

Outcome of lung cancer patients admitted to the intensive care unit with acute respiratory failure

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Abstract

Background: Previous studies have shown that the outcome of lung cancer patients who were admitted to the Intensive Care Unit (ICU), especially those requiring mechanical ventilation, is extremely poor. The present study was conducted in order to assess the outcome of a recent cohort of lung cancer patients admitted to the ICU with acute respiratory failure.

Methods: A retrospective analysis of the medical records of 105 lung cancer patients who were admitted to the ICU between January 2008 and January 2011 was performed. Severity of illness on the first day of ICU admission was assessed using the acute physiology and chronic health evaluation (APACHE) II and the sequential organ failure assessment (SOFA) scoring systems. Associated organ failure was determined according to the Knaus criteria.

Results: Eighty four (80%) patients were diagnosed with non-small cell lung cancer, 14 (13.3%) with small cell lung cancer, one patient with mesothelioma, and in the remaining 6 patients, the type of lung cancer could not be determined. Significant factors on admission were APACHE II and SOFA scores, poor performance status and severe comorbidity. During ICU stay, the main risk factors for poor outcome were the long term mechanical ventilation duration, use of vasopressors, more than two organ system failures and septic condition. The overall ICU, hospital and 6-month mortality rates were 44.7% (47/105), 56.1% (59/105) and 77.1% (81/105) respectively.

Conclusions: The present data show that the medical intensive care unit outcome of lung cancer patients is improving. Further studies of patients selected to ICU admission are needed to assess long-term mortality, quality of life, ability to continue chemotherapy and economic cost.

Keywords: Lung cancer, intensive care unit, respiratory failure

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Introduction

The outcome of patients with cancer has been improved significantly during the last decade¹. Three factors are major contributors to this trend². First of all, advances in the treatment of solid tumors and hematologic malignancies produced a 20% decrease in overall mortality³. Secondly, progress has been made in selecting patients likely to benefit from Intensive Care Unit (ICU) admission. Finally, an earlier admission to the ICU has resulted in better survival rates for critically ill cancer patients. Previous studies have shown that the outcome of lung cancer patients who were admitted to the ICU, especially those requiring mechanical ventilation, is extremely poor⁴. The present study was conducted in order to assess the outcome of a recent cohort of lung cancer patients admitted to the ICU with acute respiratory failure.

Patients and Methods

Theagenio Cancer Hospital is the referral oncology center of Northern Greece. The 8-bedded multidisciplinary adult ICU is run by a full-time intensive care team. Patients are referred directly from the oncology wards. The criteria for admission to and discharge from the ICU follow the guidelines set by the American College of Critical Care Medicine and Society of Critical Care Medicine⁵. After obtaining approval from the institutional review board, a retrospective analysis of the medical records of lung cancer patients who were admitted to the ICU between January 2008 and January 2011 was performed.

The criterion for including patients in the present study was a histologically proven diagnosis of lung cancer made within the last 2 years prior to their admission to the ICU. Patients who stayed in the ICU for 24 hours and those admitted for routine postoperative care were excluded from

the study. For those patients who were admitted more than once to the ICU during the same hospitalization, only the first ICU admission was analysed. To be admitted, patients were generally considered to have a potential chance of recovering from the acute problem. In contrast, patients without any treatment options were offered end-of-life care on the referring ward and not transferred to the ICU.

Severity of illness on the first day of ICU admission was assessed using the acute physiology and chronic health evaluation (APACHE) II and the sequential organ failure assessment (SOFA) scoring systems⁶. Associated organ failure was determined according to the Knaus criteria⁷. Respiratory support was defined as the need for non-invasive or invasive mechanical ventilation. Inotropic support included the use of any inotropic or vasopressor therapy.

No information allowing identification of the patients was recorded in this retrospective observational cohort study. The institutional review board of Theagenio Cancer Hospital approved the study.

Statistical analysis

Results are reported as mean±SD or median and range. In univariate analyses, chi-square test, Fisher's exact test and Mann-Whitney U test were used for testing differences between means. All reported p-values were two-tailed and considered statistically significant at <0.05.

