Outcome of Lung Cancer Patients Admitted to the Intensive Care Unit

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Abstract: We investigate the outcome of lung cancer patients admitted to the medical intensive care unit (MICU) and examine potential predictors of mortality. A retrospective quality assurance study of primary lung cancer patients admitted to the MICUs at 2 local tertiary care university hospitals from January 1, 1994 to May 12, 2004 was conducted (n = 69). Data on demographics and tumor-related data were collected using the hospital records of all patients admitted to MICU with a diagnosis of lung cancer. Statistical analysis was performed to determine the prognostic factors associated with MICU and hospital mortality as well as MICU and hospital lengths of stay. The MICU mortality rate was 50.7% and the mean MICU length of stay was 3.0 days. Multivariate analysis determined that Acute Physiology and Chronic Health Evaluation (APACHE II) scores, Therapeutic Intervention Scoring System scores, and non-small cell lung cancer were significantly associated with MICU mortality, whereas age and APACHE II scores were associated with hospital mortality. Respiratory failure upon admission and use of a Swan Ganz monitor were predictors of increased MICU length of stay, and chemotherapy administration and mechanical ventilation predicted increased hospital length of stay. The 50.7% mortality rate for patients with previously or newly diagnosed primary lung cancer admitted to the MICU is lower than the previously reported mortality rate of 66.7% for a period of 1986. Although the mortality remains high, an improvement over the previous decade has occurred and is comparable to that for patients requiring MICU admission for other indications.

Key Words: lung cancer, critical care, outcomes research, intensive care

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Although breast and prostate are the most common cancers, lung cancer remains the leading cause of cancer deaths both in men and women. In Canada, an estimated 30% of cancer deaths in men and 25% of cancer deaths in women have been reported recently as a result of lung cancer. In 2006, there will be an estimated 22,700 new cases of lung cancer resulting in 18,900 deaths in Canada.[1] In general, these patients are diagnosed later in the course of disease when symptoms related to incurable advanced local or metastatic lung cancer develop. Their overall survival is directly related to the stage of lung cancer at the time of diagnosis. Patients with stage IA non-small cell lung cancer (NSCLC) have a 5-year survival rate of 67% which contrasts with 1% for patients with advanced stage IV NSCLC.[2]

Many patients with lung cancer initially present critically ill with respiratory failure even before a diagnosis has been made and require admission to the medical intensive care unit (MICU) for respiratory support, including intubation and mechanical ventilation. Other lung cancer patients require MICU admission for a variety of reasons, including inotropic support for sepsis or postoperative support after surgery. Both these groups of patients are considered to have high mortality. Because of the critical nature of their disease, it is not known how many of these patients are discharged from the MICU and leave the hospital. Currently, it is suspected that overall and hospital survival from lung cancer is influenced by factors such as comorbid illnesses and performance status at the time of presentation. Predictors of high mortality were previously studied in the early 1990s, but may have changed in light of new procedures and treatment modalities. For example, Azoulay et al performed retrospective analyses on cancer patients requiring mechanical ventilation from 1990 to 1995 and from 1996 to 1998, and noted better outcomes in the second time period and in patients treated with noninvasive mechanical ventilation for acute respiratory failure.[3] Similar improvements in mortality rates have also been seen in critically ill cancer patients who require management of acute renal failure or shock.[4,5]

In designing this study, our objective was 2-fold. First, we sought to determine the outcomes of patients with a known or new diagnosis of primary lung cancer admitted to the MICU from 1994 to 2004. Second, we aimed to determine the risk factors that predicted a poor prognosis in the same cohort of patients.

PATIENTS AND METHODS

Patient Population and Data Collection

We performed a retrospective study of all primary lung cancer patients admitted to the MICU at the 2 local tertiary care university hospitals (Health Sciences Centre and St. Boniface General Hospital) in Winnipeg, Canada from January 1, 1994 to May 12, 2004. A computerized search of the Winnipeg Regional Health Authority (WRHA) Critical Care database identified 111 patients who were admitted to the MICU and classified as follows: (a) admitted for thoracotomy for possible lung cancer; (b) admitted primarily for other problems with a recent thoracotomy for lung cancer in the past 6 weeks; or (c) primarily admitted for other problems along with lung cancer. Chart review excluded patients diagnosed with nonprimary lung cancer, including pulmonary lymphoma and metastatic rectal carcinoma, or a final nonneoplastic pathologic diagnosis, including bronchiectasis and bronchiolitis obliterans. Four patient records were unavailable for review to determine eligibility. In total, 69 patients with a previously known diagnosis of primary lung cancer or new diagnosis of primary lung cancer were included in this study. The data were retrospectively collected using hospital records of the admission that resulted in transfer to the MICU. For patients who had more than one admission to the MICU, the first admission during the study period was used for analysis to assure independence of observations.

