Prognostic Value of Blood Urea Nitrogen to Serum Albumin Ratio in Intensive Care Unit Patients with Lung Cancer

Xiulan Peng1,*, Yali Huang1,*, Haifeng Fu2,*, Zhi Zhang3, Anbing He1, Renfeng Luo4

1Department of Oncology, The Second Affiliated Hospital of Jianghan University, Wuhan, Hubei, People’s Republic of China; 2Department of Hepatopancreatobiliary Surgery, Sinopharm Dongfeng General Hospital, Hubei University of Medicine, Wuhan, Hubei, People’s Republic of China; 3Department of Intensive Care Unit, The Second Affiliated Hospital of Jianghan University, Wuhan, Hubei, People’s Republic of China; 4Department of Diagnostics, JiangHan University, Wuhan, Hubei, People’s Republic of China

*These authors contributed equally to this work

Background: We aimed to evaluate the prognostic ability of blood urea nitrogen (BUN) to serum albumin ratio (BAR) to predict in-hospital mortality in patients with lung cancer in the intensive care unit (ICU).

Methods: Medical Information Mart for Intensive Care IV (MIMIC-IV v1.0) database was used to identify patients who were diagnosed with lung cancer. The primary outcome was in-hospital mortality. Multivariate COX regression was used to investigate the association between BAR and in-hospital mortality and propensity score matching (PSM) and inverse probability of treatment weighting (IPTW) were also used to ensure the robustness of our findings. eICU-CRD database (validation cohort) was also applied to validate our findings.

Results: The optimal cut-off value for BAR was 6.8mg/g. Among 1202 patients who were diagnosed with lung cancer, 287 high-BAR group (≥6.8mg/g) patients and 287 low-BAR group (<6.8mg/g) patients, who had similar propensity scores were included in this study. After matching, the high-BAR group had significantly higher in-hospital mortality (hazard ratio, HR, 2.24, 95% confidence interval, 95% CI, 1.57–3.19, P<0.001) even after adjustment for confounding factors. Moreover, the performance of BAR was superior to that of BUN and serum albumin alone and could add net benefit in predicting in-hospital mortality. Those results were further confirmed in the validation cohort.

Conclusion: As an easily accessible and cost-effective parameter, BAR could serve as a good prognostic predictor for lung cancer patients in ICU.

Keywords: blood urea nitrogen to serum albumin ratio, lung cancer, intensive care unit, Medical Information Mart for Intensive Care, eICU-CRD, prognosis

Introduction

Despite great progress in our understanding of risk, development, and treatment options, lung cancer, which usually consists of small cell lung cancer and non-small cell lung cancer, remains one of the most common diagnosed cancers and the leading cause of cancer-related death worldwide.1–4 Due to the nature of the disease and the aggressive treatments, lung cancer patients usually require admission to intensive care units (ICU) for invasive monitoring or treatment.5–7 Compared with other solid tumors, lung cancer patients admitted to ICU tend to have one of the poorest ICU and in-hospital survival rates.8–10 Hence, it is essential for clinicians to identify lung cancer patients at high risk of mortality.

Serum albumin is one of the most familiar nutritional indexes and has been demonstrated to be a prognostic factor for different types of cancers.11–14 Blood
urea nitrogen (BUN) is an important parameter reflecting the relationship between kidney condition and nutritional status of patients and has also been found to be associated with mortality.\textsuperscript{15} Moreover, the combination of serum albumin and bun, bun to serum albumin ratio (BAR), which is calculated from the quotient between BUN and albumin, was introduced as an important predictor of mortality in various diseases, including gastrointestinal bleeding, community-acquired pneumonia and so on.\textsuperscript{16–18} However, to the best of our knowledge, no study has been constructed to investigate the association between BAR and in-hospital mortality for critical care patients with lung cancer. Hence, in the current study, we initially investigated the correlation between BAR and prognosis of ICU patients with lung cancer using data from the Medical Information Mart for Intensive Care IV (MIMIC-IV version 1.0) database. Then, propensity score matching (PSM) and propensity score-based inverse probability of treatment weighting (IPTW) was introduced to ensure the robustness of our results, we further verified this finding in another big public database (eICU Collaborative Research Database, eICU-CRD v2.0).