Results

From 635 cancer patients admitted to ICU with acute respiratory failure, 105 lung cancer patients (16.5%) fulfilled the eligibility criteria and constituted the study population. Eighty four (80%) patients had non-small cell lung cancer, 14 (13.3%) patients had small cell lung cancer, one patient had mesothelioma, and in the remaining 6 patients, the type of lung cancer could not be determined, based on the available medical records. In patients with non-small cell lung cancer, 76 patients had stage IV, 6 patients had stage III, one patient had stage II, and one patient had stage I disease. In patients with small cell lung cancer, three patients had limited disease and eleven patients had extensive disease. There were no significant differences in the baseline clinical characteristics between survivors and non-survivors during the ICU admission. The main respiratory causes for admission to the ICU are summarized in Table 1.

The main patients' clinical characteristics are depicted in Table 2. The possible risk factors for poor outcome are presented in Table 3. Factors are distinguished as at ICU

admission and during ICU stay. Statistically significant factors on admission are APACHE II and SOFA scores, poor performance status and severe comorbidity. During ICU stay, the main risk factors for poor outcome are the long term mechanical ventilation duration, use of vasopressors, more than two organ system failures and septic condition. Main laboratory variables on admission to the ICU were recorded and compared between survivors and non-survivors, as shown in table 4.

The overall ICU, hospital and 6-month mortality rates were 44.7% (47/105), 56.1% (59/105) and 77.1% (81/105) respectively.

Discussion

Lung cancer is the second most common malignancy (after prostate cancer in males and breast cancer in females) in the USA, and remains the leading cause of cancer-related death in both men and women worldwide. However, the 5-year survival rate (all stages combined) is only 16%, and ranges from 50% in localized cancer to 3% in metastatic cancer⁸. Despite this poor prognosis, patients with lung cancer are increasingly admitted to medical intensive care units for critical illnesses related either to the underlying malignancy (regardless of the cancer stage) or to co-morbidities^{9,10}. Previous studies showed poor outcomes in lung cancer patients admitted to the ICU and most notably those requiring mechanical ventilation¹¹. Nevertheless, overall survival rates in these patients have improved over the last decade¹². Our study has several limitations. We used a retrospective design and were therefore unable to determine the criteria used to select patients for ICU admission. It was conducted in a single center, so possible selection biases concerning differences in patterns of care cannot be ruled out. Consequently, we cannot assess the selection bias induced by ICU triage process. Secondly, our small sample size (n=105) produced limited statistical power. Most of the previous studies on patients with advanced lung cancer were done in highly heterogeneous populations^{10,13,14}. Our study is the second one following Andrejak's study to focus exclusively on ICU admission of patients with lung cancer and acute respiratory failure and to classify reasons for ICU admission according to their link with lung cancer¹⁵. Furthermore, the patients' health-related quality of life was not evaluated. The ideal assessment of the patients' outcome must include multidimensional parameters other than mortality.

In our highly-selected population, we found an ICU mortality rate of 47.4% and an in-hospital mortality rate of 64.5%. These results are in accordance with the data recently reported by Reichner et al. (43% ICU mortality and

Table 1: Main indications for intensive care unit admission for all lung cancer patients; survivors and non-survivors.

Indications	All patients (n=105)	Survivors	Non-survivors
Pneumonia	69	28	41
Pulmonary edema	11	7	4
COPD exacerbation	11	5	6
Hemoptysis	7	2	5
Pleural effusion	5	3	2
Post-bronchoscopy	2	2	0

COPD: Chronic Obstructive Pulmonary Disease.

Table 2: Baseline clinical characteristics of all lung cancer patients; survivors and non-survivors.

	All patients	Survivors	Non-survivors	p
Subjects	105	47	58	-
Age (years)	68.3±10.4	66.5±10.6	69.8±9.5	0.190
Sex (male)	51	23	28	0.160
Hospital days prior to ICU admission	3	2	3	0.720
Median Interquartile Range	1-8	1-6	1-9	
APACHE II score on admission	23.4	21.3	25.1	0.010
Median Interquartile Range	7.2	6.5	7.6	
SOFA score on admission	9.4	7.2	10.2	0.010
Median Interquartile Range	4.0	3.3	4.2	
Performance Status				
0-1	57/105	30/57	27/57	0.010
2-4	48/105	17/48	31/57	
Smoking history				
Yes	92/105	46/92	46/92	0.350
No	13/105	1/13	12/13	
Previous treatment				
Chemotherapy	58/105	20/58	38/58	0.126
Radiotherapy	22/105	8/22	14/22	
Combination	25/105	19/25	6/25	
Severe comorbidity				
Yes	61/105	7/61	54/61	0.001
No	44/105	40/44	4/44	

Table 3. Possible risk factors for poor outcome.

