Neutrophil-to-lymphocyte Ratio as a Predictor of Mortality in ICU Patients: An Analysis of MIMIC-III Database

Xie Wu  
Chinese Academy of Medical Sciences & Peking Union Medical College Fuwai Hospital

Zhanhao Su  
Chinese Academy of Medical Sciences & Peking Union Medical College Fuwai Hospital

Qipeng Luo  
Chinese Academy of Medical Sciences & Peking Union Medical College Fuwai Hospital

Yinan Li  
Chinese Academy of Medical Sciences & Peking Union Medical College Fuwai Hospital

Hongbai Wang  
Chinese Academy of Medical Sciences & Peking Union Medical College Fuwai Hospital

Qiao Liu  
Chinese Academy of Medical Sciences & Peking Union Medical College Fuwai Hospital

Fuxia Yan (yanfuxia@sina.com)  
Chinese Academy of Medical Sciences and Peking Union Medical College Fuwai Hospital  
https://orcid.org/0000-0001-5054-0775

Research

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Abstract

**Background:** Identifying high-risk patients in intensive care unit (ICU) is very important because of the high mortality rate. Existing scoring systems are numerous but lack effective inflammatory markers. Our objective was to identify and evaluate a low-cost, easily accessible and effective inflammatory marker that can predict mortality in ICU patients.

**Methods:** We conducted a retrospective study using data from the Medical Information Mart for Intensive Care Ill database. We first divided the patients into the survival group and the death group based on in-hospital mortality. Receiver operating characteristic analyses were performed to find the best inflammatory marker (i.e. neutrophil-to-lymphocyte ratio, NLR). We then re-divided the patients into three groups based on NLR levels. Univariate and multivariate logistic regression were performed to evaluate the association between NLR and mortality. The area under the curve (AUC), Net Reclassification Improvement (NRI) and Integrated Discrimination Improvement (IDI) were used to assess whether the incorporate of NLR can improve the predictive power of existing predictive model.

**Results:** A total of 21,822 patients were included in this study, with an in-hospital mortality rate of 14.43%. Among all inflammatory marker in routine blood test results, NLR had the best predictive ability, with a median (interquartile range) NLR of 5.40 (2.95, 10.46) in the survival group and 8.32 (4.25, 14.75) in the death group. We then re-divided the patients into low (≤1), medium (1-6) and high (≥6) groups based on NLR levels. Compared with the median NLR group, the in-hospital mortality rates were significantly higher in the low (odds ratio [OR] = 2.09; 95% confidence interval [CI], 1.64 to 2.66) and high (OR=1.64; 95%CI, 1.50-1.80) NLR groups. The addition of NLR to Simplified Acute Physiology Score II (SAPS II) improved the AUC from 0.789 to 0.798 (P<0.001), with NRI of 16.64% (P<0.001) and IDI of 0.27% (P<0.001).

**Conclusion:** NLR is a good predictor of mortality in ICU patients, both low and high levels of NLR are associated with elevated mortality rate. The inclusion of NLR might improve the predictive power of SAPS II.

**Introduction**

Patients admitted to intensive care unit (ICU) are usually severely ill with high mortality rates and high hospital costs[1]. Therefore, it is very important to identify patients with high risk of mortality. There are many existing scoring systems to predict the risk of mortality in the ICU, such as Simplified Acute Physiology Score (SAPS) and Acute Physiology and Chronic Health Evaluation[2], but effective inflammatory markers were not included. C-reactive protein and procalcitonin are widely recognized as indicators of inflammation [3–5], however, routine testing are not always available for every ICU patients due to cost-effective considerations, especially for those patients without infectious complications. Thus, identifying low-cost, easily accessible and effective inflammatory indicators might help predict mortality in ICU patients.
Blood examination is a routine inspection for every patients who admitted to the ICU. In addition to total white blood cell (WBC) and differential counts, combined markers such as neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) have also attracted extensive attention in recent years. A lot of research has focused on the prognostic value of the inflammatory markers in routine blood test[6–13], but which one is the most sensitive indicator, and how exactly does this indicator predict the mortality of all ICU patients are still not clear. Therefore, we performed this study to find the best inflammatory predictor of mortality in ICU patients, and to further assess its prognostic value.