**Materials and Methods**

**Study Population**

We obtained data from the MIMIC IV database and eICU-CRD database in accordance with the ethical standards of the Institutional Review Board (IRB) of the Massachusetts Institute of Technology (MIT). eICU-CRD contains data of more than 200 thousand ICU admissions in 2014 and 2015 at 208 US hospitals while MIMIC-IV includes information of more than 70,000 patients admitted to the ICUs of Beth Israel Deaconess Medical Center in Boston, MA, from 2008 to 2019.\textsuperscript{19,20} This study was conducted in accordance with the Helsinki Declaration and authors had successfully accomplished the National Institutes of Health’s (NIH) online training course and the Protection of Human Research Participants Examination and got permission to extract data from MIMIC IV and eICU databases. Moreover, the study protocol was reviewed and successfully approved by the Ethics Committee of the Second Affiliated Hospital of Jianghan University. Considering that this was a retrospective study and all patients in this study were extracted from public database, informed consent was waived.

**Selection of Participants**

Adult patients who were diagnosed with lung cancer based on the ninth or tenth revision of International Classification of Diseases (ICD-9/10) code during their admissions were included in this study. Moreover, for patients readmitted to the ICU, only the first ICU and first hospital admissions were included in this study. We also excluded patients with missing bun or serum albumin or who spent less than 48 hours in the ICU (Figure 1).

**Variable Extraction**

Baseline characteristics and admission information: age, gender, weight, tumor type, and severity score measured by the sequential organ failure assessment (SOFA) score, the Oxford acute severity of illness score (OASIS), acute physiology score III (APSIII) and the Charlson comorbidity score were calculated as described in previous studies.\textsuperscript{21–24} Comorbidities including hypertension, diabetes, chronic kidney disease (CKD), congestive heart failure (CHF), myocardial infarct and liver disease were also collected for analysis based on the (ICD-9/10) codes. Complications including sepsis based on sepsis 3.0 criteria,\textsuperscript{25} acute kidney injury based on KDIGO guideline in 48 hours,\textsuperscript{26} acute heart failure (AHF) and acute respiratory failure (ARF) based on ICD codes were also included in this study. Use of mechanical ventilation (MV), vaso-pressors and renal replacement therapy during their hospital stay were also recorded in this study. Moreover, initial vital signs and laboratory results were also extracted by structured query language with PostgreSQL 9.6.

The BAR (mg/g) was calculated by initial serum BUN (mg/dL) / serum albumin (g/dL).

The primary outcome in this study was in-hospital mortality.

**Statistical Analyses**

Continuous variables were expressed as mean (standardized mean difference, SMD), categorical covariates were reported as number (percentage). X-tile software (version 3.6.1) was applied to determine the best cutoff values for BAR in MIMIC-IV database. Then, clinical features between high BAR and low BAR groups were analyzed with either Student’s t-test or Chi-squared test as appropriate. Propensity score matching (PSM) and propensity score-based inverse probability of treatment weighting (IPTW) were also applied to adjust the imbalance of the covariates between two groups to...
ensure the robustness of our results. One-to-one nearest neighbor matching with a caliper width of 0.2 was applied in the current study. Multivariate COX regression and adjusted hazard ratio (HR) were also conducted in the original cohort, matched cohort, weighted cohort and validation cohort to investigate the association between BAR and in-hospital mortality. Receiver operating characteristic curve (ROC) was used to compare the predictive performance of BAR, BUN and albumin in predicting in-hospital mortality in different cohorts. Finally, the decision curve analysis (DCA) was also performed to evaluate the potential clinical usefulness and benefits of the GLR. All analyses were performed using R (version 4.1.0) and X-tile (version 3.6.1) software and p<0.05 was considered statistically significant.

