



Influence of neutrophil granulocyte/lymphocyte ratio (NLR) on poor prognosis of elderly AECOPD patients during hospital stay

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ABSTRACT

Objective: To discuss the influence of neutrophil granulocyte/lymphocyte ratio(NLR) to the poor prognosis of elderly AECOPD patients during the stay in hospital. **Method:** A total of 133 cases elderly patients with AECOPD admitted in our hospital from March 2013 to September 2014 were selected, and divided them into death group (31 cases) and survival group (102 cases) according to in-hospital death occurrence; To compare the on admission general clinical data, therapy method, lung function, blood routine examination [white blood cell count (WBC), neutrophil granulocyte/lymphocyte ratio(NLR)], C-reactive protein (CRP), blood gas analysis and blood biochemical indexes in both groups, and drew ROC curve for a analysis of the clinical value of NLR in the prediction of death. **Results:** Among 133 cases of elderly AECOPD patients: the proportion of combined pulmonary heart disease and mechanical ventilation in death group was higher than that in survival group, PaCO₂, WBC count, neutrophil count, NLR, CRP level in death group was higher, but lymphocyte count, serum albumin(ALB) in death group was lower; multiple logistic regression analysis showed that NLR presented independent positive correlation with the in-hospital death in elderly AECOPD patients; ROC curve analysis showed that the ROCAUC of NLR to the in-hospital death in elderly AECOPD patients was 0.787, the best diagnostic node value was 7.3, sensitivity and specificity were 77.4% and 74.5% respectively; bounded by NLR(7.3), divided patients into NLR >7.3 group and NLR <7.3 group, hospital stays, CRP level and mortality in NLR >7.3 group were higher than that in NLR <7.3 group. **Conclusion:** NLR was the high risk factor of the in-hospital death in elderly AECOPD patients, early detection of NLR level had a certain difference to the evaluation for short-term prognosis of elderly AECOPD patients and guide treatment.

1. Introduction

Chronic obstructive pulmonary disease(COPD) was one of the most common frequently-occurring respiratory system diseases in elderly people, due to the lung function and immune defense function reduction, elderly people easily suffered the acute attack of COPD because of external inducement stimulation, like infection, climatic changes and fatigue invasion etc., AECOPD was the acute progress of illness state, which not only increased medical burden of patients, but also directly affected the life quality and prognosis

of patients. Therefore, how to evaluate the AECOPD illness state as early as possible and prognosis and then give early intervention was still the clinical focus[1]. In recent years, neutrophil granulocyte/lymphocyte ratio (NLR), as a kind of inflammatory marker, has aroused the concern of the clinicians, which had multiple advantages, like cheap and convenient detection etc., many researches[2,3] showed that NLR has been applied to the evaluation of disease severity and prognosis, like cardiovascular disease, gastrointestinal disease and infectious diseases etc. However reports on the prognosis evaluation of NLR to the elderly AECOPD patients during the stay in hospital were relatively rare. In this paper, through detection of the on admission NLR level, we aimed to evaluate its influence to the poor prognosis of elderly AECOPD patients during the stay in hospital, provided reference for clinical diagnosis and treatment.

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2. Data and method

2.1. Object

A total of 133 cases elderly patients with AECOPD admitted in our hospital from March 2013 to September 2014 were selected, age 60-84 years old, average age (69.7±8.9) years old, among whom, male 85 cases, female 48 cases; all patients' diagnosis was done, with reference to literature[4]; exclusion criteria: age<60 years old; autoimmune disease or tumor; severe heart liver renal dysfunction; thyroid disease; immunosuppressant drug use; splenectomy patients; divided them into death group (31 cases) and survival group (102 cases) according to in-hospital death occurrence; age, gender constituent ratio, course of disease etc. in both groups had no obvious statistical difference ($P>0.05$). See Table 1.