The data collected included demographic data (age, sex), geographic data, MICU admitting diagnosis, MICU and hospital length of stay, MICU and hospital disposition, MICU treatment, Therapeutic Intervention Scoring System (TISS) and Acute Physiology and Chronic Health Evaluation (APACHE) II day 1 scores, MICU admission blood work, comorbid diseases, and evaluation of the tumor (histology, metastases, staging, treatment options). Information regarding the use of invasive and noninvasive (eg, BiPAP) mechanical ventilation, hemodialysis, and inotropic support was collected and analyzed as it pertained to MICU treatment.

Statistical Analysis

Data were analyzed using Microsoft Excel and Stata. Variables predictive of death during the MICU admission and hospital admission as well as MICU and hospital lengths of stay were identified. Continuous data are presented as the medians and ranges and were dichotomized into categorical variables using the median as the cutoff point. Nonparametric data were initially analyzed using the Wilcoxon rank sum test or Kruskal-Wallis test as appropriate to evaluate each variable independently for its association with MICU and hospital outcomes and lengths of stay. Nominal data were analyzed by χ^2 analysis with Fisher exact test where appropriate. Univariate analysis involving categorical data was conducted using the Spearman rank correlation test. All variables with $P < 0.1$ in univariate analysis were then subjected to a backwards stepwise logistic regression or backwards multiple linear regression to determine the prognostic factors associated with MICU and hospital death and survival, or MICU and hospital lengths of stay, respectively. Differences with a P value <0.05 were considered statistically significant.

RESULTS

Patient Demographics

A total of 69 patients with primary lung cancer were admitted to the MICU during the period of our data collection with a median age of 68 (mean = 65; 32–85 years old). Patient characteristics are described in Table 1. Of them, 37.7% were female, 20.3% had small cell lung cancer (SCLC), 68.1% had non-small cell lung cancer (NSCLC),

TABLE 1. Patient Characteristics (n = 69)

	n	%
Male	43	62.3
Female	26	37.7
Median age (yr)	68 (32–85)	
Type of lung cancer		
Non-small cell lung cancer	45	65.2
Small cell lung cancer	14	20.3
Unknown	8	11.6
Comorbidities		
Congestive heart failure/ischemic heart disease	11	15.9
Chronic renal insufficiency (Cr >120)	6	8.7
Diabetes	15	21.7
COPD	24	34.8
Entrance complaint		
Dyspnea	30	43.5
Known lung tumour	17	24.6
Hemoptysis	3	4.3
Cough	12	17.4
Reason for admission to MICU		
Postoperative	19	27.5
Respiratory failure	52	75.4
Sepsis	13	18.8
Other	35	50.7
MICU treatment		
Invasive mechanical ventilation	55	79.7
Noninvasive mechanical ventilation	9	13.0
Vasopressors	31	44.9
Renal Replacement Therapy	4	5.8
Invasive monitoring (Swan-Ganz)	23	33.3
Chemotherapy	11	15.9
Pre-admission	4	5.8
During admission	7	10.1
Radiation therapy	7	10.1
Surgery	42	60.9
Complications		
Respiratory	43	62.3
Cardiac	29	42.0
Febrile Neutropenia	3	4.3
Median MICU length of stay (days)	3 (0–30)	
Median hospital length of stay (days)	13 (0–74)	
MICU mortality	35	50.7
Hospital mortality	45	65.2

and 11.6% had an unknown type (lack of definitive pathologic differentiation).