**Material And Methods**

**Data Sources**

Data for this study were obtained from Medical Information Mart for Intensive Care III (MIMIC-III) database version 1.4, which is a large, publicly available database comprising information of over forty thousand patients who admitted to critical care units of the Beth Israel Deaconess Medical Center between June 2001 to October 2012. For more details see Johnson et al.[14]. To gain access, one of our researchers completed the required training courses and signed the data use agreement.

**Participants**

This study included all patients over 16 years old who admitted to ICU. In patients who had multiple ICU admissions, only the first admission was included. And the patients with missing values or abnormal values for key variables within 24 h after ICU entry were excluded. Abnormal values referred to WBC > 400*10^9/L, NLR > 100 or PLR > 8000, etc. Based on the inclusion and exclusion criteria, 21,822 patients were finally enrolled for data analysis.

**Data Extraction**

Data from the MIMIC-III database were extracted using Structured Query Language (SQL) with PostgreSQL version 11.2. Demographic data, laboratory parameters, patient's clinical outcomes and survival data were collected from all participants, including age, gender, ethnicity, ICU type, WBC count, lymphocyte count, neutrophil count, platelet count, severity at admission as measured by Simplified Acute Physiology Score II (SAPS II), ICU and hospital length of stay, mortality at hospital, day 90 and 1 year, and so on. The laboratory parameters were assessed during the first 24 hours post admission. NLR and PLR were calculated by dividing neutrophil or platelet count by lymphocyte count. SAPS II was calculated automatically in the database according to the published scoring criteria[15]. The extracted data were presented in comma separated value files, linked by identifiers and integrated into a whole table through Stata version 15.0.

**Statistical Analysis**
Statistical analyses were performed with Stata (version 15.0) and MedCalc (version 19.0.7). Continuous variables were presented as median with interquartile range and compared using the Wilcoxon rank sum test or Kruskal–Wallis test, whereas categorical variables were shown as frequency with percentage and compared using the Fisher’s test or binomial probability test. Receiver operating characteristics (ROC) curves were plotted to calculate the area under the curve (AUC) and were compared using DeLong’s test. Optimal cut-off values of each inflammatory markers were established with the aid of the MedCalc software. Univariate and multivariate analyses were performed with logistic regression to evaluate the prognostic value of NLR for mortality. In multivariate analyses, we adjusted for age, gender, ethnicity, ICU type and SAPS II. In addition to the classical AUC, Net reclassification improvement (NRI) and integrated discrimination improvement (IDI) were also calculated to assess the improvements in the predictive power after adding NLR. Subgroup analyses were performed to evaluate whether ICU type could influence the conclusions. All P-values of less than 0.05 were regarded as statistically significant.

Results

Study Population

Between June 2001 and October 2012, a total of 38,597 distinct adult patients (aged 16 years or above) were admitted to ICUs. After the selection criteria, 21822 patients were included in the final analysis. The mean age of the included patients was 64.89 ± 17.80 years, and 46.47% were female. The in-hospital mortality rate was 14.43%, while the 90-day and 1-year mortality rate were 20.78% and 28.57%, respectively. The median lengths of ICU and hospital stay were 2.08 (1.21, 4.13) and 6.63 (3.79, 11.79) days.

