Diagnostic and prognostic role of neutrophil-to-lymphocyte ratio (NLR) in sepsis

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Objective: To evaluate neutrophil-to-lymphocyte ratio (NLR) as diagnostic and prognostic role in sepsis.
Methods: It was a prospective, observational study, conducted in Intensive Care Unit of Mianyang Central Hospital, from August 2017 to August 2018. A total of 37 cases of newly diagnosed cases of sepsis were included in the study and 20 healthy adults were taken as controls. According to the mortality within 30 days, patients with sepsis were divided into survival group (n=15) and death group (n=22). The white blood cell (WBC), neutrophils count (NEU), lymphocyte count (LYM), and NLR in peripheral blood were recorded at 1, 3, 5, 7 days after admission for patients. Logistic regression analysis was used to evaluate the risk factors for predicting the outcome, and receiver-operating characteristic curve (ROC) was plotted for evaluating the value of these factors on the 30-day prognosis. Results: NLR on day 1 (NLR1) of sepsis was significantly higher as compared to controls (P<0.001), with far higher diagnostic efficiency (AUC=0.959) than WBC (AUC=0.788) and equivalent to NEU% (AUC=0.942); WBC and NLR on day 7 (NLR7) is independent risk factors for 30-day mortality of sepsis patients and is helpful to predict the prognosis of sepsis. Conclusion: NLR can be a convenient and useful diagnostic and prognostic marker in sepsis and is of great clinical applicative value for primary hospitals without ability to detect other costly biomarkers and for emergency department.

1. Introduction

Sepsis is a systemic, harmful host response caused by an infection that can progress to severe sepsis and septic shock. Every year, the number of people suffering from sepsis in the world exceeds 19 million, and the mortality rate is more than 1/4. The mortality rate of septic shock can be as high as 40%-70%[1,2]. Studies have shown that the 72-hour survival rate will decrease by about 7.7%/h[3] within 72 hours after the onset of the disease, so early recognition of sepsis can effectively improve the prognosis and reduce the mortality rate.

Peripheral blood neutrophil to lymphocyte ratio as an indicator of the body’s inflammatory state, its convenient, low price, has been widely used in the evaluation of a variety of malignant tumors[4,5], while in infectious diseases such as acute appendicitis, lung applications in areas such as infection have also been reported[6,7]. In recent years, it has been found that it has a good clinical value[8,9,10,11,12] in assessing the severity and prognosis of patients with sepsis. This study analyzes and discusses the diagnosis and prognosis of peripheral blood in patients with sepsis by monitoring the peripheral blood nlr in patients with sepsis. The role.

2. Information and methods

2.1. Study subjects

A total of 37 patients with sepsis in the Department of Critical Care Medicine, Mianyang Central Hospital from August 2017 to August 2018, and 20 healthy adults from the physical examination center of our hospital were selected as a prospective observational study. Control group A total of 50 patients met the inclusion criteria,
8 of whom were included in the hospital history, 5 were excluded due to the length of stay, and 24 were included in the study. There were 17 males (45.9%) and 20 females (54.1%). The average age was 64.54±14.43 years old, 10 cases (27.0%) were positive for blood culture, and 22 cases (59.6%) were followed up to 30 days. There were 20 healthy controls, 10 males (50.0%) and 10 females (50.0%) with an average age of 53.70±11.79 years old. See Table 1.

2.1.1. Inclusion criteria

2.1.2. Exclusion criteria
Inpatient medical history information is complete. Check in time <24 h.

2.1.3. Ethics
This study meets the medical ethics standards and is approved by the hospital ethics committee (approval number: s2016013). The patient or his authorized client volunteers to participate and fully understand the study and sign a written informed consent form.

2.2. Observation indicators
Observed the patient's baseline data (age, sex, body mass index, primary infection site, etc.), the ratio of wbc, neu, lym, nrl in the peripheral blood of the patients on the 1st, 3rd, 5th, and 7th day and the first day lactic acid, bnp, platelet count; 30-day survival.

2.3. Statistical methods
The data were statistically analyzed by SPSS 19.0. The continuous variables were all tested by normality. The measurement data that conformed to the normal distribution were expressed as mean±standard deviation. The t test was used for comparison between the two groups, and the independent sample t test was used for variance. Non-parametric tests were used for variance variance. The count data was analyzed by χ² test. The receiver operating characteristic curve (ROC) was plotted for each indicator, and the area under the ROC curve (AUC) was calculated for multivariate stepwise logistic regression analysis. P <0.05 was considered statistically significant.