On presentation to the hospital, 43.5% of patients complained of dyspnea and 17.4% complained of cough. Interestingly, only 3 patients presented with hemoptysis. Respiratory failure was seen in 75.4% of patients who were admitted to the MICU, and postoperative status and sepsis accounted for 27.5% and 18.8%, respectively. Other reasons included pericardial tamponade, congestive heart failure, myocardial infarction, cardiac arrest, cardiogenic shock, acute renal failure, and pulmonary embolism.

Although in the MICU, almost all the patients required mechanical ventilation, either invasive (79.7%) or noninvasive (13.0%). In addition, nearly 45% of patients required vasopressor support at some point during their MICU admission. A smaller percentage of patients required renal replacement therapy (5.8%). Of the 42 patients who underwent surgical procedures as noted in Table 1, 21 underwent bronchoscopy (30.4%), 11 underwent pulmonary lobectomy (15.9%), 5 underwent pericardial window (7.2%), and 1 underwent a pneumonectomy (1.4%).

The MICU mortality rate was 50.7%; the median length of MICU stay was 3 days (range 0–30 days). The median hospital length of stay was 13 days (range 0–74 days) with a mortality rate of 65.2%. The higher hospital mortality rate compared with MICU mortality rate occurred upon transfer of patients from the MICU to the general ward.

Predictive Factors for Outcomes and Lengths of Stay

Multivariate analysis revealed that APACHE II scores, TISS scores and a diagnosis of non-small cell lung cancer (NSCLC) were significantly associated with MICU mortality. A history of chronic obstructive pulmonary disease (COPD) and postoperative admission status were predictive of transfer from the MICU to the wards (Table 2). Age and APACHE II scores were associated with an increase in hospital mortality, while COPD and having elective surgery were predictive of being sent home from the hospital.

An increased length of stay in the MICU was predicted in patients who were admitted secondary to respiratory failure and those who required invasive hemodynamic monitoring with the use of a Swan Ganz monitor. Hospital length of stay was prolonged in patients who received chemotherapy during their hospital admission and those who required mechanical ventilation during their MICU admission.

Because the data collected in this article extend from 1994 to 2004, a comparison was done between subjects admitted to MICU from 1994 to 1998 versus subjects for the period 1999 to 2004. The mortality rates in MICU were similar (50.7% vs. 51.2%), whereas a non statistical difference was found vis-à-vis hospital deaths 67.4% versus 61.5%. The length of MICU and hospital stay was also not significantly different between the 2 periods, a median of 3 versus 2.5 days and 13 versus 10 days, respectively.

TABLE 2. Prognostic Factors as Determined by Multivariate Analysis

	Variable	Adjusted Odds Ratio	95% Confidence Limits
MICU death	APACHE	1.277	1.093–1.493
	TISS	1.091	1.009–1.181
	NSCLC	9.461	1.431–62.554
Transfer from MICU to wards	Postoperative	7.322	1.281–41.831
	COPD	14.230	2.562–79.036
Hospital death	Age	1.164	1.053–1.287
	APACHE	1.232	1.034–1.467
Transfer from hospital to home	COPD	4.94	1.033–21.332
	Elective surgery	27.412	2.429–309.331

DISCUSSION

Despite significant improvements in supportive critical care over the past few decades, the prognosis of patients admitted to the MICU remains unfavorable. This is especially true in patients with malignancies and is often a topic of much debate in view of the scarce MICU and financial resources available to support hospitalized cancer patients who have developed complications either due to their disease or treatment. Our study demonstrated a mortality rate of 50.7% among 69 primary lung cancer patients admitted to the MICU from 1994 to 2004, which contrasts with the 66.7% mortality rate seen in a smaller group of 38 lung cancer patients retrospectively studied from 1986 to 1996.[6]

Kroschinsky et al examined the outcome and prognostic features in patients with hematological malignancies admitted to the MICU and reported an overall MICU mortality rate of 44% with a statistically significant difference between patients requiring mechanical ventilation and nonventilated patients (74% vs. 12%, $P < 0.001$).[7] Multivariate analysis revealed only SAPS II as an independent predictor of MICU mortality, whereas both SAPS II and mechanical ventilation predicted long-term survival. Similarly, Kress et al reported a 67% mortality rate among 153 cancer patients admitted to the MICU who received mechanical ventilation from 1993 to 1996,[8] and Azoulay et al reported a 60.9% mortality rate in a group of 105 cancer patients who received mechanical ventilation in the MICU from 1996 to 1998.[3] The mortality rate among the 64 ventilated patients in our study was 52.3%. Because the number of patients who did not receive mechanical ventilation was too small, a statistically significant difference in mortality rate between the 2 groups could not be determined.

