Short-term mortality among patients with non–small cell lung cancer and respiratory failure: a retrospective study

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Abstract

Lung cancer remains the number one cause of malignancy-related mortality in the United States. Identifying risk factors that are predictive of short-term mortality among patients with non-small cell lung cancer will allow the patients, their families and health care providers to be better prepared emotionally for the fatal outcome and may attenuate the cost and distress associated with often futile measures. The objective of this study was to measure the 3-month mortality among patients with non-small cell lung cancer who developed respiratory failure. This retrospective study reviewed the outcome of all patients with inoperable non-small cell lung cancer who were admitted to our hospital with respiratory failure. Respiratory failure was defined as need for mechanical ventilation, noninvasive ventilation, or at least 50% fraction of inspired oxygen. Short-term mortality was defined as death in the hospital or within 3 months of discharge, as well as discharge to hospice; short-term mortality was found to be 94.4% in the study population. The prognosis of patients with inoperable non-small cell lung cancer and respiratory failure is grave. Short-term mortality among this patient population is close to 100%.

Introduction

Trachea, lung, and bronchus cancer remains the number one cause of malignancy-related mortality in the United States. It is responsible for close to 160,000 deaths annually and represents 28% of all cancer deaths.[1] Unlike the leading cause of mortality- major cardiovascular diseases- cancer-related death is generally much more predictable once the diagnosis is established. Extensive data exist on lung cancer survival rates by stage.[2,3] The available information about expected short-term mortality among patients with lung cancer who develop certain potentially predictive symptoms or complications is much more limited. Identifying risk factors for short-term mortality will allow health care professionals to better mentally prepare the patients, their families and themselves for an unfavorable outcome. The focus of patient management can be shifted to less aggressive care and to comfort.

Survival will be poorer in the subset of patients having lung cancer who develop respiratory failure compared with patients having the same-stage lung neoplasm who do not develop respiratory failure. In a study 25 years ago among a population with unresectable small cell lung cancer and non-small cell lung cancer who required mechanical ventilation, Ewer et al. found that mortality exceeded 95%.[4] Eighty-five percent died while on mechanical ventilation. Groeger et al. documented 76% in-hospital mortality among patients requiring mechanical ventilation who had a diagnosis of any malignancy.[5] In 2003, Lin *et al.* studied patients with lung cancer who required mechanical ventilation for longer than 24 hours and found that an Acute Physiology and Chronic Health Evaluation (APACHE) III score less than 70 and a fraction of inspired oxygen (FIO2) less than 0.6 were predictive of somewhat better chance of weaning from the respirator. The overall hospital mortality still exceeded 85%.[6] Studies evaluating mortality among patients with lung cancer requiring intensive care for any reason reveal a broader range of findings because of different criteria used for intensive care unit admission.[7,8]

The objectives of this study were to measure short-term mortality (death occurring in the hospital or within 3 months of discharge) among patients having inoperable non-small cell lung cancer admitted with respiratory failure and to identify risk factors for death at the time of acute respiratory failure. In contrast to previously reported data, this study targets a more homogeneous and narrowly defined population with surgically incurable non-small cell lung cancer.

Materials and Methods

The study design was approved by the Institutional Review Board at University of Southern California (USC). Medical records of patients admitted to USC University Hospital/Norris Comprehensive Cancer Center between January 1999 and December 2009 who met the following criteria were reviewed: diagnosis of unresectable non-small cell lung cancer (or inoperable patient) and respiratory failure at the time of admission or any time before discharge. For the purpose of this study, respiratory failure was defined as need for intubation unrelated to a procedure, use of noninvasive ventilation, or requirement of at least 50% FIO_2 (Table 1). The collected data included patient demographics, type and stage of non-small cell lung cancer,[9] length of hospital and intensive care unit stay, discharge to hospice or death in the hospital or within 3 months of discharge (short-term mortality) (Table 1), APACHE-II score at the time of admission or respiratory failure, evidence of carbon dioxide retention (partial carbon dioxide tension >45 mm Hg), history of chronic obstructive pulmonary disease (COPD), and duration of mechanical ventilation. Mortality among the admitted patients was measured as a percentage (95% confidence interval) based on binomial distribution. The study design included multiple regression analysis to identify risk factors for short-term mortality.

Results

Eighteen patients met the study criteria (Table 2). There were 8 cases of adenocarcinoma, 5 cases of squamous cell carcinoma, 2 cases of bronchoalveolar carcinoma, and 3 cases of poorly differentiated non-small cell lung cancer.

Seventeen of 18 patients (94.4%, 95% confidence interval, 72.7-99.9%) met the criteria for short-term mortality. The single patient who was alive 3 months after leaving the hospital died 1 month later at a nursing home. Because of the extremely high mortality, no regression analysis could be performed to identify risk factors for death. Respiratory failure with a

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Key words: lung cancer, mortality, respiratory failure.

Contributions: all authors have contributed equally.

Conflict of interest: the authors report no conflicts of interest.

Received for publication: 9 April 2011.
Accepted for publication: 9 June 2011.

Chest Disease Reports 2011; 1:e7
doi:10.4081/cdr.2011.e7

diagnosis of surgically incurable lung cancer appeared to be the major determinant of short-term mortality irrespective of underlying COPD, APACHE score, acute etiology of respiratory failure, or other factors. No patient was managed with noninvasive ventilation alone. Hypercapnia was uncommon (one-third of all cases). Three patients (16.6%) were discharged to Hospice. One patient was placed in a nursing home at the time of discharge. The rest of the study population all died in the hospital after a mean hospital stay of 13.6 days.

Table 1. Study definitions of respiratory failure and short-term mortality.