2.2. Observational index

Taking a record of the general on admission clinical data, like age, gender, course of disease, complication (atrial fibrillation, coronary disease, diabetes mellitus and pulmonary heart disease etc.) etc.; on admission therapy method: mechanical ventilation, inhaled corticosteroid χ^2 receptor stimulant treatment, hospital stays and in-hospital mortality; detection of the next-morning blood biochemical indexes after admission, like serum creatinine (Scr), blood urea nitrogen (BUN), serum albumin (ALB), which were detected by Japanese model-OLYMPUS automatic biochemical analyzer; detection of the blood gas index, like (PaO₂); detection of the blood routine examination:white blood cell count (WBC); neutrophile granulocyte/lymphocyte ratio (NLR); C-reactive protein (CRP); blood cell count was detected by automatic blood cell analyzer (Sysmex XE5000).

2.3. Statistical method

Using SPSS 17.0 statistical software for analysis, measurement

data using Mean±SD to show, using grouping t test for processing; enumeration data expression in the form of rate or constituent ratio, data processing using χ^2 test; relative factors analysis of in-hospital death occurrence using unconditional dichotomy Logistic regression model, using ROC curve to evaluate the predictive value of NLR to in-hospital death, $P<0.05$ showed the difference had obvious statistical significance.

3. Results

3.1. Comparison of the general clinical data, laboratory examination index in both groups

Among 133 cases of elderly AECOPD patients: death (31 cases), mortality (23.3%); compared with survival group, the proportion of combined pulmonary heart disease and mechanical ventilation in death group was higher ($P<0.05$), PaCO₂, WBC count, neutrophil count, NLR, CRP level in death group was higher ($P<0.05$), but lymphocyte count, serum albumin(ALB) in death group was lower($P<0.05$); see Table 1.

3.2. Multivariate logistic regression analysis of the in-hospital death in elderly AECOPD patients

Multivariate logistic regression analysis showed that combined pulmonary heart disease, NLR, CRP, high PaCO₂, low ALB presented independent positive correlation with the in-hospital death of elderly AECOPD patients ($P<0.05$); see Table 2.

3.3. ROC curve evaluation on the predictive value of NLR to in-hospital death

ROC curve analysis showed that the ROCAUC of NLR to the in-hospital death in elderly AECOPD patients was 0.787 (95%CI=0.536-0.927, $P<0.05$), the best diagnostic node value was

Table 1. Comparison of the general clinical data, laboratory examination index in both groups.

Group	n	Age (years old)	Gender (n,%)		Course of disease (year)	Smoking (n, %)	Complication (n,%)				
			Male	Female			Atrial fibrillation	Hypertension	Coronary disease	Pulmonary heart disease	Diabetes mellitus
Death	31	71.1±10.2	19(61.3)	12(38.7)	9.6±2.3	18(58.1)	4(12.9)	11(35.5)	5(16.1)	21(67.7)	5(16.1)
Survival	102	67.9±7.8	66(64.7)	36(35.3)	9.1±2.1	50(49.0)	7(6.9)	26(25.5)	14(13.7)	40(39.2)	13(12.7)
t/ χ^2		1.797	0.120	1.135	0.778	0.487	1.183	0.002	7.792	0.033	
P		0.075	0.729	0.258	0.378	0.484	0.277	0.966	0.005	0.855	

Group	n	PaCO ₂ (mmHg)	Neutrophile Granulocyte(10 ⁹ /L)	Lymphocyte(10 ⁹ /L)	NLR	WBC(10 ⁹ /L)	CRP(mg/L)
Death	31	56.4±7.4	8.73±2.10	1.04±0.25	8.62±2.03	11.12±3.21	42.5±8.2
Survival	102	43.2±5.8	7.51±1.89	1.48±0.33	5.21±1.42	9.30±2.44	10.4±2.4
t/ χ^2		10.376	3.066	-6.844	10.641	4.928	35.140
P		0.000	0.003	0.000	0.000	0.000	0.000

Group	n	Scr (μmol/L)	BUN (mmol/L)	ALB (g/L)	Therapy Method (n, %)		
					Inhaled corticosteroid	Mechanical ventilation	β_2 receptor stimulant
Death	31	84.0±14.3	7.1±2.0	30.2±4.5	9(29.0)	13(41.9)	14(45.2)
Survival	102	79.3±12.3	6.5±2.2	35.3±4.8	19(18.6)	23(22.5)	35(34.3)
t/ χ^2		1.792	1.357	-5.769	1.549	4.526	1.202
P		0.075	0.177	0.000	0.213	0.033	0.273

7.3, sensitivity and specificity were 77.4% and 74.5% respectively; see Figure 1.