	All patients	Survivors	Non-survivors	p
Subjects	105	47	58	-
MV Duration				
<24h	32/105	23/32	9/32	0.005
>24h	73/105	24/73	49/73	
Vasopressors				
Yes	87/105	30/105	57/87	0.005
No	18/105	17/18	1/18	
Associated organ failures				
<2	53/105	45/53	8/53	0.005
>2	52/105	2/52	50/52	
Renal dysfunction				
Yes	37/105	24/37	13/37	0.190
No	68/105	23/68	45/68	
Septic condition				
Yes	47/105	17/47	30/47	0.005
No	58/105	30/58	28/58	

Table 4. Main laboratory variables on intensive care unit admission for survivors and non-survivors.

	Survivors	Non-survivors	p
Subjects	47	58	-
Hemoglobin (g/dL)	11.0±2.2	10.4±1.8	0.080
Platelets (x10 ³ /mm ³)	296.5±135.1	205.4±115.5	0.010
Creatinine (mg/dL)	1.7±0.8	1.5±0.9	0.650
Calcium (mg/dL)	8.1±1.9	7.9±2.2	0.300
Albumine (mg/dL)	1.8±1.4	1.6±1.2	0.205
Positive blood culture	6/47	39/58	0.001

60% hospital mortality)⁴, Soares et al (44% ICU mortality and 60% hospital mortality)¹⁰, and Rocques et al¹².

Mortality rates in lung cancer patients admitted to the ICU have decreased over time. In early studies, mortality ranged from 75 to 91%^{11,13,16}. Although Adam and Soubani recently reported a relatively low ICU mortality rate of 22%, only 49% of their patients required mechanical ventilation and mortality was highest in the mechanically ventilated patients¹⁷. The improved outcome of lung cancer patients admitted to the ICU reported in the present study may be related to: improved mechanical ventilation strategies that minimize further lung injury; better management of sepsis and a multidisciplinary approach to the management of these cases. However, prospective studies and more strict inclusion criteria are necessary to confirm and address the reasons for the improved survival noticed.

Several studies have tried to identify the clinical variables that are associated with poor ICU outcome. The outcome predictors reported by Reichner et al⁴ were the need for mechanical ventilation, advanced lung cancer stage and higher sequential organ failure assessment score. In the study by Boussat et al¹³ acute pulmonary disease and Karnofsky performance status <70 were associated with higher mortality. In the recent study by Soares et al¹⁰ the predictors of poor ICU outcome were the severity of comorbid illnesses, the number of organ system failures, cancer recurrence or progression, and airway infiltration or obstruction by cancer. In our study, it was possible to identify several predictors of poor ICU outcome that include high admission APACHE II and SOFA scores, the need for mechanical ventilation, the use of vasopressors, positive blood cultures and the presence of two or more organ system failures. Type of cancer seems to have a role regarding survival; lung cancer patients admitted to the ICU are characterized by poor survival rates, according to the international literature².

Azoulay et al² suggest that, when there is uncertainty regarding a patient's outcome, a trial of 3 to 4 days of full intensive care should be offered. The appropriateness of continuing this treatment will be determined by the subsequent patient's clinical response. In a recent study of patients with severe sepsis, mortality was closely associated with early changes in the severity of organ dysfunctions. Even improvements in organ functions on subsequent days had only a modest impact on the probability of survival.

In the multivariate analysis, thrombocytopenia was significantly associated with higher mortality. Moreau et al¹⁸ also reported that thrombocytopenia had prognostic significance in a large cohort of ICU patients and the platelet count is included in the SOFA score. Moreover, thrombocytopenia is considered a marker of cancer-related coagulation abnormalities^{19,20}.

In conclusion, the present data has shown that the medical intensive care unit outcome of lung cancer patients is improving. Further studies of patients selected to ICU admission are needed to assess long-term mortality, quality of life, ability to continue chemotherapy and economic cost.

Conflict of Interest

The authors declare no conflict of interest.

