DISTRIBUTION OF PATHOGENS IN PATIENTS WITH VENTILATOR-ASSOCIATED PNEUMONIA AND CLINICAL VALUES OF NLR AND PLR FOR PROGNOSIS

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ABSTRACT

We aimed to study pathogen distribution in patients with ventilator-associated pneumonia (VAP) and diagnostic values of neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR). Sixty-eight VAP patients treated from June 2016 to February 2018 were enrolled as an observation group and subdivided into a survival group (n=50) and a death group (n=18) according to 28th-day prognosis. Thirty VAP-free patients receiving ventilator therapy were included as a control group. The purulent fluid or sputum was collected. Venous blood was taken at intubation (T0), 24 h (T1) and 120 h (T2) after diagnosis. The correlation between NLR and PLR was analyzed, and their evaluation values for prognosis were confirmed by ROC analysis. A total of 358 microbial strains were isolated. Gram-negative bacteria (222) were the main pathogens, accounting for 35.64%. Gram-positive bacteria (124) accounted for 34.64%, and 12 fungal strains were detected (3.35%). At T1 and T2, NLR and PLR of observation group significantly exceeded those of control group, and the values of death group significantly surpassed those of survival group (P<0.05). NLR was significantly positively correlated with PLR upon diagnosis (r=0. 362, P=0.008, P<0.05). AUC of NLR at T1 was 0.756, with the sensitivity and specificity of 71.2% and 85.6%, respectively (P=0.015). AUC of PLR was 0.832, with the sensitivity and specificity of 79.54% and 86.2%, respectively (P=0.028). Gram-positive bacteria were the dominant pathogens in VAP patients. NLR and PLR are potentially eligible indices for timely severity assessment and prognosis determination.

Keywords: *ventilator-associated pneumonia, pathogen distribution, neutrophil-to-lymphocyte ratio, platelet-to-lymphocyte ratio.*

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Introduction

Critically ill patients are prone to respiratory failure. To improve respiratory function and lung ventilation, ventilators are often used to replace normal physiological breathing. This process requires intubation or incision to establish an artificial airway for mechanical ventilation, thereby easily causing ventilator-associated pneumonia (VAP)[1]. VAP has high morbidity and mortality rates. The incidence rate of VAP in intensive care units is approximately 20%, and the mortality rate is as high as 15%-45%, so the survival and prognosis are seriously affected[2]. Meanwhile, prolonging the length of hospital stay and increasing the treatment expenditure also economically burden the patients' families. Affected by changes in the medical environment, the distribution of pathogens in VAP patients continuously changes, so timely monitoring the changes is beneficial to effective therapies[3].

Since VAP patients are in an inflammatory state, assessing the degree of inflammation is of great significance to clinical treatment. The neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) can visually reflect the inflammatory state and immunity level[4], but the values of VAP patients have never been reported hitherto. Thereby motivated, we herein analyzed the distribution of pathogens in VAP patients, and explored the clinical values of NLR and PLR for prognosis, providing valuable reference for clinical diagnosis and treatment.

Materials and methods

Baseline clinical data

This study has been approved by the ethics committee of our hospital, and written consent has been obtained from all patients. Sixty-eight patients with VAP diagnosed and admitted to our hospital from June 2016 to February 2018 were selected as an observation group. All the enrolled patients were in accordance with the diagnostic criteria of "Guidelines for the Diagnosis, Prevention and Treatment of VAP" (Chinese Medical Association, 2013 Revision). This group included 40 males and 28 female s, with an average age of (56.68±5.59) years old. They were then subdivided into a survival group (n=50) and a death group (n=18) according to prognosis on the 28th day. Inclusion criteria: 18 years old and above; ≥48 h of mechanical ventilation performed for the first time or within 48 h after extubation; with four of the following five symptoms:

- New or progressive infiltrating shadows disclosed by X-ray;
- Fever at over 38°C;
- Appearance of purulent substances in respiratory secretions;
- Detection of the same pathogens in two culture samples of sputum or deep bronchial secretions;
- Increase of white blood cell number to above 10×109/L measured by routine blood test.

Exclusion criteria

Quitting from this study or hospital transfer; complication with lung tumors or advanced malignant tumors; obvious infection during mechanical ventilation; incomplete clinical data. Meanwhile, 30 patients who received ventilator therapy but without VAP were included as a control group. All enrolled patients had comparable baseline clinical data (P>0.05). This study has been approved by the ethics committee of our hospital, and written consent has been obtained from all patients.

Detection of pathogens

The sputum sample of infected site or the sample of patient without using ventilator was collected through a tracheal intubation tube or a tracheotomy cannula, stored in a sterile swab and examined immediately. The samples were initially observed under a low-power microscope. To avoid severe contamination, the samples with <10 squamous cells and >25 white blood cells were further tested. Two replicate samples were collected from each patient. The samples were cultured on the medium, from which pure cultures were obtained for pathogen identification with ARIS 2X automated system (Thermo Scientific, USA).