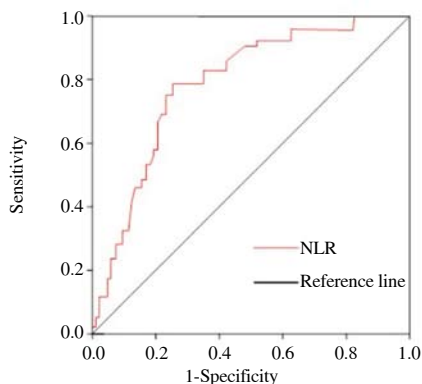


Figure 1. ROC curve evaluation on the predictive value of NLR to in-hospital death.

3.4. CRP, hospital stays and mortality comparison in NLR 7.3 group and NLR<7.3 group

Bounded by NLR (7.3), divided patients into NLR 7.3 group and NLR<7.3 group, hospital stays, CRP level and mortality in NLR 7.3 group were higher than that in NLR<7.3 group ($P<0.05$). See Table 3.

4. Conclusion

Accordingly, reports differed in the in-hospital mortality of AECOPD patients. As was reported by Chang[5], in-hospital mortality was about 2.8%-34.7% in AECOPD patients; as was reported by domestic Tan Xiaoxia[6], in-hospital mortality was 18.1%; as was reported by Shi Guoqiang[7], in-hospital mortality was 28.6% in 126 cases of small sample AECOPD patients; as was reported by foreign Roberts[8], in-hospital mortality was 17.5% in 1 274 cases of AECOPD patients among more than 30 hospital in

England, and as was reported in this paper, in-hospital mortality was 23.3% and death cases was 31 among 133 cases of AECOPD patients, which was in accordance with the above reports.

Current studies showed that COPD pathogenesis was essentially a kind of nonspecific inflammatory process in lung tissue and airway, various cytokines and inflammatory mediators involved in the pathological process of the whole COPD occurrence development[9]. Due to the lung function and immune defense function reduction, elderly people easily suffered the acute attack of COPD under the influence of various external incentives. At this time, the balance between anti-inflammatory and proinflammatory mechanism was disturbed, various immune cells activated caused a series of cascading inflammatory response, besides, a large number of inflammatory mediator and cytokines, like TNF- α , IN-6, IN-8 etc., released, which damaged the lung vascular endothelial cell, increased the vasopermeability and then caused pulmonary interstitial edema, further worsened the lung lesions, exacerbated lung tissue ischemia hypoxia, seriously, would lead to air-flow ratio imbalance, respiratory failure and even death[10]. As was reported by Warwick[11], CRP, as a non-specific index reflecting inflammation degree, in AECOPD patients was high than that in stable phase COPD patients, and the higher the CRP level was, the higher the short-term mortality risk occurrence was; Wang Hongyang[12] found that serum CRP, TNF- α , IL-6 etc. in in-hospital respiratory failure patients were obviously higher than that in in-hospital non-respiratory failure patients through detection of the serum inflammatory medium in AECOPD patients, and serum CRP, TNF- α , IL-6 etc. presented positive correlation with PaCO₂, negative correlation with FEV₁/FVC. All of which indicated that inflammatory response had important significance in AECOPD occurrence and its short-term prognosis.

Neutrophile granulocyte/lymphocyte ratio (NLR) was considered as a kind of marker, which could effectively reflect the inflammation response, multiple researches showed that NLR has been applied to the evaluation of severity of the diseases (like cardiovascular disease, community-acquired pneumonia and digestive system disease etc.) and its prognosis, and NLR could better reflect the inflammation degree and evaluate the prognosis of clinical value, compared with

Table 2. Multivariate logistic regression analysis of the in-hospital death in elderly AECOPD patients.