Comparison of survival and death group

Based on in-hospital mortality data, patients were divided into survival and death groups. The baseline characteristics and clinical data were shown in Table 1. The death group was older and had more females than the survival group. Compared with overall in-hospital mortality, the mortality rate in MICU was significantly higher (16.31%). Blood examinations showed significant differences between the survival and death group: WBC, neutrophil count, NLR and PLR were much higher in the death group, whereas lymphocyte and platelet counts were much lower.
Table 1
Baseline characteristics according to survivors and death

|                         | Overall (n = 21,822) | Survival group (n = 18,673) | Death group (n = 3,149) | P value |
|-------------------------|----------------------|-----------------------------|-------------------------|---------|
| Age, years              | 66.68 (52.76, 79.55) | 65.37 (51.65, 78.41)        | 75.05 (61.16, 83.58)    | < 0.001 |
| Gender, n (%)           |                      |                             |                         | 0.004   |
| Female                  | 10,140 (46.47)       | 8,602 (46.07)               | 1,538 (48.84)           |         |
| Male                    | 11,682 (53.53)       | 10,071 (53.93)              | 1,611 (51.16)           |         |
| Ethnicity, n (%)        |                      |                             |                         | < 0.001 |
| White                   | 15,875 (72.75)       | 13,619 (72.93)              | 2,256 (71.64)           |         |
| Black                   | 2,080 (9.53)         | 1,857 (9.94)                | 223 (7.08)              |         |
| Other                   | 3,867 (17.72)        | 3,197 (17.12)               | 670 (21.28)             |         |
| ICU type                |                      |                             |                         | < 0.001 |
| CCU                     | 3,331 (15.26)        | 2,864 (15.34)               | 467 (14.83)             |         |
| CSRU                    | 2,443 (11.20)        | 2,279 (12.20)               | 164 (5.21)              |         |
| MICU                    | 10,411 (47.71)       | 8,713 (46.66)               | 1,698 (53.92)           |         |
| SICU                    | 3,775 (17.30)        | 3,201 (17.14)               | 574 (18.23)             |         |
| TSICU                   | 1,862 (8.53)         | 1,616 (8.65)                | 246 (7.81)              |         |
| SAPS II                 | 34 (25, 43)          | 32 (24, 40)                 | 48 (37.5, 60)           | < 0.001 |
| Periphery blood index   |                      |                             |                         |         |
| WBC (10⁹/L)             | 9.9 (7.1, 13.9)      | 9.7 (7.1, 13.6)             | 11.4 (7.6, 16.6)        | < 0.001 |
| Lymphocyte (10⁹/L)      | 1.30 (0.83, 1.91)    | 1.34 (0.87, 1.94)           | 1.06 (0.67, 1.62)       | < 0.001 |
| Neutrophil (10⁹/L)      | 7.56 (4.88, 11.45)   | 7.34 (4.82, 11.07)          | 9.16 (5.49, 13.60)      | < 0.001 |
| Platelet (10⁹/L)        | 208 (150, 275)       | 210 (155, 275)              | 192 (119, 277)          | < 0.001 |
| NLR                     | 5.75 (3.09, 11.13)   | 5.40 (2.95, 10.46)          | 8.32 (4.25, 14.75)      | < 0.001 |

Data are presented as median and interquartile range or number and percentage.

ICU, intensive care unit; CCU, coronary care unit; CSRU, cardiac surgery recovery units; MICU, medical ICU; SICU, surgical ICU; TSICU trauma surgical ICU; SAPS, Simplified Acute Physiology Score; WBC, white blood cell; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio.
| Overall (n = 21,822) | Survival group (n = 18,673) | Death group (n = 3,149) | P value |
|---------------------|-----------------------------|-------------------------|---------|
| **PLR**             |                             |                         |         |
| 177.9 (115.4, 287.4) | 175.1 (115.1, 280.0)       | 199.1 (117.8, 334.9)   | < 0.001 |

Data are presented as median and interquartile range or number and percentage.

ICU, intensive care unit; CCU, coronary care unit; CSRU, cardiac surgery recovery units; MICU, medical ICU; SICU, surgical ICU; TSICU, trauma surgical ICU; SAPS, Simplified Acute Physiology Score; WBC, white blood cell; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio.

**Determination of the best inflammatory marker and its cut-off value**

The optimal cut-off values of the inflammatory markers were shown in Table 2. The NLR showed the highest ability to predict in-hospital mortality (AUC = 0.609, p < 0.001). The percentages of in-hospital mortality in different NLR stages was shown as a bar diagram (Fig. 1). We found both high NLR level (> 6) and low NLR level (< 1) were associated with increased mortality rate. Therefore, we selected NLR as our best inflammatory marker, with cut-off points of 1 and 6.