**Results**

**Patient Clinical Features**

A total of 2209 patients (1202 patients in the original cohort, 1007 patients in the validation cohort) with lung cancer were analyzed in this study. The best cut-off value for BAR, determined using X-tile software, was 6.8mg/g. We grouped the patients according to the measurements of BAR. In the original cohort, compared to patients with low BAR (<6.8mg/g), those with high BAR were older, higher proportion of males, had metastatic cancer and interventions during hospital stay, had more comorbidities and complications, had higher levels of severity scores, total bilirubin, white blood counts, anion gap, creatinine and potassium, and lower level of mean arterial pressure (MAP), hemoglobin, platelets and bicarbonate. Moreover,
patients in high BAR group had prolonged ICU stays and higher in-hospital mortality. After PSM and IPTW, almost all covariates in the matched cohort and in the weighted cohort were balanced between two groups (Supplemental Figure 1). Moreover, patients in the validation cohort exhibited similar characteristics to those in the original cohort (Table 1).

Prognostic Value of BAR for Primary Endpoint
As described in Table 1, compared with patients in low-BAR group, high-BAR group had a relatively higher in-hospital mortality in original cohort (38.7% versus 14.2%, P<0.001), in matched cohort (29.6% versus 18.5%, P=0.002) as well as in validation cohort (38.2% versus 14.3%, P<0.001). Those findings were further confirmed by Kaplan-Meier curves. As described in Figure 2A–C, high BAR group had a poor in-hospital mortality in original cohort, in matched cohort and in validation cohort.

The univariate COX regression analysis indicated that high BAR group patients were associated with increased in-hospital mortality, with a crude hazard ratio (HR) of 2.60 (95% confidence index, 95% CI, 2.03–3.33, P<0.001) and the association remained robust after PSM (HR=2.04, 95% CI 1.44–2.89, P<0.001) and IPTW (HR= 2.00, 95% CI 1.42–2.82, P<0.001) (Table 2). These findings were further confirmed by the results of the multivariate analyses. High BAR was still an independent predictor for in-hospital mortality in original cohort (HR=2.09, 95% CI 1.58–2.76, P<0.001), in matched cohort (OR=2.24, 95% CI 1.57–3.19, P<0.001) and in weighted cohort (OR=2.77, 95% CI 2.03–4.58, P<0.001) after adjustment for age, gender, weight, tumor type, comorbidities, complications, score system, interventions, vital signs and laboratory results (Table 2). Moreover, patients in the validation cohort showed similar results, which indicated that BAR was a significant and robust predictor for in-hospital mortality in lung cancer patients in ICU.

To further investigate whether BAR remained a prognostic factor in certain patient subgroups, we performed exploratory subgroup analyses. Forest plot demonstrated that BAR was an independent prognostic factor in the original cohort in all subgroups (Figure 3A). Moreover, patients from the validation cohort showed similar results. BAR can predict patient survival in almost all subgroups except for patients with acute heart failure and chronic kidney disease (Figure 3B).

Clinical Usefulness of BAR
BAR exhibited better predictive abilities for in-hospital mortality when compared with BUN or serum albumin alone in the original cohort, in the matched cohort, as well as in the validation cohort (Figure 2D and Table 3).

A DCA curve was also introduced to evaluate the clinical use of BAR for in-hospital mortality. According to the DCA, when the threshold probability for a patient was within the range of 0–100%, the BAR added more net benefit than the “treat all” or “treat none” strategies both in the original cohort, in the matched cohort, and in the validation cohort, which indicated that BAR could have clinical usefulness (Figure 4A–C).

Discussion
In the current study, we retrospectively enrolled 2209 ICU patients with lung cancer and found that high BAR group patients had increased in-hospital mortality and concluded that initial BAR could be an independent predictor for in-hospital mortality after adjusting confounding factors. In addition, the predictive performance of BAR was superior to that of serum albumin or BUN alone and could add more net benefit in terms of in-hospital mortality rather than “treat all” or “treat none”. Hence, those results suggested that BAR might be a good predictor for identifying patients at high risk of in-hospital mortality among lung cancer patients in ICU.

As one of the leading causes of cancer-related deaths all over the world, lung cancer patients often need invasive monitoring or treatment and have a relatively low survival rate, especially patients in ICU. Using the data from surveillance, epidemiology, and end results-medicare registry, Christopher et al demonstrated that the in-hospital mortality was 24% in patients with lung cancer who were admitted to an ICU for reasons other than surgical resection of their tumor. In the current study, the in-hospital mortality rate for ICU patients with lung cancer was 26.0% in the original cohort and 26.4% in the validation cohort.

