# Predictors of mortality in cancer patients who need intensive care unit support: a two center cohort study

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**Background/aim:** Cancer patients frequently need intensive care support due to respiratory failure. We aimed to evaluate the predictors of mortality in cancer patients who were admitted to the intensive care unit (ICU).

**Materials and methods:** This study was performed in the ICUs of two centers between 1 January 2008 and 31 December 2015. Demographic data, cancer type, causes of respiratory failure, comorbidities, APACHE II scores, treatments, and mortality rates were recorded.

**Results:** A total number of 583 cancer patients (477 males) were enrolled from the two centers. Of those, 472 patients had lung cancer (81%), while 111 had extrapulmonary malignancies (19%), having similar mortality rates. Causes of respiratory failure were mostly invasion of the cancer itself in 84% of cases and due to infection in 12%. ICU mortality rate was 53% and the 1-year mortality rate was 80%. APACHE II scores were significantly higher in nonsurvivors (P < 0.001). One-year survival was found to be significantly shorter in females than males (9 days vs. 12 days) in patients with lung cancer.

**Conclusion:** Mortality rates of cancer patients who need ICU support are higher than overall ICU mortality. High APACHE II scores and female sex seem to be related to mortality in these patients.

**Key words:** Intensive care unit, cancer, respiratory failure, mortality

## 1. Introduction

Respiratory failure requiring intensive care support holds an important place among cancer patients. Due to an increase in the incidence of cancer and treatment facilities together with improvements, the number of cancer patients is increasing in intensive care units (ICUs). The main causes of respiratory failure in patients with malignancies are commonly infections, pulmonary embolism, direct tumoral involvement of the respiratory system, cancer-related medical disorders, and anticancer drug-induced respiratory distress (1). Accompanying diseases such as chronic obstructive pulmonary disease (COPD) and complications of the primary disease requiring ICU support may also lead to respiratory failure and cause higher mortality (2).

Today, developing techniques and intensive care support may be life-saving in selected patients undergoing oncologic treatment. ICU admission is costly, so predicting cancer patients who may benefit from ICU treatment is important, especially in developing countries. To select patients for ICU admission, information on factors associated with ICU mortality is required.

In this study, we aimed to evaluate the outcome and factors affecting survival of patients with advanced lung cancer and other cancers (breast, prostate cancer, etc.) who were admitted to the ICU.

## 2. Materials and methods

This study was performed in the medical ICUs of two teaching hospitals specializing in pulmonary diseases. After obtaining approval from the institutional review board, a retrospective analysis of the medical records of cancer patients who were admitted to the two ICUs was performed between 1 January 2008 and 31 December 2015. Patients who were treated in the ICU for less than 24 h 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

744

same hospitalization, only the first ICU admission was analyzed.

Demographic, physiological, and clinical data including age, sex, race, smoking history, and comorbidities upon admission to the ICU were retrieved.

The Acute Physiology and Chronic Health Evaluation (APACHE) II score was calculated retrospectively for each patient based on data obtained within the first 24 h after their admission to ICU.

## 2.1. Statistical analysis

All patients were evaluated longitudinally to determine their ICU and hospital outcomes. Values were reported as medians (interquartile ranges) and compared by the Mann–Whitney U test. All percentages were approximated to round numbers. Nominal data were analyzed using the chi-square test. Multiple logistic regression analysis was used to identify the variables that were independently associated with mortality. Each variable that was found to be significant at $P < 0.05$ by univariate analysis was introduced into a backward, stepwise, logistic regression model. Risk estimations were expressed as odds ratios with 95% confidence intervals (OR, 95% CI). $P < 0.05$ was used to indicate statistical significance.

## 3. Results

Between 1 January 2008 and 31 December 2015, there were 583 admissions of patients with cancer in the two ICUs. Of these patients, 82% were male and 18% were female. Median age was 64 (57–71) years. Comorbidities were reported in 71 patients. A total of 472 patients had lung cancer, while 111 patients had extrapulmonary cancer. Cancer invasion was the most frequent respiratory indication for ICU admission (391 patients); the second most common respiratory condition was pneumonia (57 patients) and other respiratory conditions included acute exacerbation of COPD, hemoptysis, and malignant pleural effusions. Initially, 451 patients required invasive mechanical ventilation (IMV), 98 patients were treated with noninvasive ventilation, and 34 patients had only medical or symptomatic (NIV) treatment. Median ICU stay length was 5 (2–10) days (Table 1). One-year mortality was 80%.