Table 2
The optimal cut-off values based on in-hospital mortality

| Peripheral blood index | Cut-off value | AUC  | P value |
|------------------------|---------------|------|---------|
| WBC (10^9/L)           | 12            | 0.575| < 0.001 |
| Lymphocyte (10^9/L)    | 1.17          | 0.593| < 0.001 |
| Neutrophil (10^9/L)    | 9.57          | 0.576| < 0.001 |
| Platelet (10^9/L)      | 128           | 0.554| < 0.001 |
| NLR                    | 6             | 0.609| < 0.001 |
| PLR                    | 267           | 0.536| < 0.001 |

WBC, white blood cell; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio.

**Outcomes of patients with different NLR level**

We re-divided patients into three groups based on their NLR levels: low NLR group (NLR ≤ 1, n = 580), medium NLR group (1 < NLR < 6, n = 10691), and high NLR group (NLR ≥ 6, n = 10551) and compared the
clinical outcomes of the three groups (Table 3). Compared with the medium NLR group, low and high levels of NLR were both significantly associated with poor prognosis. Their in-hospital, 90-day and 1-year mortality rates were significantly increased, and the hospital stay and ICU stay were also significantly longer.

| Clinical outcomes             | Overall (n = 21822) | NLR ≤ 1 (n = 580) | NLR 1–6 (n = 10691) | NLR ≥ 6 (n = 10,551) | P value |
|------------------------------|--------------------|-------------------|---------------------|---------------------|---------|
| Hospital mortality, n (%)    | 3149 (14.43)       | 122 (21.03)       | 1,009 (9.44)        | 2,018 (19.13)       | < 0.001 |
| 90-Day mortality, n (%)      | 4534 (20.78)       | 155 (26.72)       | 1,511 (14.13)       | 2,868 (27.18)       | < 0.001 |
| 1-Year mortality, n (%)      | 6234 (28.57)       | 211 (36.38)       | 2,311 (21.62)       | 3,712 (35.18)       | < 0.001 |
| ICU length of stay (d)       | 2.08 (1.21, 4.13)  | 2.04 (1.08, 4.38) | 1.96 (1.13, 3.46)   | 2.38 (1.33, 5.04)   | < 0.001 |
| Hospital length of stay (d)  | 6.63 (3.79, 11.79) | 7.35 (3.34, 15.86)| 6.08 (3.63, 10.79)  | 7.00 (3.96, 12.67)  | < 0.001 |

Data are presented as median and interquartile range or number and percentage.
## Prognostic value of NLR for mortality

The added predictive value of NLR were evaluated by calculating AUC, NRI and IDI. As shown in Fig. 2, the addition of NLR to the SAPS II significantly improved the AUC from 0.789 (95% CI, 0.785–0.796) to 0.798 (95% CI, 0.793–0.804; \( p < 0.001 \), DeLong’s test). The NRI and IDI for NLR in relation to the SAPS II were 16.64% (\( p < 0.001 \)) and 0.27% (\( p < 0.001 \)), respectively.

## Subgroup analysis

We also performed a subgroup analysis based on different ICU patients (Table 5). The prognostic value of NLR in the subgroups were almost similar to the total, except for the patients in TSICU with low NLR level.

