Is C-Reactive Protein/Albumin Ratio of Advanced-Stage Non-small Cell Lung Cancer Patients Able to Predict Mortality in the Admission for Palliative Care?

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Abstract

Context: Lung cancer is frequent and mortal cancer. The predicting mortality may be helpful for cancer management. **Aim:** The purpose of the study was to evaluate the role of baseline C-reactive protein (CRP)/albumin ratio (CAR) in relation to hospital mortality, the setting of advanced stage non-small cell lung cancer (NSCLC). **Materials and Methods:** The present study is a retrospective analysis and included 77 adult patients with Stage IV NSCLC who were hospitalized for supportive care. All patients are divided into two groups as survivors and nonsurvivors. CAR on the admission was compared between groups. The correlation between CAR and the death time was investigated. The cutoff level of CAR was calculated, and patients with a high level were described in two groups. **Results:** For all participants, the mean age was 63.0 ± 9.9 years, and the median values of CRP and albumin levels were 15.3 mg/dl (1–51.5) and 5.7 g/dl (0.02–22.7), respectively. CAR was significantly lower in the survivor group. By receiver operation curve analysis, the cutoff levels of CRP and CAR were determined as 10.8 and 3.5, respectively. The odds ratio of mortality was 3.85 (1.49–9.94 95% confidence interval [CI], \(P = 0.006\)) for higher than cutoff levels of CAR. The odds ratio was 3.38 (1.32–8.65 95% CI, \(P = 0.01\)) for higher CRP levels. There was a significant but weak negative correlation between the time of death and both CRP and CAR in the nonsurvivor group (\(r = -0.46, P = 0.002; r = -0.48, P = 0.001,\) respectively). **Conclusion:** The present study showed that CAR was significantly increased in nonsurvivors. CAR may be a cheap, easy, and effective tool for predicting the death and its time of hospitalized NSCLC patients.

Keywords: Albumin, C-reactive protein, lung cancer, mortality

Introduction

Lung cancer is still a major death cause from cancer, and non-small cell lung cancer (NSCLC) accounts for approximately 85% of lung cancer patients.[1]

The predicting of mortality is crucial for disease management. Many studies have tried to find the best predictor for mortality. These predictors such as tumor stage, C-reactive protein (CRP)/albumin ratio (CAR), neutrophil/lymphocyte ratio (NLR), and platelet/lymphocyte ratio (PLR) were described by different trials.[2-4]

CRP reflects systemic inflammatory response. CRP/CAR was found as a prognostic factor for septic patients,[5] hepatocellular carcinomas,[6] esophageal squamous cell carcinoma,[7] and colorectal adenocarcinomas.[8] Systemic inflammation was associated with disease progression and worse outcomes according to findings of these trials.

The studies that were designed with CAR, often research for survival analysis. There is a lack of knowledge about the relation between CAR on the 1st day of admission and mortality in that hospitalization. The aim of this study was to evaluate the role of baseline CAR in relation to hospital mortality in the setting of advanced stage NSCLC.

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MATERIALS AND METHODS
The retrospective study included 77 adult patients with Stage IV NSCLC that were admitted in Kırıkkale University, School of Medicine, Department of Medical Oncology, for supportive and palliative care between January 2018 and January 2019 were evaluated. Forty-one patients died, and 36 patients discharged from the hospital. Discharged patients were defined as “Survivors,” and deceased patients were defined as “Nonsurvivors.” Medical records of laboratory parameters such as complete blood cell parameters, especially CRP and albumin levels, on the 1st day of hospitalization were noted. Neutrophil/lymphocyte and PLRs were calculated. The time of death after the admission was calculated as day. CAR was calculated by CRP/albumin formula. Between two groups, baseline characteristics and CAR were compared. The correlation between the day of death after admission and CAR was evaluated. The cutoff levels of CAR were calculated, and the risk of mortality was tried to determine.

Statistical analysis
For all statistical analysis, IBM Corp. Released 2017. IBM SPSS Statistics for Windows, Version 25.0. (Armonk, NY: IBM Corp.) was used. Normally distributed values were given as mean ± standard deviation, whereas abnormally distributed values were given as median (minimum–maximum). The Mann–Whitney U-test was performed for two group comparisons. The receiver operation curve (ROC) analysis was used for detecting a cutoff level of significant values. The Fisher’s exact test was used, and the odds ratio was calculated according to cutoff levels between the two groups. Spearman’s analysis was used for correlations. P < 0.05 was considered statistically significant.

Ethical consideration
The approval has been obtained from the Ethical Committee, Kırıkkale University.