Median 1-year survival of all patients was 12 (95% CI: 10–14) days (Figure 1). One-year survival was slightly longer in males compared to females (log-rank P: 0.07, Figure 2). When only patients with lung cancer were evaluated, 1-year survival was found to be significantly shorter in females than males (log-rank P: 0.015, Figure 3)

## 3.1. Factors predicting ICU mortality

Of the 583 patients, 311 died in the ICU (53%) and 272 patients were discharged from ICU. In univariate analysis, age, comorbidities, and sex did not influence ICU mortality. Patients with lung cancer and those with extrapulmonary cancer did not differ in terms of mortality rate. APACHE II severity scores significantly predicted ICU mortality ($P < 0.001$). A need for intubation and IMV was associated with higher mortality rates ($P < 0.001$) (Table 2).

Multivariate analysis identified three factors independently associated with higher ICU mortality: female sex (OR: 2.07, 95% CI: 1.23–3.49, P = 0.006), need for intubation and IMV (OR: 2.84, 95% CI: 1.73–4.68, P < 0.001), and APACHE II score (OR 1.10, 95% CI: 1.07–1.13, P < 0.001) (Table 3).

**Table 1.** Demographic data of cancer patients in the ICU.

| | |
|---|---|
| Age, median (IQR) | 65 (57–72) |
| Males, n (%) | 477 (82) |
| APACHE II score, median (IQR) | 24 (18–30) |
| Existence of comorbidity, n (%) | 74 (13) |
| Cancer type, n (%)<br>　　　Pulmonary<br>　　　Extrapulmonary | <br>472 (81)<br>111 (19) |
| Cause of respiratory failure, n (%)<br>　　　Invasion of the cancer<br>　　　Infection<br>　　　Other | <br>391 (67)<br>92 (16)<br>100 (17) |
| Need for intubation and IMV, n (%) | 453 (78) |

APACHE: Acute Physiologic and Chronic Health Evaluation, IMV: invasive mechanical ventilation, IQR: interquartile range.
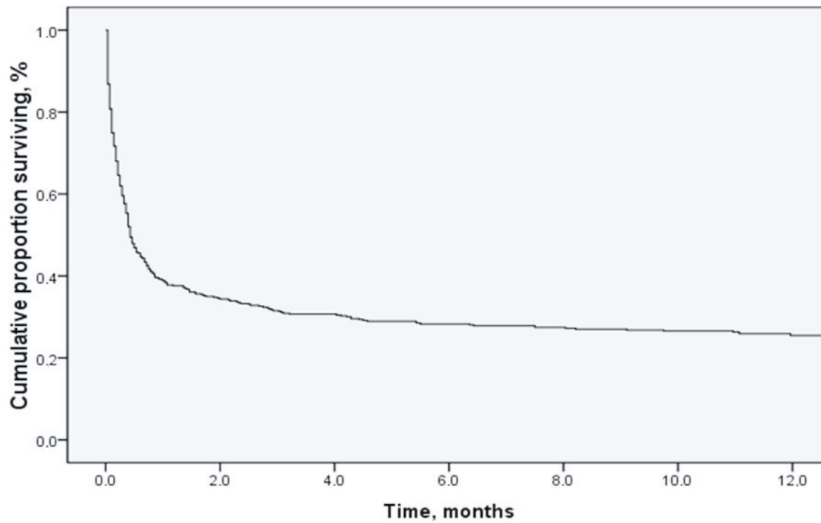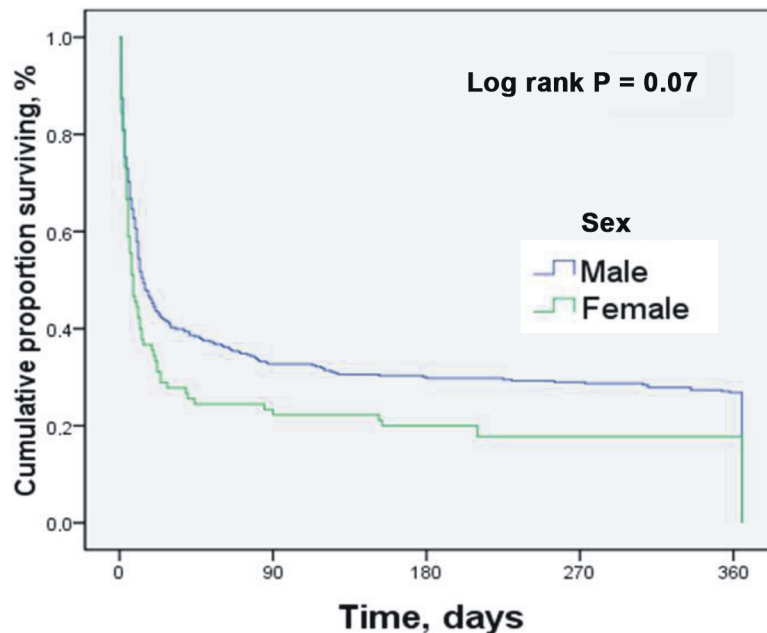
**Figure 1.** Kaplan–Meier survival of all patients.