### Table 4
Association between NLR and mortality

| Exposure       | Non-adjusted | Adjusted       |
|----------------|--------------|----------------|
|                | OR (95% CI)  | P value        | OR (95% CI)  | P value        |
| In-hospital mortality |              |                |              |                |
| ≤ 1            | 2.56 (2.07, 3.15) | < 0.001 | 1.61 (1.26, 2.05) | < 0.001 |
| 1–6            | 1            | 1              |              |                |
| ≥ 6            | 2.27 (2.09, 2.46) | < 0.001 | 1.59 (1.46, 1.74) | < 0.001 |
| 90-Day mortality |              |                |              |                |
| ≤ 1            | 1.96 (1.65, 2.33) | < 0.001 | 1.48 (1.18, 1.85) | < 0.001 |
| 1–6            | 1            | 1              |              |                |
| ≥ 6            | 2.08 (1.95, 2.22) | < 0.001 | 1.60 (1.48, 1.43) | < 0.001 |
| 1-Year mortality |              |                |              |                |
| ≤ 1            | 2.07 (1.74, 2.47) | < 0.001 | 1.51 (1.23, 1.86) | < 0.001 |
| 1–6            | 1            | 1              |              |                |
| ≥ 6            | 1.97 (1.85, 2.09) | < 0.001 | 1.38 (1.29, 1.48) | < 0.001 |

Adjusted confounders: age, sex, ethnicity, ICU type and SAPS II.

**Prognostic value of NLR for mortality**

The added predictive value of NLR were evaluated by calculating AUC, NRI and IDI. As shown in Fig. 2, the addition of NLR to the SAPS II significantly improved the AUC from 0.789 (95% CI, 0.785–0.796) to 0.798 (95% CI, 0.793–0.804; \( p < 0.001 \), DeLong’s test). The NRI and IDI for NLR in relation to the SAPS II were 16.64% (\( p < 0.001 \)) and 0.27% (\( p < 0.001 \)), respectively.

**Subgroup analysis**

We also performed a subgroup analysis based on different ICU patients (Table 5). The prognostic value of NLR in the subgroups were almost similar to the total, except for the patients in TSICU with low NLR level.
Table 5
Subgroup analyses of the association between in-hospital mortality and NLR levels.

| Subgroups | NLR | \( \leq 1 \) | 1–6 | \( \geq 6 \) |
|-----------|-----|-------------|-----|------------|
| CCU       | n (%) | 74 (2.22) | 1,712 (51.4) | 1,545 (46.38) |
|           | OR (95%CI) | 2.43 (1.21, 4.86) | 1 | 1.82 (1.44, 2.31) |
|           | P value | 0.012 | < 0.001 |
| CSRU      | n (%) | 46 (1.88) | 1,812 (74.17) | 585 (23.95) |
|           | OR (95%CI) | 3.72 (1.45, 9.54) | 1 | 3.25 (2.29, 4.61) |
|           | P value | 0.006 | < 0.001 |
| MICU      | n (%) | 350 (3.36) | 4,635 (44.52) | 5,426 (52.12) |
|           | OR (95%CI) | 1.77 (1.30, 2.41) | 1 | 1.44 (1.27, 1.63) |
|           | P value | < 0.001 | < 0.001 |
| SICU      | n (%) | 73 (1.93) | 1,767 (46.81) | 1,935 (51.26) |
|           | OR (95%CI) | 2.43 (1.24, 4.78) | 1 | 1.71 (1.39, 2.10) |
|           | P value | < 0.001 | < 0.001 |
| TSICU     | n (%) | 37 (1.99) | 765 (41.08) | 1,060 (56.93) |
|           | OR (95%CI) | 1.99 (0.79, 5.00) | 1 | 1.55 (1.13, 2.12) |
|           | P value | 0.144 | 0.007 |

Confounders adjustment were performed as before (Table 4).

ICU, intensive care unit; CCU, coronary care unit; CSRU, cardiac surgery recovery units; MICU, medical ICU; SICU, surgical ICU; TSICU trauma surgical ICU.

Discussion

The primary objective of this study was to find a low-cost, easily accessible and effective inflammatory marker that can predict ICU mortality, and to further evaluate its predictive power. To achieve this goal, we first divided the patients into the survival and death group to investigate the correlation between inflammatory markers of blood routine examination and in-hospital mortality in ICU patients, and it turned out that NLR had the best predictive ability. Then we determined the cutoff value of NLR and re-grouped the patients by NLR levels. We found that patients with lower or higher NLR levels were more likely to have higher mortality rate and longer ICU and hospital stay. Next, we incorporated NLR into the SAPS II and found that the addition of NLR can significantly improve the predictive power of SAPS II. Finally, we
conducted a subgroup analysis based on ICU type, and the results were basically consistent with the overall population.