RESULTS
There were 11 female and 66 male patients. For all participants, the mean age was 63.0 ± 9.9 years, and the median value of CRP and albumin levels was 15.3 mg/dl (1–51.5) and 5.7 g/dl (0.02–22.7), respectively. The age, sex, Charlson comorbidity scores, NLR, and PLR were similar by group comparisons. CAR was significantly lower in the survivor group. CAR has been calculated by CRP/albumin formula. Between two groups, baseline characteristics and CAR were compared. The correlation between the day of death after admission and CAR was evaluated. The cutoff levels of CAR were calculated, and the risk of mortality was tried to determine.

The CAR may reflect not only inflammatory conditions but also the nutritional status of cancer patients. Both malnutrition may affect CRP and albumin levels. Inflammation and nutrition relations had been demonstrated by many studies. It was demonstrated which the nutritional supports could decrease the CAR, reduce inflammation, and improve immune status. Therefore, the CAR could be used to evaluate nutritional status. Moreover, perhaps, the hospital mortality of NSCLC inpatients may be related to both inflammation and malnutrition.

The CAR has been investigated for survival analysis. Zhang et al. showed that CAR can predict long-term disease progression and death in patients with operable NSCLC independently. Investigators have discussed this condition with inflammation and malnutrition mechanisms too. In this study, NLR has found as predictable for disease outcomes. They thought that increasing of neutrophils and decreasing of lymphocytes may cause cytokine activation, restrain

Figure 1: The time of death and C-reactive protein/albumin ratio
lymphocyte associate killing. Furthermore, our study design
was different, but NLR was similar in study groups.

Ni et al.\(^{[21]}\) compared prognostic factors such as
Glasgow prognostic score, NLR, PLR, and CAR in advanced NSCLC patients. They have found that CAR may be a better
prognostic factor than the other inflammatory markers. They
discussed the mechanism of adverse outcomes about CAR that
was unclear. However, they thought it could be related to the
IL-6/JAK-STAT signaling pathway.

Koh and Lee\(^{[22]}\) studied the prognostic impact of CAR on
the overall survival of patients with advanced NSCLC receiving palliative chemotherapy. CAR has found as an
independent prognostic factor in patients, especially with
advanced lung adenocarcinomas receiving platinum-based chemotherapy.

This study has several limitations. Once, retrospective design
with the Turkish population and single-institution results
are some of them. The sample size was small. Also, CRP
and albumin can be influenced by numerous factors such as
infections, nutrition, and diabetes. The other inflammatory
markers could not be researched.

### Conclusion

The present study showed that CRP and CAR were significantly
increased in deceased patients by comparing survivors. CAR
may be slightly more predictive than CRP. CAR may be a
cheap, easy, and effective tool for predicting the death of
hospitalized NSCLC patients. Further larger investigations
are needed to clarify for explaining the role of inflammation
on cancer mortality and time of death.

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### Conflicts of interest
There are no conflicts of interest.

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### Table 1: Patient characteristics and laboratory values by group comparisons

|                      | Survivor (n=36) | Nonsurvivor (n=41) | P    |
|----------------------|----------------|-------------------|------|
| Age, year            | 62.8±9.9       | 63.5±10.0         | 0.71 |
| Female/male sex (n)  | 4/32           | 7/34              | 0.52 |
| Diagnosis            |                |                   |      |
| Squamous cell carcinoma (n) | 20          | 22                | 0.94 |
| Adenocarcinoma (n)   | 12             | 15                |      |
| Others (n)           | 4              | 4                 |      |
| Charlson comorbidity index | 8 (6-12)  | 8 (6-11)          | 0.90 |
| Time of death after admission, day | NA           | 6 (1-30)         |      |
| CRP, mg/dl           | 6.2 (0.1-39.7) | 16.1 (1.9-51.5)   | <0.001 |
| Albumin, g/dl        | 3.5 (1.9-4.3)  | 2.8 (1.8-4.1)     | <0.001 |
| CRP/albumin ratio    | 2.4 (0.02-1.4) | 7 (0.36-22.7)     | <0.001 |
| Neutrophil/lymphocyte ratio | 6.7 (0.3-38.4)| 10.3 (0.3-65.4)  | 0.10 |
| PLR                  | 229 (15.00-697.4) | 234.4 (2.50-5215.80) | 0.36 |

CRP: C-reactive protein, NA: Not available, PLR: Platelet/lymphocyte ratio

### Table 2: The patient distribution according to the cutoff level

|                   | Nonsurvivor (n) | Survivor (n) |
|-------------------|----------------|--------------|
| Patients with CAR ≥3.5 | 27            | 12           |
| Patients with CAR <3.5  | 14            | 24           |

CAR: C-albumin ratio

### Table 3: The patient distribution according to the cutoff level

|                    | Survivor (n) | Nonsurvivor (n) |
|--------------------|--------------|-----------------|
| Patient with CRP ≥10.8 | 19          | 8               |
| Patient with CRP <10.8  | 11          | 29              |

CRP: C-reactive protein

### Figure 2: The time of death and C-reactive protein
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