Respiratory failure	Short-term mortality
Intubation (other than anesthesia related)	Death in the hospital
Need for noninvasive ventilation	Death within 3 months of discharge
FIO_2 ≥50%	Discharge to hospice

FIO_2, fraction of inspired oxygen

Table 2. Study population demographics.

Study population (n=18)	94.4% Value
Age, mean (SD), (years)	63.9 (14.0)
Male/female ratio	13/5
Lung cancer Stage I	0
Stage II	0
Stage III	5
Stage IV	13
ICU stay, mean (SD), (days)	10.9 (10.4)
Hospital stay, mean (SD), (days)	13.6 (16.2)
Duration of mechanical ventilation, mean (SD), (days)	12.4 (11.3)
APACHE II score, mean (SD)	12.7 (3.0)
Carbon dioxide retention (% patients)	33.3
Time since diagnosis of lung cancer was established, mean (SD), (months)	12.3 (11.8)
History of COPD (% patients)	17

APACHE, Acute physiology and chronic health evaluation; COPD, chronic obstructive pulmonary disease; ICU, intensive care unit.

Discussion

This study confirms that the prognosis of patients with non-small cell lung cancer and respiratory failure is grave. Because of the anatomic location and natural course of non-small cell lung cancer, respiratory failure is a common terminal complication in incurable cases. Owing to the almost universal mortality found in our study, we were unable to identify any additional risk factors beyond the presence of respiratory failure.

The study institution does not have an emergency department. This explains the relatively small number of patients meeting the study criteria. It also introduces a potential for selection bias. Although we can speculate that patients with more severe respiratory failure may have been admitted and treated on an emergent basis at other institutions (therefore not invalidating our high-mortality findings), the exact effect and bias potential of this fact cannot be completely ignored.

In our study, all patients who met the inclusion criteria had stage 3 or stage 4 lung cancer, with more than two-thirds having stage 4. This is understandable considering that it is difficult from an anatomic standpoint for stage 1 or stage 2 lung cancer to independently cause respiratory failure. We would be reluctant to apply our findings to patients with early-stage non-small cell lung cancer who develop respiratory failure presumably as a result of some additional cardiopulmonary compromise (e.g., nonobstructive pneumonia, congestive heart failure, or COPD exacerbation). Also, we limited our patient population to those with non-small cell lung cancer, and no conclusions should be extrapolated to patients with small cell lung cancer. It is well known that the pathophysiologic behavior of small cell lung cancer is completely different. The latter type of lung neoplasm is distinguished clinically by its rapid doubling time, high growth fraction, and early development of metastases. The responsiveness of small cell lung cancer to chemotherapy is much greater than that of non-small cell lung cancer, and cure is achieved by combination chemotherapy and radiation therapy in 10% to 15% of patients with limited-stage disease.[10]

Watching a loved one die is a difficult experience to endure. The physical and emotional tolls on the patient himself are even greater considering the uncertain benefit of procedures performed to treat his terminal disease. Better prognostic tools can aid in designing a more appropriate care plan that allows patients and family members to more effectively use their remaining time together and will likely reduce the number of futile, painful, and expensive procedures. Patients with chronic illness account for 32% of total Medicare spending in their last 2 years of life; this amounts to more than $46,000 per chronically ill beneficiary.[11] With continuously increasing costs of health care, the cost-benefit ratio of any therapeutic or diagnostic modality is scrutinized more than ever. Proper cost-effectiveness analysis is a necessity in today's health care and is an integral part of any health policy. In summary, our study adds to the literature a more precise measurement of the grave prognosis among patients with inoperable non-small cell lung cancer complicated by respiratory failure. The short-term mortality among this patient population is close to 100%. In view of the ever-increasing financial burden of end-of-life care to the health system, as well as the high emotional toll and pain that patients and family members incur during the final days of life, more accurate data about expected mortality will benefit those facing end of life, health care professionals, and society at large.

References

1. Heron M, Hoyert DL, Murphy SL, Xu J. Deaths: final data for 2006. Nati Vital Stat Rep 2009;57:1-134.
2. Mountain CF. Revisions in the International System for Staging Lung Cancer. Chest 1997;111:1710-7.
3. Yano T, Morodomi Y, Ito K, et al. Verification of the newly proposed T category (seventh edition of the tumor, node, and metastasis classification) from a clinicopathological viewpoint in non-small cell lung cancer-special reference to tumor size. J Thorac Oncol 2010;5:45-8.
4. Ewer MS, Ali MK, Atta MS, et al. Outcome of lung cancer patients requiring mechanical ventilation for pulmonary failure. JAMA 1986;256:3364-6.
5. Groeger JS, White P Jr, Nierman DM, et al. Outcome for cancer patients requiring mechanical ventilation. J Clin Oncol 1999; 17:991-7.
6. Lin YC, Tsai YH, Huang CC, et al. Outcome of lung cancer patients with acute respiratory failure requiring mechanical ventilation. Respir Med 2004;98:43-51.
7. 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.
8. Soares M, Darmon M, Salluh JI, et al. Prognosis of lung cancer patients with life-threatening complications. Chest 2007;131: 840-6.
9. Greene FL, Page DL, Fleming ID, et al., editors. AJCC cancer staging handbook. Berlin: Springer Verlag; 2002.
10. Jänne PA, Freidlin B, Saxman S, et al. Twenty-five years of clinical research for patients with limited-stage small cell lung carcinoma in North America. Cancer 2002;95:1528-38.
11. Wennberg JE, Fisher ES, Goodman DC, Skinner JS. Tracking the Care of Patients with Severe Chronic Illnes- The Dartmouth Atlas of Health Care 2008. Dartmouth Institute for Health Policy and Clinical Practice; 2008.