The predictive value of NLR has been widely studied, particularly in cardiovascular disease[11, 16], infectious disease[12, 17–19] and cancer[7–10, 20, 21]. Most previous studies suggested that the higher the NLR level, the worse the prognosis[7–11, 13, 16–18, 20, 21]; however, other studies suggest that low NLR level also impart poor prognosis[12, 19]. If we equally divided the patients into 3–5 groups based on NLR level, we can draw the conclusions that high NLR level indicate poor prognosis (Additional le 1: Table S1). But before analysis, we noted that patients with lower NLR level also seem to have poor prognosis. Thus we took a different grouping scheme and confirmed our conjecture by further analysis. This finding was in line with clinical experience and therefore easy to explain. Indeed, the prognosis is generally good when the clinical indicators are within the normal range, too high or too low are more likely associated with poor prognosis. The possible reason of elevated NLR leading to poor prognosis has been mentioned in many literatures, which mainly reflects enhanced systemic inflammation and stress response[7, 13, 22, 23]. However, the reason why low NLR levels are associated with poor prognosis remains unclear, and we speculated the following reasons for this. Decreased NLR is mainly due to decreased neutrophils. Neutrophils play a key role in the innate immune response, including directly killing pathogens by phagocytosis, releasing a variety of cytokines, activating T cells and so on[12, 24]. Therefore, a reduction in the circulating neutrophil count could lower the body’s response to microbial invasion. In addition, the reduced circulating neutrophil count could be ascribed to increased neutrophil adhesion to the vascular endothelium[25], which could also cause endothelial damage, leading to leukocyte aggregation and microvascular thrombosis[26]. Thus, the compromise of innate immunity and the increase in endothelial damage could collectively impair the prognosis of the patients[27].

Many previous studies have overlooked that low NLR levels can also lead to poor prognosis, this may be caused by the following reasons. 1) The number of patients with low NLR levels was small. There are only 580 patients with NLR ≤ 1, which was 2.66% of the total population. Together with the overall trend that higher NLR level is associated with worse prognosis, the small number of patients with low NLR and poor prognosis may have been neglected; 2) The main outcome indicators may have a certain influence on the conclusion. Previous studies have mostly focused on late-death (≥ 5 days)[8, 10, 13, 20, 22] and found that high NLR level could predict poor prognosis. But Riché et al. reported that low NLR level was associated with early death (< 5 days), while high NLR level was associated with late death[12]. Duggal et al have also suggested that increased NLR was a biomarker for increased length of stay in ICU patients[23]. Therefore, it is reasonable to draw conclusions that high NLR indicate high mortality from previous studies focusing on late death. However, in our study, around half of the in-hospital deaths (1512/3149, 48.02%) occurred within 5 days, so low NLR level may also lead to increased mortality could be noted in our study; 3) The study population may also have an impact on the conclusion. Multiple previous studies were conducted in patients with specific diseases, while our study focused on the universality of all ICU patients, so we included all ICU patients with no case selection. For patients in MICU, many diseases can present with lymphocytosis and neutropenia, including hematological malignancies such as acute lymphocytic leukemia and myelodysplastic syndrome[27–30]; hematopoietic system diseases like
aplastic anemia[31]; rheumatic diseases like systemic lupus erythematosus[32]; and infectious etiology such as HIV, HBV and Epstein-Barr virus, etc. These patients are at elevated risk of bacterial and fungal infections, which accordingly have poor prognosis[33, 34]. This may be the reason for over-representation of the MICU patients with NLR ≤ 1 (3.36%). For postoperative patients in SICU, TSICU and CSRU, surgery will normally lead to elevated levels of NLR[35, 36]. On the one hand, tissue damage caused by trauma or surgery induced an acute inflammatory reaction, which leads to the accumulation of neutrophils[36, 37]; on the other hand, surgery and anesthesia exposed the body to a state of stress, which induces catecholamine and adrenocorticotropic hormone release, inducing the bone marrow, liver and spleen to produce neutrophils constantly and resulting in a massive recruitment of immature neutrophils into circulation[38]. In addition, cortisol inhibited the synthesis of lymphocyte nucleic acids, which leads to lymphopenia[39]. Therefore, postoperative patients should have a higher NLR. If the NLR is still at abnormally low levels for the postoperative patients, then the predominantly neutrophilic inflammatory response are probably not activated, but only lead to a transient type of lymphocytosis[40] and therefore cause poor prognosis. This is also consistent with previous reports that the mortality rate is significantly higher among trauma patients with lymphocytosis[41].