Azouley and Afessa hypothesized that the improved mortality rates among critically ill cancer patients in recent years may be attributed to 3 factors: (1) patients with poor functional status and underlying comorbidities and no available treatment for their underlying medical conditions may be denied ICU admission; (2) improved understanding of the pathophysiology of malignancy-related complications has resulted in the development of more effective treatment options with less complications; and (3) the development of noninvasive mechanical ventilation has reduced the need for endotracheal intubation and the associated mortality rate.[9]

Abbas et al examined gynecologic oncology patients admitted to the surgical intensive care unit (SICU) to determine the risk factors for outcome and survival.[10] They noted that 27.4% (20 of 73 patients) died in the hospital and that survival was negatively impacted by multiple medical conditions that predicted an ICU stay of longer than 5 days. Ovarian cancer patients were noted to have longer hospital stays and a poorer survival.

In our study, patients who underwent elective surgery were more likely to have shorter hospital length of stay, which probably reflects a better prognosis in a subset of patients with good physical condition, minimal or no comorbidities and good performance status. Neutropenia, a common occurrence in cancer patients after chemotherapy, was not associated with mortality or prolonged length of stay. Good performance status and acceptable stable comorbidities are likely to lead to chemotherapy compared with those not eligible for treatment. Presence of COPD was also associated with significantly better ICU and hospital survival, thus possibly selecting out patients requiring hospitalization with COPD exacerbation concomitant to lung cancer.

Treatment of patients with intravenous chemotherapy within the ICU has been examined for patients with newly diagnosed malignancies or specific malignancy-related organ involvement. A recently published article by Benoit et al assessed the outcome of severely ill patients with hematological malignancy, who received intravenous chemotherapy in the ICU for a life-threatening malignancy-related complication. A total of 37 patients with a variety of complications, including extensive disease with or without organ involvement and severe disseminated intravascular coagulation, received chemotherapy treatment.[11] Only mechanical ventilation during the ICU admission was associated with in-hospital mortality in this population. The in-hospital mortality rate was 43%, and the 6-month mortality rate was 67%. A similar study by Darmon et al examined a mixed population of hematological and solid tumor malignancies to determine the outcomes of these patients requiring both ICU management for acute organ failures and immediate chemotherapy.[12] The independent predictors for 30-day mortality were vasopressor drugs usage, mechanical ventilation, and hepatic failure. The authors also noted a strong association between patient survival and number of organ failures, especially respiratory and cardiovascular failure, which predicted a greater risk of death. In our study, among the 11 patients who received chemotherapy in the MICU, the mortality rate was 62%, and chemotherapy status was not a predictor of prognosis.

In a single center study by Wallace et al, the authors reported their data from 22 other studies published between 1967 and 2001 that documented the outcome of cancer patients who received in-hospital cardiopulmonary resuscitation (CPR).[13] Eleven of the 22 studies noted no survivors, and higher survival rates were documented at specialized cancer centers but still ranged from 9.6% at M.D. Anderson Cancer Center in Houston, Texas to 15.6% at Memorial Sloan-Kettering Cancer Center in New York. The authors noted that over an 8-year period at the M.D. Anderson Cancer Center, 406 patients underwent CPR out of a total of 5196 admissions. Of these patients, 37% patients survived the initial cardiac arrest. However, only 2% of patients with solid tumors and an equally dismal number of patients undergoing hematopoietic stem cell transplantation or those diagnosed with leukemia that underwent CPR survived to hospital discharge. The authors concluded that "once a patient with cancer becomes critically ill and develops cardiac arrest, the chances of survival to discharge are poor." Thus, they advocate full supportive care for cancer patients who require admission to the ICU, excluding CPR.