**Figure 2.** Comparison of survival curves of male and female patients.

## 4. Discussion

A large proportion of cancer patients experience acute life-threatening episodes related to their malignancy, treatment, or comorbidities. Until recently, ICU admission of patients with advanced cancer was controversial and generally discouraged (3). However, over the last decade, several studies found increased survival rates in this population (4,5). Advances in both oncology and intensive care may have contributed to improved survival rates, along with better selection of the patients most likely to benefit from ICU admission (6).

We found an ICU mortality rate of 53%. These results are in accordance with the data recently reported by Reichner et al. (7), Rocques et al. (8), and Andréjak et al. (9). However, our patients had more advanced disease than those in the earlier studies, and also some of our patients had extrapulmonary cancer (but most of them had pulmonary cancer), suggesting that ICU mortality rates may have improved as noticed in other recent studies.

Mortality rates in lung cancer patients admitted to the ICU have decreased over time. In early studies, mortality ranged from 75% to 91% (10–12). Although Adam et al.
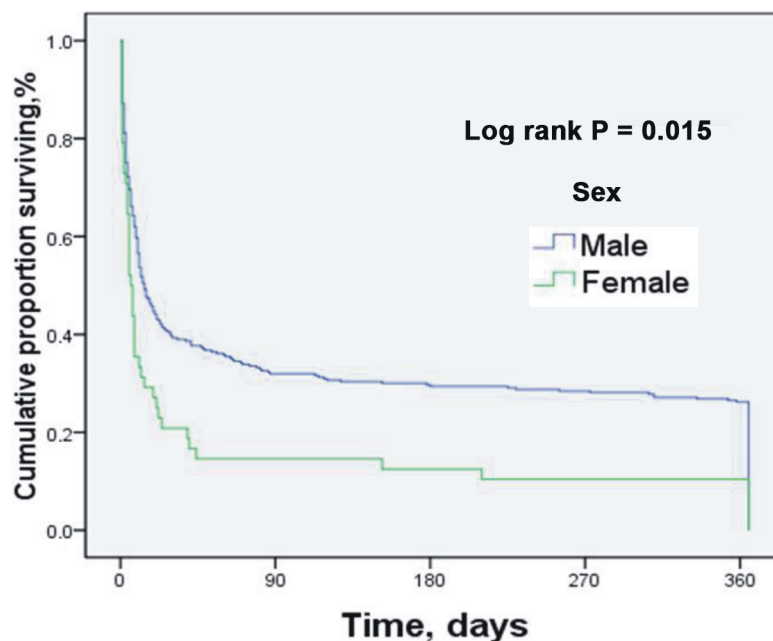
**Figure 3.** Comparison of survival curves of male and female lung cancer patients.

**Table 2.** Comparison of data between survivors and nonsurvivors in the ICU.

| Variable | Survivors n = 272 | Nonsurvivors n = 311 | P |
|---|---|---|---|
| Age, median (IQR) | 64 (57–70) | 65 (57–72) | 0.23 |
| Sex, n (%) Female Male | 42 (16) 230 (84) | 64 (20) 247 (80) | 0.13 |
| Existence of comorbidity, n (%) | 39 (14) | 35 (11) | 0.32 |
| Cancer type, n (%) Pulmonary Extrapulmonary | 216 (79) 56 (21) | 256 (82) 55 (18) | 0.39 |
| APACHE II, median (IQR) | 19 (15–25) | 27 (22–32) | <0.001 |
| Length of ICU stay, days, median (IQR) | 6 (3–11) | 4 (2–10) | 0.01 |
| Need for intubation and IMV, n (%) | 171 (63) | 282 (91) | <0.001 |

APACHE: Acute Physiologic and Chronic Health Evaluation, ICU: intensive care unit, IMV: invasive mechanical ventilation, IQR: interquartile range.

