II - Acute Physiology and Chronic Health Disease Classification System II. Results expressed as median (interquartile range). Variables analyzed using the Mann-Whitney test.

DISCUSSION

The results of this study suggest a worse outcome for patients with lung cancer admitted to the ICU, with a 44.1% in-hospital mortality rate and 35.3% ICU mortality rate.

These data are in accordance with the overall mean mortality in the ICU, similar to other recently published studies, which showed overall ICU mortality ranging from 22 to 51% and in-hospital mortality ranging from 46 to 66%.⁽⁹⁻¹⁷⁾ Conversely, the study by Lin⁽⁶⁾ showed an 85.2% hospital mortality rate.

The patients' epidemiological profile coincides with the profiles reported in previous studies, wherein the female gender and the mean age group above 60 years predominate, and the histological types epidermoid and adenocarcinoma, recently diagnosed active cancer and disease with distant metastasis were further prevalent.^(6,9,18) Approximately 40% of patients with non-small cell lung cancer (NSCLC) were in an advanced disease stage, with metastasis or locally advanced involvement.⁽¹⁹⁾

According to some studies,⁽⁹⁻¹³⁾ patients admitted to the ICU with lung cancer have NSCLC in a more advanced disease stage, and the admission is directly related to lung cancer. The use of the ICU for patients with advanced lung cancer has increased. The performance status and ability to control tumor growth are key factors assessed upon patient admission to the ICU, where the overall mortality is 40-50%, with reductions in mortality attributed to advances in ICU care.⁽²⁰⁾

Infectious complications, from localized to generalized infections with sepsis and septic shock, are the most common reasons for ICU admission among the indications for intensive therapy in patients with cancer.^(2,6,10,13,14) In this study, the most frequent reasons were respiratory failure (47%) and sepsis (17.6%). A total of 61.8% of the patients were found to have some type of infection during the ICU stay. Similar results were found in earlier studies.^(6,9,10) Typically, cancer patients admitted to the ICU with infection are unresponsive to the initial therapy and show signs of spread of the infectious agent.⁽²⁾ This tendency leads to longer ICU stays, MV, and the use of vasoactive drugs.

Most patients included in this study received some type of ventilatory support during the ICU stay. The data in this study corroborate prior research studies, which showed the use of IMV during the ICU stay of most cancer patients.⁽¹²⁻¹⁵⁾

This study also showed that the need for dialysis

and the duration of IMV use were factors significantly associated with mortality. D'Avila showed that an MV duration longer than 6 days was associated with higher mortality risk.⁽²¹⁾ Other studies also showed a direct correlation between lethality and longer stays on IMV and dialysis.^(6,21) Roques et al.⁽⁹⁾ showed an association between mortality and admission to the ICU for acute respiratory failure, cancer progression, vasopressor use, IMV use, and APACHE II.⁽¹⁸⁾

Although it is known that patients using vasoactive drugs or IMV and patients suffering from infections during hospitalization have an increased risk of mortality, no significant association was found in this study, most likely because of the reduced sample size, but some other studies do show that correlation.^(9,12,18)

The current study had some limitations. First, the main study limitation is its sample size, which makes it practically descriptive, as the interpretation of associations considering only univariate analyses is very limited and compromises the associations between variables and the main outcome. Second, the study was based on data collected from a single center, which might have potential biases given the target population's characteristics, including access to health services, for example. New studies with more patients are needed to confirm those results and relate other factors and outcomes.

CONCLUSION

Although patients with lung cancer may benefit from intensive care in the ICU because many therapeutic advances have been pursued that can increase their survival and improve their quality of life, this study showed a high mortality rate in such patients, related to the time of use of IMV and the use of dialysis.

RESUMO

Objetivo: Este estudo objetivou avaliar o desfecho de pacientes com câncer de pulmão admitidos na unidade de terapia intensiva e verificar o perfil clínico e demográfico deles.

Métodos: Estudo analítico observacional, retrospectivo, em que foi avaliado o desfecho de pacientes com diagnóstico de câncer de pulmão que internaram na unidade de terapia intensiva de um hospital universitário de janeiro de 2010 até fevereiro de 2011.

Resultados: Foram incluídos 34 prontuários de pacientes. Vinte e seis (76,5%) receberam algum tipo de suporte ventilatório, 21 (61,8%) utilizaram ventilação mecânica invasiva e 11 (32,4%) utilizaram ventilação não invasiva em algum momento durante a estadia na unidade de terapia intensiva. Conside-

rando a letalidade, 12 (35,3%) foram a óbito durante o período de internação na unidade de terapia intensiva, totalizando 15 (44,1%) óbitos durante todo o período de hospitalização; 19 (55,9%) pacientes obtiveram alta do hospital para casa. A análise das variáveis mostrou que os pacientes que foram a óbito permaneceram um período maior em ventilação mecânica invasiva 5,0 (0,25-15,0) dias do que os sobreviventes (1,0 (0-1,0) dias) ($p=0,033$) e realizaram diálise durante a estadia na

unidade de terapia intensiva ($p=0,014$).

Conclusões: A mortalidade dos pacientes com câncer de pulmão admitidos em unidade de terapia intensiva está associada com o tempo de permanência na ventilação mecânica invasiva e a necessidade de diálise.

Descritores: Neoplasias pulmonares/mortalidade; Unidade de terapia intensiva; Prognóstico

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