In recent years, we have seen overall improvements in long-term survival rates for many types of cancers due to increased detection of early stage disease and more effective treatments that often involve multimodality therapy such as surgery and radiation therapy and also second- and even third- line chemotherapeutic regimens.[14] In NSCLC, the advent of targeted therapies such as erlotinib as used in the advanced disease setting after first or second line regimens fail, can prolong survival and improve symptom control.[15] Unfortunately, this has not translated into significant improvements in terms of 20-year relative survival rate, which remains extremely poor in contrast to other malignancies.[14] As these patients survive longer, it is inevitable that complications that may warrant admission to the MICU may arise secondary to either their disease or the treatment they receive. Chemotherapy-related organ toxicities or immunosuppressant related infections are a few such complications. It is also conceivable that the advances over the past few decades in supportive and critical care, such as invasive and noninvasive mechanical ventilation, renal replacement therapy, management of sepsis, and supportive therapy for organ failure, would have resulted in significantly better outcomes for cancer patients admitted to the MICU. However, the current mortality rates indicate that even though progress has been made, there remain ample expectations for improvement.

We conclude that there is a high mortality rate associated with MICU admission for patients with previously or newly diagnosed primary lung cancer. However, it has improved over the previous decade and is comparable to that among patients requiring MICU admission for other illness such as pneumonia, adult respiratory distress syndrome, sepsis, and cardiac arrest.[16] Increased mortality is associated with higher APACHE II scores, TISS scores, and NSCLC. An increase in length of ICU stay was predicted by respiratory failure, use of a Swan Ganz monitor, concurrent chemotherapy, and mechanical ventilation.

REFERENCES

1. Canadian Cancer Society, National Cancer Institute of Canada. *Canadian Cancer Statistics 2006.* Toronto, Canada: Canadian Cancer Society; 2005.
2. Spira A, Ettinger DS. Multidisciplinary management of lung cancer. *N Engl J Med*. 2004;350:379–392.
3. Azoulay E, Alberti C, Bornstain 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.
4. Benoit DD, Hoste EA, Depuydt PO, et al. Outcome in critically ill medical patients treated with renal replacement therapy for acute renal failure: comparison between patients with and those without haematological malignancies. *Nephrol Dial Transplant*. 2005;20:552–558.

5. Larche J, Azoulay E, Fieux F, et al. Improved survival of critically ill cancer patients with septic shock. *Intensive Care Med*. 2003;29:1688–1695.
6. Boussat S, El'rini T, Dubiez A, et al. Predictive factors of death in primary lung cancer patients on admission to the intensive care unit. *Intensive Care Med*. 2000;26:1811–1816.
7. Kroschinsky F, Weise M, Illmer T, et al. Outcome and prognostic features of intensive care unit treatment in patients with hematological malignancies. *Intensive Care Med*. 2002;28:1294–1300.
8. Kress JP, Christenson J, Pohlman AS, et al. Outcomes of critically ill cancer patients in a university hospital setting. *Am J Respir Crit Care Med*. 1999;160:1957–1961.
9. Azoulay E, Afessa B. The intensive care support of patients with malignancy: do everything that can be done. *Intensive Care Med*. 2006;32:3–5.
10. Abbas FM, Sert MB, Rosenshein NB, et al. Gynecologic oncology patients in the surgical ICU. Impact on outcome. *J Reprod Med*. 1997;42:173–178.
11. Benoit DD, Depuydt PO, Vandewoude KH, et al. Outcome in severely ill patients with hematological malignancies who received intravenous chemotherapy in the intensive care unit. *Intensive Care Med*. 2006;32:93–99.
12. Darmon M, Thiery G, Ciroldi M, et al. Intensive care in patients with newly diagnosed malignancies and a need for cancer chemotherapy. *Crit Care Med*. 2005;33:2488–2493.
13. Wallace SK, Ewer MS, Price KJ, et al. Outcome and cost implications of cardiopulmonary resuscitation in the medical intensive care unit of a comprehensive cancer center. *Support Care Cancer*. 2002;10:425–429.
14. Brenner H. Long-term survival rates of cancer patients achieved by the end of the 20th century: a period analysis. *Lancet*. 2002;360(9340):1131–1135.
15. Shepherd FA, Rodrigues Pereira J, Ciuleanu T, et al. Erlotinib in previously treated non-small-cell lung cancer. *N Engl J Med*. 2005;353:123–132.
16. Staudinger T, Stoiser B, Mullner M, et al. Outcome and prognostic factors in critically ill cancer patients admitted to the intensive care unit. *Crit Care Med*. 2000;28:1322–1328.