In this study, SAPS II was chosen as a tool for predicting the mortality. Although SAPS III had a better predictive ability, there were too many missing values due to the need for data within 1 hour after admission[42], so we chose to use SAPS II. Some studies had suggested that PLR also had the ability to predict mortality[10, 43, 44], therefore, we evaluated the predictive power of the PLR, and found that it does have prediction ability but not as good as NLR. When we continued to add PLR to the new SAPS II scoring model with NLR, the AUC value did not increase significantly, so we did not incorporate PLR into this model.

The major strengths of our study were the large sample size and including all ICU patients without selection bias. Furthermore, we also noticed that the mortality rate was elevated in patients with low NLR levels. Of course, there were some limitations of this study. First, this was a retrospective study, and therefore some important data might be missing. Some patients were excluded because of missing data on neutrophil or lymphocyte, and it was hard to explore the reasons for the missing data based on currently available information. Second, the conclusion of this study was qualitative, but not quantitative. We can only conclude that the addition of NLR can improve the performance of the SAPS II, but the NLR scores can’t be directly included into SAPS II and construct a new scoring model. However, we believed the results of the current study would be an important prompt to later scoring systems. Finally, although we conducted subgroup analysis in different types of ICU, in depth analyses were not undertaken because it’s not the aim of our study.

**Conclusion**

Among all inflammatory indicators in routine blood tests, NLR has the best predictive ability. Abnormally elevated or decreased NLR are both associated with higher mortality. Adding NLR to SAPS II can improve the predictive power for ICU mortality.
Abbreviations

AUC: area under the curve; CI: confidence interval; ICU: intensive care unit; IDI: Integrated Discrimination Improvement; MIMIC: Medical Information Mart for Intensive Care; NLR: neutrophil-to-lymphocyte ratio; NRI: Net Reclassification Improvement; OR: odds ratio; PLR: platelet-to-lymphocyte ratio; ROC: Receiver operating characteristics; SAPS: Simplified Acute Physiology Score; WBC: white blood cell.

Declarations

Ethics approval and consent to participate

The study was an analysis of a third party anonymized publicly available database, which was approved by the Massachusetts Institute of Technology (Cambridge, MA) and Beth Israel Deaconess Medical Center (Boston, MA). Therefore we were not required to take the Institution Review Board permission.

Consent for publication

Not applicable.

Availability of data and materials

The datasets presented in the current study are available in the MIMIC III database (https://physionet.org/works/MICIIIClinicalDatabase/files/).

Competing interests

The authors declare that they have no competing interests.

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None.

Authors' contributions

As principal investigator, XW is fully responsible for all stages of the study, including design, data extraction, statistical analysis, and manuscript writing. FXY was involved in the design of the original protocol. QPL and YNL participated in data curation and analyses. HBW and QL contributed to the discussion and interpretation of data. ZHS helped to draft the final manuscript. All authors read approved the final manuscript.

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Figures

**Figure 1**

Association of in-hospital mortality rates and different NLR levels.
Figure 2

Receiver operating characteristic curves for SAPS II and SAPS II+NLR. SAPS, Simplified Acute Physiology Score; NLR, Neutrophil-to-Lymphocyte Ratio; AUC, area under the receiver-operating characteristic curve; IDI, integrated discrimination improvement; NRI, net reclassification improvement.

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