The association between BAR and prognosis in patients with disease of the respiratory system has been investigated in previous studies. Seung et al conducted a retrospective study of 443 patients who were admitted to emergency department and concluded that BAR was a useful prognostic factor of 28-day mortality in aspiration pneumonia patients. A similar result has also been found in critically ill patients with acute pulmonary embolism. Using the data extracted from MIMIC-III, Fang et al...
Table 1: Comparisons of Baseline Characteristics Between the Original Cohort, Matched Cohort, and Validation Cohort

| Covariates         | Original Cohort | Matched Cohort | Validation Cohort | P value |
|--------------------|-----------------|----------------|-------------------|---------|
|                    | Low BAR         | High BAR       | P                 | Low BAR | High BAR | P          | Low BAR | High BAR | P value |
| N                  | 621             | 581            | -                 | 287     | 287      | -          | 496     | 511      | -       |
| Age, years         | 64.7 (12.0)     | 69.7 (12.2)    | <0.001            | 67.8 (11.7) | 67.9 (12.0) | 0.941  | 64.5 (11.5) | 69.2 (11.2) | <0.001 |
| Gender, male, n (%)| 296 (47.7)      | 339 (58.3)     | <0.001            | 15 (54.4) | 160 (55.7) | 0.801 | 238 (48.0) | 282 (55.2) | 0.026  |
| Weight (kg)        | 71.7 (19.3)     | 75.7 (20.0)    | 0.001             | 73.5 (19.6) | 73.3 (19.3) | 0.866 | 73.8 (21.3) | 76.1 (21.3) | 0.088  |
| Tumor type, n (%)  |                 |                |                   | 162 (56.4) | 159 (55.4) |       | 380 (76.6) | 374 (73.2) | 0.238  |
| Metastatic         | 371 (59.7)      | 290 (49.9)     |                   | 125 (43.6) | 128 (44.6) |       | 116 (23.4) | 137 (26.8) |         |
|                     | 250 (40.3)      | 291 (50.1)     |                   |         |         |       |         |         |         |
| Interventions, n (%)|                |                |                   |          |          |       |          |          |         |
| MV                 | 436 (70.2)      | 355 (61.1)     | 0.014             | 186 (64.8) | 190 (66.2) | 0.792 | 280 (56.5) | 345 (67.5) | <0.001 |
| CRRT               | 4 (0.6)         | 15 (2.6)       | <0.001            | 3 (1.0)  | 3 (1.0)  | 1.000 | 1 (0.2)  | 4 (0.8)  | 0.388  |
| Vasopressors       | 121 (19.5)      | 211 (36.3)     | <0.001            | 79 (27.5) | 77 (26.8) | 0.925 | 78 (15.7) | 144 (28.2) | <0.001 |
| Score system       |                |                |                   |          |          |       |          |          |         |
| SOFA               | 3.4 (1.2)       | 5.8 (1.6)      | <0.001            | 4.4 (1.1) | 4.5 (1.8) | 0.821 | 2.9 (1.2) | 4.8 (1.1) | <0.001 |
| OASIS              | 31.1 (8.0)      | 34.5 (9.0)     | <0.001            | 32.5 (8.3) | 32.4 (7.9) | 0.935 | 24.4 (10.3) | 27.8 (10.1) | <0.001 |
| APSIII             | 41.0 (10.4)     | 60.5 (14.5)    | <0.001            | 48.9 (19.3) | 48.9 (15.9) | 0.989 | 41.4 (18.9) | 54.6 (24.2) | <0.001 |
| Comorbidities, n (%)|                |                |                   |          |          |       |          |          |         |
| Hypertension       | 259 (41.7)      | 220 (37.9)     | 0.193             | 133 (46.3) | 125 (43.6) | 0.557 | 84 (16.9) | 92 (18.0) | 0.716  |
| Diabetes           | 88 (14.2)       | 152 (26.2)     | <0.001            | 56 (19.5) | 53 (18.5) | 0.831 | 84 (16.9) | 133 (26.0) | 0.001  |
| CKD                | 40 (6.4)        | 161 (27.7)     | <0.001            | 36 (12.5) | 35 (12.2) | 1.000 | 21 (4.2)  | 61 (11.9) | <0.001 |
| Myocardial infarct | 38 (6.1)        | 69 (11.9)      | <0.001            | 26 (9.1)  | 26 (9.1)  | 1.000 | 39 (7.9)  | 40 (7.8)  | 1.000  |
| CHF                | 68 (11.0)       | 136 (23.4)     | <0.001            | 49 (17.1) | 43 (15.0) | 0.569 | 39 (7.9)  | 71 (13.9) | 0.003  |
| COPD               | 222 (35.7)      | 212 (36.5)     | 0.836             | 100 (34.8) | 96 (33.4) | 0.792 | 171 (34.5) | 179 (35.0) | 0.906  |
| Liver disease      | 42 (6.8)        | 69 (11.9)      | <0.001            | 28 (9.8)  | 25 (8.7)  | 0.773 | 8 (1.6)   | 12 (2.3)  | 0.542  |
| Charlson index     | 9.3 (2.2)       | 10.5 (2.5)     | <0.001            | 9.8 (2.4) | 9.7 (2.3) | 0.831 | 6.5 (1.5) | 7.8 (2.7) | <0.001 |
| Complications, n (%)|                |                |                   |          |          |       |          |          |         |
| Sepsis             | 244 (39.3)      | 355 (61.1)     | <0.001            | 152 (53.0) | 145 (50.5) | 0.616 | 145 (29.2) | 272 (53.0) | <0.001 |
| AKI                | 264 (42.5)      | 389 (67.0)     | <0.001            | 157 (54.7) | 151 (52.6) | 0.676 | 181 (36.5) | 238 (46.6) | <0.001 |
| AHF                | 27 (4.3)        | 74 (12.7)      | <0.001            | 27 (9.4)  | 20 (7.0)  | 0.361 | 10 (2.0)  | 16 (3.1)  | 0.359  |
| ARF                | 179 (28.8)      | 259 (44.6)     | <0.001            | 121 (42.4) | 105 (36.6) | 0.200 | 191 (38.5) | 232 (45.4) | 0.031  |