Calculation of NLR and PLR

Venous blood was drawn from the observation group at intubation (T0), VAP diagnosis (T1) and 120 h after diagnosis (T2). The blood collection time of the control group was the same as that of the observation group. Routine blood test was performed by MC6600 automated analyzer (Shenzhen Mexcom Electronic Co., Ltd., China), and lymphocytes were counted using DxFLEX flow cytometer (Beckman Coulter, USA). Then NLR and PLR were calculated.

Statistical analysis

All data were analyzed by SPSS20.0 software. Continuous categorical data were expressed as mean ± standard deviation. NLR and PLR differences between two groups were performed by the t test, and the correlation between them was subjected to Pearson's correlation analysis. ROC curve was plotted to evaluate the diagnostic values of NLR and PLR on the first day. P<0.05 was considered statistically significant.

Results

Distribution of pathogens in VAP patients

A total of 358 microbial strains were isolated from the 68 VAP patients. Gram-negative bacteria (222) were the main pathogens of VAP patients, accounting for 35.64%, of which Pseudomonas aeruginosa (27.03%) had the highest proportion, followed by Acinetobacter baumannii (20.72%). Besides, gram-positive bacteria (124) accounted for 34.64%, with Staphylococcus aureus (31.45%) and Staphylococcus epidermidis (25.81%) being most abundant. In addition, 12 fungal strains were detected (3.35%), mainly including Candida albicans (66.67%) (Tab. 1).

NLR and PLR of different groups

There was no significant difference in NLR and PLR between observation and control groups, or survival and death groups at T0 (P>0.05). Compared with the control group, NLR and PLR were significantly higher in the observation group at T1 and T2 (P<0.05). Compared with the survival group, NLR and PLR were significantly higher in the death group at T1 and T2 (P<0.05) (Tab. 2 and 3).

Pathogen	Number of strains	Composition ratio (%)
Gram-positive cocci	124	34.64%
S. aureus	39	10.89%
S. epidermidis	32	8.94%
Streptococcus pneumoniae	10	2.79%
Group G hemolytic streptococci	8	2.23%
Enterococcus faecium	6	1.68%
Group F hemolytic streptococci	9	2.51%
Bacillus cereus	6	1.68%
Streptococcus pyogenes	5	1.40%
Other gram-positive bacteria	9	2.51%
Gram-negative bacteria	222	62.01%
P. aeruginosa	60	16.76%
A. baumannii	46	12.85%
Escherichia coli	32	8.94%
Enterobacter cloacae	26	7.26%
Serratia marcescens	16	4.47%
Klebsiella pneumoniae	19	5.31%
Enterobacter aerogenes	8	2.23%
Stenotrophomonas maltophilia	6	1.68%
Other gram-negative bacteria	9	2.51%
Fungi	12	3.35%
C. albicans	8	2.23%
Other fungi	4	1.12%
Total	358	100.00%

Table 1: Distribution of pathogens in VAP patients.

Time	NLR		t	P	PLR		t	P
	Observation group (n=68)	Control group (n=30)			Observation group (n=68)	Control group (n=30)		
T0	1.93±0.43	1.91±0.52	0.199	0.843	155.96±12.66	153.74±18.66	0.688	0.493
T1	2.42±0.62	1.75±0.46	5.304	0.000	168.72±18.42	135.12±15.15	8.762	0.000
T2	2.31±0.21	1.64±0.17	15.379	0.000	172.48±16.75	127.42±10.52	13.578	0.000

Table 2: NLR and PLR of observation and control groups.

Time	NLR		t	P	PLR		t	P
	Death group (n=18)	Survival group (n=50)			Death group (n=18)	Survival group (n=50)		
T0	1.92±0.25	1.88±0.44	0.364	0.717	153.74±18.88	155.69±12.42	0.494	0.623
T1	2.55±0.63	2.11±0.57	2.731	0.008	178.21±19.75	150.35±16.54	5.817	0.000
T2	2.83±0.76	1.89±0.26	7.667	0.000	196.23±20.56	142.63±13.96	12.246	0.000

Table 3: NLR and PLR of survival and death groups.

Correlation between NLR and PLR

Pearson's correlation analysis revealed that NLR was significantly positively correlated with PLR upon diagnosis (r=0. 362, P=0.008, P<0.05) (Fig. 1).