References

1. Staudinger T, Stoiser B, Müllner M, Locker GJ, Laczika K, Knapp S, et al. Outcome and prognostic factors in critically ill cancer patients admitted to the intensive care unit. *Crit Care Med.* 2000; 28: 1322-1328.
2. Azoulay E, Alberti C, Bornstain C, Leleu G, Moreau D, Recher C, et al. Improved survival in cancer patients requiring mechanical ventilatory support: impact of noninvasive mechanical ventilatory support. *Crit Care Med.* 2001; 29: 519-525.
3. Brenner H. Long-term survival rates of cancer patients achieved by the end of the 20th century: a period analysis. *Lancet.* 2002; 360: 1131-1135.
4. Reichner CA, Thompson JA, O'Brien S, Kuru T, Anderson ED. Outcome and code status of lung cancer patients admitted to the medical ICU. *Chest.* 2006; 130: 719-723.
5. Guidelines for intensive care unit admission, discharge, and triage. Task Force of the American College of Critical Care Medicine, Society of Critical Care Medicine. *Crit Care Med.* 1999; 27: 633-638.
6. Vincent JL, Moreno R, Takala J, Willatts S, De Mendonça A, Bruining H, et al. The SOFA (Sepsis-related Organ Failure Assessment) score to describe organ dysfunction/failure. On behalf of the Working Group on Sepsis-Related Problems of the European Society of Intensive Care Medicine. *Intensive Care Med.* 1996; 22: 707-710.
7. Knaus WA, Draper EA, Wagner DP, Zimmerman JE. Prognosis in acute organ-system failure. *Ann Surg.* 1985; 202: 685-693.
8. Jemal A, Siegel R, Ward E, Hao Y, Xu J, Thun MJ. Cancer statistics, 2009. *CA Cancer J Clin.* 2009; 59: 225-249.
9. Groeger JS, White P Jr, Nierman DM, Glassman J, Shi W, Horak D, et al. Outcome for cancer patients requiring mechanical ventilation. *J Clin Oncol.* 1999; 17: 991-997.
10. Soares M, Salluh JI, Torres VB, Leal JV, Spector N. Short- and long-term outcomes of critically ill patients with cancer and prolonged ICU length of stay. *Chest.* 2008; 134: 520-526.
11. Lin YC, Tsai YH, Huang CC, Hsu KH, Wang SW, Tsao TC, et al. Outcome of lung cancer patients with acute respiratory failure requiring mechanical ventilation. *Respir Med.* 2004; 98: 43-51.
12. Roques S, Parrot A, Lavole A, Ancel PY, Gounant V, Djibre M, et al. Six-month prognosis of patients with lung cancer admitted to the intensive care unit. *Intensive Care Med.* 2009; 35: 2044-2050.
13. Boussat S, El'rini T, Dubiez A, Depierre A, Barale F, Capellier G. Predictive factors of death in primary lung cancer patients on admission to the intensive care unit. *Intensive Care Med.* 2000; 26: 1811-1816.
14. Kress JP, Christenson J, Pohlman AS, Linkin DR, Hall JB. Outcomes of critically ill cancer patients in a university hospital setting. *Am J Respir Crit Care Med.* 1999; 160: 1957-1961.
15. Andréjak C, Terzi N, Thielen S, Bergot E, Zalcmán G, Charbonneau P, et al. Admission of advanced lung cancer patients to intensive care unit: a retrospective study of 76 patients. *BMC Cancer.* 2011; 11: 159.
16. Ewer MS, Ali MK, Atta MS, Morice RC, Balakrishnan PV. Outcome of lung cancer patients requiring mechanical ventilation for pulmonary failure. *JAMA.* 1986; 256: 3364-3366.
17. Adam AK, Soubani AO. Outcome and prognostic factors of lung cancer patients admitted to the medical intensive care unit. *Eur Respir J.* 2008; 31: 47-53.
18. Moreau D, Timsit JF, Vesin A, Garrouste-Orgeas M, de Lassence A, Zahar JR, et al. Platelet count decline: an early prognostic marker in critically ill patients with prolonged ICU stays. *Chest.* 2007; 131: 1735-1741.
19. Salluh JI, Soares M, De Meis E. Antiphospholipid antibodies and multiple organ failure in critically ill cancer patients. *Clinics (Sao Paulo).* 2009; 64: 79-82.
20. de Meis E, Pinheiro VR, Zamboni MM, Guedes MT, Castilho IA, Martinez MM, et al. Clotting, immune system, and venous thrombosis in lung adenocarcinoma patients: a prospective study. *Cancer Invest.* 2009; 27: 989-997.