(Continued)
| Covariates | Original Cohort | Matched Cohort | Validation Cohort | P value |
|------------|----------------|----------------|------------------|---------|
| MAP, mmHg  | 85.8 (16.9)    | 81.9 (17.9)    | 84.6 (18.4)      | <0.001  |
| Heart rate, bpm | 97.3 (22.2)    | 97.4 (21.3)    | 97.1 (21.8)      | 0.915   |
| RR, bpm    | 21.0 (6.5)     | 21.3 (6.4)     | 20.9 (6.3)       | 0.398   |
| SpO2, %    | 96.0 (3.7)     | 95.8 (4.2)     | 96.1 (3.6)       | 0.282   |
| Vital signs|                |                |                  |         |
|             |                |                |                  |         |
| WBC, ×10^9/L| 11.7 (4.4)     | 13.6 (4.8)     | 12.6 (4.9)       | <0.001  |
| HGB, g/dL  | 110.2 (2.2)    | 102.2 (2.1)    | 105.2 (2.1)      | <0.001  |
| PLT, ×10^9/L| 275.0 (58.2)   | 249.9 (48.3)   | 225.7 (74.7)     | 0.001   |
| Bilirubin, mmol/L | 0.9 (0.3)     | 1.5 (0.6)      | 12.0 (0.4)       | <0.001  |
| Anion gap, mEq/L | 150.0 (3.8)    | 166.6 (4.9)    | 154.4 (4.2)      | <0.001  |
| Bicarbonate, mEq/L | 240.0 (4.6)    | 223.3 (5.5)    | 233.5 (4.9)      | <0.001  |
| Chloride, mmol/L | 100.9 (6.6)    | 100.9 (7.2)    | 101.0 (6.8)      | <0.001  |
| Creatinine, mg/dL | 0.9 (0.3)      | 1.6 (0.5)      | 1.0 (0.4)        | <0.001  |
| Potassium, mmol/L | 4.1 (0.7)      | 4.5 (0.8)      | 4.2 (0.7)        | <0.001  |
| Sodium, mmol/L | 136.6 (5.4)    | 136.5 (5.9)    | 136.6 (5.5)      | <0.001  |
| ICU LOS, days | 2.2 (1.2, 3.9) | 2.5 (1.5, 5.2) | 2.5 (1.3, 4.2)   | 0.001   |
| Hospital LOS, days | 9.0 (5.6, 14.7)| 9.7 (5.6, 15.4)| 10.0 (6.2, 16.1)| <0.001  |
| Death n(%)  | 88.0 (14.2)    | 225.0 (38.7)   | 53.0 (18.5)      | 0.001   |