(13) recently reported an ICU mortality rate of only 22%, only 49% of their patients required mechanical ventilation (versus 78% intubation and mechanical ventilation requirement in our study). Moreover, the study by Adam et al. included patients with all stages of lung cancer. In our study, mortality was highest in the intubated and mechanically ventilated patients, as well as in Adam et

al.'s study. Our study also included patients with locally advanced and advanced lung cancer and extrapulmonary cancers.

ICU mortality was not significantly influenced by age or comorbidities in the present study. Female sex was associated with poor survival. Andréjak et al. found that ICU mortality was not significantly influenced by age, sex,

**Table 3.** Risk factors for mortality of cancer patients in the ICU.

| Variable | Odds ratio (95% CI) | P |
|---|---|---|
| Female sex | 2.07 (1.23–3.49) | 0.006 |
| APACHE II | 1.10 (1.07–1.13) | <0.001 |
| Need for intubation and IMV | 2.84 (1.73–4.68) | <0.001 |

CI: Confidence interval, APACHE: Acute Physiologic and Chronic Health Evaluation, ICU: intensive care unit, IMV: invasive mechanical ventilation.

or comorbidities. A history of thoracic radiotherapy was associated with significantly higher mortality, suggesting a link between radiation-induced pneumonitis and acute respiratory failure (9). Azevedo et al. reported that in multivariate logistic regression, medical admission, active underlying malignancy newly diagnosed, underlying malignancy in recurrence or progression, tumor as reason for ventilatory support, poor performance status, noninvasive ventilation followed by mechanical ventilation, only use of IMV, and higher SOFA scores (each point, excluding the respiratory domain) were independently associated with hospital mortality (1). In contrast to a report by Reichner et al. (7) that stage IV non-small-cell lung cancer was independently associated with higher mortality, we found no significant influence on ICU mortality of the pulmonary and extrapulmonary cancers and type of pulmonary cancer.

APACHE II score significantly predict ICU mortality in our patients with cancer. On the other hand, the SAPS II and APACHE II scores did not significantly predict ICU mortality in advanced lung cancer. Similar results have been reported for the SAPS III and APACHE III scores (8,13,14).

The other variable available at admission and independently associated with ICU mortality by multivariate logistic regression was the need for intubation and mechanical ventilation. Roques et al. (15), Azoulay et al. (16), and Slatore et al. (17) found that need for mechanical ventilation was an independent factor for a worse prognosis in lung cancer.

The present study has important limitations, including the retrospective nature of the analysis, which may have resulted in selection bias, and the lack of assessment of potentially significant predictors of outcome, such as the role of progression of cancer, airway infiltration, severity of comorbid illnesses, complications of cancer therapy, or performance status in predicting the ICU outcome of cancer patients. Because the two centers are pulmonary centers, most of the patients had lung cancer, and for this reason, our results cannot be generalized for other cancer types. Moreover, improvements in cancer therapy and ICU treatment standards may lead to some bias. Prospective, multicenter trials are necessary to address these issues. In addition to data on mortality, we need information on outcomes in survivors after ICU and hospital discharge. We assessed 1-year survival of patients whose advanced stage cancer might have had poor prognosis. Postdischarge survival is strongly dependent on the malignancy type and its treatment (1). In the present study, females had poor survival. There was no relationship between sex and APACHE II score, mechanical ventilation requirement, and comorbidities. This result may be incidental; we need further information.

The present data suggest that the medical ICU outcome of cancer patients is improving but still worse than that of other critically ill patient populations. We know that ICU admission is costly, but we did not select patients who were likely to benefit from ICU admission. In addition, the patient and family should not be unnecessarily exposed to the burden associated with an ICU stay. Further studies concerning patients with cancer admitted to the ICU are needed to assess long-term mortality, quality of life, ability to continue chemotherapy, and socioeconomic cost.

In conclusion, the mortality rates of advanced stage cancer patients who need ICU support are still higher than overall ICU mortality. High APACHE II scores, female sex, and need for intubation and mechanical ventilation seem to be related to mortality in cancer patients who need ICU support. These predictors must be taken into account for the survival expectancy of these patients in the ICU.

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