3. Results

3.1. The value of peripheral blood WBC, NEU%, NLR in the early diagnosis of sepsis
Peripheral blood WBC, NEU, LYM, and NRL were compared with healthy controls on the first day of sepsis (independent sample t test), and the results showed statistically significant differences (P<0.001), as shown in Table 2. The ROC curve was used to analyze the early diagnosis value of WBC, NEU% and NLR on the first day of sepsis in patients with sepsis. The results showed that NLR had higher diagnostic efficacy on early sepsis on the first day of sepsis. AUC=0.959), far superior to WBC (AUC = 0.788), which is equivalent to NEU% (AUC=0.942). When NLR=18.245 is used as the cut-off point, the Yoden index is the largest, the sensitivity is 70.0%, and the specificity is 83.8%. see picture 1.

3.2. Multivariate logistic regression analysis of 30-day mortality in patients with sepsis
On the first day of admission, lactic acid, BNP, platelets, and NLR and WBC on the 1st, 3rd, 5th, and 7th day were included in the multivariate logistic regression equation for predicting 30-day mortality. The results showed that on the 7th day, WBC and NLR were predicted for 30 days. Independent prognostic indicators of mortality (P<0.05); see Table 3.

Table 1
Comparison of general data between survival group and death group sepsis patients.

<table>
<thead>
<tr>
<th>Group</th>
<th>Number of cases (example)</th>
<th>age (year old)</th>
<th>Gender (example)</th>
<th>BMI (Kg/m²)</th>
<th>Lung</th>
<th>Abdominal cavity</th>
<th>Urinary</th>
<th>other</th>
</tr>
</thead>
<tbody>
<tr>
<td>Survival group</td>
<td>15</td>
<td>62.07±17.15</td>
<td>male 7 female 8</td>
<td>23.54±4.18</td>
<td>9(60.0)</td>
<td>4(26.7)</td>
<td>2(13.3)</td>
<td>0(0.0)</td>
</tr>
<tr>
<td>Death group</td>
<td>22</td>
<td>66.23±12.39</td>
<td>male 10 female 12</td>
<td>21.78±2.89</td>
<td>11(50.0)</td>
<td>8(36.4)</td>
<td>2(9.1)</td>
<td>1(4.5)</td>
</tr>
<tr>
<td>χ²/t</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>P</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.005</td>
</tr>
</tbody>
</table>

Table 2
Comparison of peripheral blood NLR between sepsis group and healthy person group.

<table>
<thead>
<tr>
<th>Grouping</th>
<th>Number of cases (example)</th>
<th>WBC</th>
<th>NEU</th>
<th>LYM</th>
<th>NLR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sepsis group</td>
<td>37</td>
<td>12.27±1.25</td>
<td>10.82±1.20</td>
<td>0.75±0.89</td>
<td>21.49±3.11</td>
</tr>
<tr>
<td>Health group</td>
<td>20</td>
<td>5.72±0.27</td>
<td>3.21±0.22</td>
<td>1.98±0.16</td>
<td>17.68±3.72</td>
</tr>
<tr>
<td>t</td>
<td></td>
<td>3.822</td>
<td>4.605</td>
<td>8.381</td>
<td>4.659</td>
</tr>
<tr>
<td>P</td>
<td></td>
<td>P&lt;0.001</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Note: WBC, NEU, LYM, NLR are laboratory indicators for patients with sepsis on day 1.
3.3. Analysis of the prognostic value of wbc and nlr on the prognosis of patients with sepsis on the 7th day

The 30-day mortality roc curve for predicting sepsis was plotted on day 7 wbc, nlr. The results showed that the predicted value of wbc was lower on the 7th day (auc: 0.633). On the 7th day, nlr had a certain predictive value (auc: 0.806). When nlr=15.445 was used as the cut-off point, the Yoden index was the largest, and the sensitivity was 73.0%. The specificity is 64.5%, see Table 4, Figure 2.

![Figure 1](image1.png) ![Figure 2](image2.png)

**Figure 1** Day 1 nlr identifies sepsis roc curve. **Figure 2**: Day 7 wbc, nlr predicts sepsis 30-day mortality roc curve.

4. Discussion

Neutrophils are innate immune cells. In the case of sepsis, the release of neutrophils is increased by stimulation of bone marrow, and apoptosis is slowed down, so that peripheral blood neutrophil cell counts are increased, and the role of phagocytizing pathogenic microorganisms is exerted. Release bioactive substances to enhance the body's ability to remove pathogenic microorganisms. Lymphocytes are a major component of the acquired immune system. Lymphocyte apoptosis is significantly increased in sepsis, and peripheral blood lymphocyte counts are significantly reduced, leading to decreased immunosuppression and pathogen elimination[12,13]. Therefore, the ratio of NLR in patients with sepsis will increase, and it can reflect the balance between the body's inflammatory response and immune status compared with single inflammation indicators such as white blood cell count, neutrophil count, and lymphocyte count.