Note: For all continuous covariates, the mean values and standard deviations are reported.

Abbreviations: BAR, blood urea nitrogen to serum albumin ratio; MV, mechanical ventilation; CRRT, continuous renal replacement therapy; SOFA, sequential organ failure assessment; OASIS, Oxford acute severity of illness score; APSII, acute physiology score II; CKD, chronic kidney disease; CHF, congestive heart failure; COPD, chronic obstructive pulmonary disease; AKI, acute kidney injury; AHF, acute heart failure; ARF, acute respiratory failure; MAP, mean arterial pressure; RR, respiratory rate; WBC, white blood cell; HGB, hemoglobin; PLT, platelet; ICU, intensive care unit; LOS, length of stay.
investigated the correlation between BAR and prognosis of 1048 ICU patients with acute pulmonary embolism and concluded that BAR was an independent predictor for ICU mortality as well as 28-day mortality after ICU admission and the predictive performance of BAR was superior to the SOFA score and APSIII score. Moreover, Huang et al conducted a retrospective, observational study of 602 patients and demonstrated that elevated BAR at admission is an independent risk factor for in-hospital mortality in coronavirus disease patients (2019). Our study added the evidence that BAR was a reliable predictor for prognosis of patients with disease of the respiratory system. We firstly found that initial BAR could be an independent predictor for in-hospital mortality even after adjusting confounding factors in patients with lung cancer who were admitted to ICU. Moreover, the predictive

| Table 2 Summary of Results of Primary Outcome |
|----------------------------------------------|
| **Original Cohort** | **Matched Cohort** | **Weighted Cohort** | **Validation Cohort** |
| HR (95% CI) | P value | HR (95% CI) | P value | HR (95% CI) | P value | HR (95% CI) | P value |
| Unadjusted | 2.60 (2.03–3.33) | <0.001 | 2.04 (1.44–2.89) | <0.001 | 2.00 (1.42–2.82) | <0.001 | 2.21 (1.68–2.91) | <0.001 |
| Model 1 | 2.66 (2.07–3.41) | <0.001 | 2.10 (1.48–2.99) | <0.001 | 2.05 (1.44–2.91) | <0.001 | 2.41 (1.83–3.17) | <0.001 |
| Model 2 | 2.45 (1.89–3.19) | <0.001 | 2.13 (1.50–3.03) | <0.001 | 2.22 (1.54–3.22) | <0.001 | 2.36 (1.79–3.10) | <0.001 |
| Model 3 | 2.04 (1.56–2.69) | <0.001 | 2.28 (1.60–3.25) | <0.001 | 2.40 (1.63–3.52) | <0.001 | 2.30 (1.75–3.02) | <0.001 |
| Model 4 | 2.09 (1.58–2.76) | <0.001 | 2.24 (1.57–3.19) | <0.001 | 2.77 (2.03–4.58) | <0.001 | 2.20 (1.67–2.90) | <0.001 |

**Notes:** Model 1 adjusted for age, gender, weight, tumor type. Model 2 adjusted for model 1 plus comorbidities and complications. Model 3 adjusted for model 2 plus score system, interventions and Charlson index. Model 4 adjusted for model 3 plus vital signs and laboratory results.

**Abbreviations:** HR, hazard ratio; 95% CI, 95% confidence index.
The performance of BAR was superior to that of serum albumin or BUN alone and could add more net benefit in terms of in-hospital mortality rather than “treat all” or “treat none”.