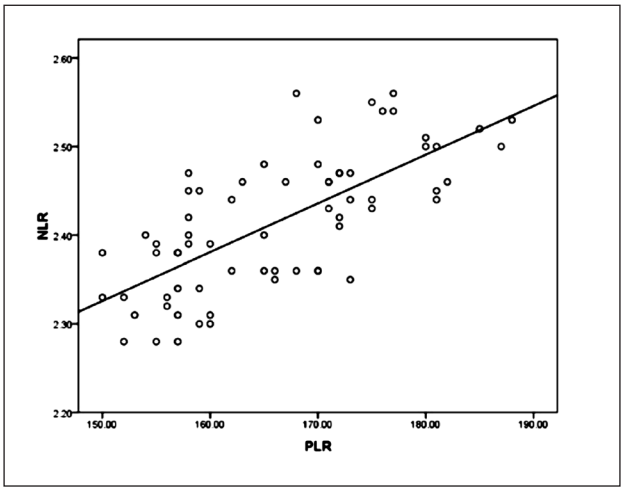

Fig. 1: Correlation between NLR and PLR upon diagnosis.

ROC analysis for prognosis evaluation of NLR and PLR

AUC of NLR at T1 was 0.756, and the optimal cutoff value was 2.580, with the sensitivity and specificity of 71.2% and 85.6%, respectively (P=0.015). At this time, AUC of PLR was 0.832, and the optimal cutoff value was 186.320, with the sensitivity and specificity of 79.54% and 486.2%, respectively (P=0.028) (Tab. 4).

Item	AUC	Optimal cutoff value	95%CI	Sensitivity (%)	Specificity (%)	P
NLR	0.756	2.580	0.638~0.863	71.2	85.6	0.015
PLR	0.832	186.320	0.762~0.896	79.54	86.2	0.028

Table 4: ROC analysis results for prognosis evaluation of NLR and PLR.

Discussion

With the continuous advancement of medical technology, mechanical ventilation is a commonly used method for the rescue of critically ill patients. Because of its strong invasiveness, severely ill patients often have serious illnesses, and their immunity is underground, and pathogenic bacteria are sticky. The probability of attachment and colonization in the respiratory tract is greatly increased, so VAP is one of the main complications of mechanical ventilation[5]. The prevention and treatment of VAP is a difficult problem that urgent medical treatment needs to solve.

Since the use of antibiotics and other antibiotics is more common than other treatment options, although there have been many literatures about the statistical analysis of the distribution of pathogens in VAP patients[6,7], there are certain geographical differences[8]. Regular analysis of the distribution of pathogens in patients with VAP in our hospital can provide guidance for clinical use.

The results of this study showed that gram-negative bacteria (62.01%) were the main infectious bacteria in VAP patients, similar to the results of most scholars, including A. baumannii and P. aeruginosa, of which P. aeruginosa had the highest proportion, probably due to the formation of a film on the wall of the tube, which has strong adhesion and is difficult to remove. Gram-positive bacteria accounted for 35.64% of the pathogens, and the highest proportion of strains are S. aureus and S. epidermidis. Fungi (3.35%) had the lowest proportion, and the main strain was C. albicans.

Under stresses such as inflammation, it is one of the hotspots of VAP clinical research to obtain the current biological state[9], such as procalcitonin, lactic acid and C-reactive protein, which can objectively evaluate physiology and pathology. Although the efficacy characteristics of patients with VAP have been extensively studied, there are no gold standards for the indices used for VAP prognosis evaluation[10]. In the process of regulation of inflammatory response, central granulocytes and lymphocytes play an important role as markers of inflammation. Neutrophils are elevated in the inflammatory states to invade tissues, so tissue damage is aggravated with the increase of inflammatory factors secreted by them[11]. Platelets increase with the release of inflammatory factors, and the severity of the disease can be judged in microbial pneumonia. There are few studies on NLR and PLR in inflammatory diseases[12], but existing studies have shown that it is of great significance for the judgment of the severity of pneumonia and the evaluation of clinical prognosis. Lee et al. reported that the differences between NLR and PLR of healthy subjects and patients with pneumonia were statistically significant, which both increased along with disease aggravation[13]. In another study, patients with pneumonia underwent acute exacerbation, with increased inflammatory status as well as NLR and PLR[14]. The results of this study showed that there were significant differences in NLR and PLR between the different groups. Compared with the control group, the NRP and PLR of the VAP group were significantly decreased at the T1 and T2 time points, and the two died in the death group and the survival group. The group also showed a significant decrease compared with the survival group at the above time, and the difference was statistically significant ($P<0.05$). The correlation analysis of NLR and PLR shows that there is a positive correlation of the same trend. In addition, when the observation group was diagnosed with VAP, that is, at time T1, the ROC curve analysis showed that NLR and PLR have higher sensitivity and specificity for the evaluation of prognosis.

In summary, Gram-positive bacteria are the main pathogens in patients with VAP. NLR and PLR can be used as good indices for VAP patients in timely assessment of disease status and prognosis. It is worthy of clinical research and discussion. There are some inevitable defects in this study, such as the small sample size, and the VAP patients are complicated, it is necessary to increase the sample size for further research.

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