Early recognition of sepsis can effectively improve the prognosis and reduce the mortality rate. As a gold standard for the diagnosis of sepsis, blood culture is mostly studied because of its long time-consuming, low positive rate and prone to false positives, and is currently used to evaluate the novel biomarkers of patients with sepsis and prognosis. Stages or tests are expensive and limited in application, making it difficult to meet clinical needs, especially in primary hospitals[9,10,14]. Gurol et al[15] found that NLR has the same accuracy as procalcitonin in the diagnosis of sepsis in 1 468 patients. When NLR<5, sepsis can be ruled out. A prospective study found that NLR pair on day 1 Patients with sepsis have better diagnostic efficacy (sensitivity and intentionality of 87.5% and 90%, respectively)[11]. This study also found that NLR has a higher diagnostic efficacy for early sepsis on day 1 Better than WBC. However, a recent meta-analysis (8 patients with a total of 7093 sepsis) showed that NLR as a single test had a lower predictive value for sepsis diagnosis (AUC=0.69, SEN=0.723, and SPE=0.59)[16].

There is no uniform conclusion about the prognosis of NLR in patients with sepsis. Hwang et al[17] performed a retrospective study of 1 728 patients with sepsis and found that initial NLR was an independent risk factor for predicting 28-day mortality in patients with sepsis, and sustained low NLR and sustained high NLR versus 28 d Increased mortality risk.Rajnish Kaushik et al. dynamically monitored NLR on day 1 and 5 of sepsis patients and found that NLR was significantly associated with 28-day mortality on day 5 (P=0.009)[11]. While ustín et al[18] underwent an observational cohort study of 5056 patients with ICU, no significant correlation was found between NLR and 28-day mortality in patients with sepsis. This study found that the 7-day NLR value can predict the prognosis of sepsis. The higher the value, the higher the mortality rate of sepsis patients, and the first, third, and fifth days have no significant correlation with the prognosis of sepsis.

NLR can be used as an important auxiliary indicator for early recognition of sepsis, and dynamic monitoring of NLR changes may be more meaningful for the prognosis evaluation of sepsis patients, especially for emergency and primary hospitals. However, sepsis is a dynamic and complex pathophysiological process, and the mechanism of NLR in the development of sepsis is still unclear. It is difficult to accurately and accurately evaluate the early detection and prognosis of sepsis. There is still a need to combine multiple methods for comprehensive assessment in clinical work.

Table 3

<table>
<thead>
<tr>
<th>Laboratory indicators</th>
<th>P value</th>
<th>OR(95%CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lactic acid</td>
<td>0.974</td>
<td>1.004(0.774-1.303)</td>
</tr>
<tr>
<td>BNP</td>
<td>0.776</td>
<td>1.002(0.991-1.013)</td>
</tr>
<tr>
<td>Platelet</td>
<td>0.166</td>
<td>1.000(1.000-1.000)</td>
</tr>
<tr>
<td>Day 1 WBC</td>
<td>0.089</td>
<td>0.881(0.761-1.020)</td>
</tr>
<tr>
<td>Day 3 WBC</td>
<td>0.780</td>
<td>0.980(0.853-1.172)</td>
</tr>
<tr>
<td>Day 5 WBC</td>
<td>0.241</td>
<td>0.877(0.704-1.092)</td>
</tr>
<tr>
<td>Day 7 WBC</td>
<td>0.034</td>
<td>1.242(1.017-1.518)</td>
</tr>
<tr>
<td>Day 1 NLR</td>
<td>0.223</td>
<td>0.970(0.923-1.019)</td>
</tr>
<tr>
<td>Day 3 NLR</td>
<td>0.473</td>
<td>1.027(0.955-1.104)</td>
</tr>
<tr>
<td>Day 5 NLR</td>
<td>0.179</td>
<td>0.972(0.932-1.013)</td>
</tr>
<tr>
<td>Day 7 NLR</td>
<td>0.021</td>
<td>1.170(1.023-1.337)</td>
</tr>
</tbody>
</table>

Table 4

<table>
<thead>
<tr>
<th>Laboratory indicators</th>
<th>AUC</th>
<th>Intercept point</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>95%CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 7 WBC</td>
<td>0.633</td>
<td>17.975</td>
<td>40.9</td>
<td>86.7</td>
<td>0.454-0.812</td>
</tr>
<tr>
<td>Day 7 NLR</td>
<td>0.806</td>
<td>15.445</td>
<td>73.0</td>
<td>64.5</td>
<td>0.664-0.948</td>
</tr>
</tbody>
</table>
References