A high BAR represents a high BUN concentration and a low albumin level. As a well-known index of renal function, BUN could also reflect the complex mutuality among nutritional status, protein metabolism, and renal condition of the patient. Increasing studies have focused attention on the BUN-based index or BUN alone for the prognosis of patients with different types of diseases, such as hemodialysis, CKD, peripheral arterial disease, and so on. Serum albumin plays an important role in immune-modulation, anti-oxidation, anti-inflammatory and endothelial stabilization. Moreover, serum albumin levels could be decreased by the status of malnutrition, inflammation, hepatocellular injury, renal losses, and so on.

Table 3 Receiver Operating Curve Analysis

| Variable | Sensitivity | Specificity | AUC (95% CI) | P value |
|----------|-------------|-------------|--------------|---------|
| Original cohort | | | | |
| BAR | 71.9 | 60.1 | 0.720 (0.694–0.745) | <0.001 |
| BUN | 62.9 | 62.0 | 0.660 (0.633–0.687) | <0.001 |
| Albumin | 51.8 | 73.6 | 0.672 (0.646–0.697) | <0.001 |
| Matched cohort | | | | |
| BAR | 71.7 | 50.2 | 0.673 (0.633–0.711) | 0.003 |
| BUN | 94.2 | 17.2 | 0.532 (0.490–0.574) | 0.046 |
| Albumin | 85.5 | 35.1 | 0.613 (0.571–0.653) | |
| Validation cohort | | | | |
| BAR | 68.8 | 66.4 | 0.725 (0.697–0.753) | <0.001 |
| BUN | 74.1 | 50.1 | 0.649 (0.619–0.679) | 0.001 |
| Albumin | 58.3 | 79.6 | 0.686 (0.659–0.711) | |

Abbreviations: BAR, blood urea nitrogen to serum albumin ratio; BUN, blood urea nitrogen; AUC, area under the receiver operating curve.
some albumin-based ratio for the diagnostic and prognostic of lung cancer. However, to the best of our knowledge, limited data are available on the combination of BUN and serum albumin for the prognosis of patients with lung cancer considering that the increased BUN and decreased serum albumin levels are in agreement with previous studies. In the current study, we retrospectively enrolled 2209 ICU patients with lung cancer using two large free public databases and noted a positive correlation between BAR and the prognosis of patients. This association became robust even after PSM and IPTW were also employed to eliminate the imbalance of the covariates between high-BAR and low-BAR groups. Furthermore, this association between BAR and in-hospital mortality was further confirmed in another big database with 1007 ICU patients with lung cancer.

Despite the relatively large sample size, there were still some limitations observed in this study. Firstly, we only calculated the initial BAR after their ICU admission but did not assess changes in BAR in any patients during hospital stay. Values of serum albumin or BUN may vary over time, and dynamic monitoring of these values may be more accurate. Secondly, we did not obtain levels of serum C-reactive protein and other inflammatory or nutritional indicators, which may be helpful to investigate the mechanism of the association between BAR and prognosis of lung cancer patients. Finally, this was a retrospective study, further prospective multicenter studies are proposed to validate the conclusions of our study and to investigate the potential mechanism behind them.

**Conclusion**

In the current study, we firstly demonstrated that initial BAR could serve as an independent prognostic predictor of in-hospital mortality in lung cancer patients in ICU, with good discrimination and clinical usefulness. BAR, which is an easily accessible and cost-effective parameter, provides a helpful index for clinicians to stratify the risk of mortality. Despite the solid statistics of this study, the findings of this study need more validations.

**Data Sharing Statement**

All data in our study are available from the corresponding author upon reasonable request.

**Statement of Ethics**

This study was conducted in accordance with the Helsinki Declaration and authors had successfully accomplished the National Institutes of Health’s (NIH) online training course and the Protection of Human Research Participants Examination and got the permission to extract data from MIMIC IV and eICU databases. Moreover, the study protocol was reviewed and successfully approved by the Ethics Committee of the Second Affiliated Hospital of Jianghan University and informed consent was waived.

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**Disclosure**

The authors declare that they have no competing interests.

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