Variable	B	SE	Wald χ^2 value	df	P	OR (95%CI)
Constant term	-0.852	0.201	37.475	1	0.000	
Combined pulmonary heart disease	0.302	0.110	7.681	1	0.006	1.352(1.125-1.735)
PaCO ₂	0.259	0.102	6.592	1	0.011	1.295(1.041-1.554)
CRP	0.799	0.225	25.895	1	0.000	2.225(1.348-3.252)
NLR	0.857	0.244	6.638	1	0.010	2.358(1.378-3.584)
ALB	-0.576	0.231	3.934	1	0.042	0.562(0.253-0.761)

Table 3. CRP, hospital stays and mortality comparison in NLR 7.3 group and NLR<7.3 group[n(%)].

Group	n	Different CRP level		Hospital stays		In-hospital death	
		P75	<P75	14 d	<14 d	Death	Survival
NLR 7.3	50	21(42.0)	29(58.0)	29(58.0)	21(42.0)	24(48.0)	26(52.0)
NLR<7.3	83	13(15.7)	70(84.3)	26(31.1)	57(68.9)	7(8.4)	76(91.6)
χ^2		11.374	9.155	27.327			
P		0.001	0.003	0.000			

Note: for all patients in this study, CRP level was divided into P75 and <P75 group (according to P75); hospital stays were divide into 14 d and <14 d group (according to 14 d-node value)

single neutrophil granulocyte or lymphocyte count. As was pointed by Akpek[14], not only NLR level presented positive correlation with CRP level in myocardial infarction patients, but also was the in-hospital adverse cardiac event occurrence rate of high NLR patients obviously higher than that in survival group, through the NLR detection of ST-elevation acute myocardial infarction patients with early coronary interventional therapy. Through detection of the blood routine among patients with community-acquired pneumonia, Jage[15] found that lymphocyte count and NLR reduction could better predict the death risk of patients, compared with the traditional single biochemical index, like WBC, CRP, neutrophil granulocyte etc.. As was reported by Azab[3], NLR and lymphocyte count increased and reduced respectively in acute pancreatitis patients, if the NLR duration reduced by 1 week, there would be greater risks of multiple organ failure; along with the improvement of the systemic inflammatory response, NLR would decline gradually.

During the pathogenesis process of AECOPD, after a series of inflammatory stimulation, neutrophilic leukocytosis and activation occurred, IL-8 etc. cytokines generated, which led to the cascading amplified inflammatory response and increased the damage of lung tissue and blood vessels[12,16]; activated neutrophils could adhere to the pulmonary blood vessel walls and release the TXA₂ and leukotrienes B₄ etc., which could promote the platelet aggregation and capillary contraction, exacerbate the pulmonary vascular resistance[12,15]; in addition, activated neutrophils could also release and degrade the damage of elastin, proteolytic enzyme etc. to alveolar epithelial cells and lung vascular endothelial cell, led to the increased pulmonary vascular permeability and increase the risk of pulmonary interstitial edema[17]. Because AECOPD patients were in stress reaction conditions, circulated glucocorticoid and catecholamine level increased, which led to the lymphocyte count decrease, in addition, most COPD patients were accompanied by infection, when illness state was severe and immunologic function declined in elderly patients, lymphocyte count absolute values reduced accordingly. Therefore, in the AECOPD attack, neutrophil count increased, but lymphocyte count decreased, as a combination of both, NLR increased. In this paper, white blood cell count (WBC), neutrophil count and NLR in death group were obviously higher than that in survival group, while lymphocyte count was lower than that in survival group. Multi-variable Logistic regression model correction confounding factors showed that NLR was the independent risk factor of in-hospital death in elderly patients with AECOPD, but WBC count, neutrophil count, lymphocyte count were not included in equation, which indicated that NLR detection had close relations with the evaluation to the short-term prognosis of AECOPD patients, in addition, ROCAUC of NLR to the in-hospital death of elderly AECOPD patients was 0.787, >0.700, which indicated that the evaluation of NLR to the prognosis of elderly AECOPD patients had better clinical value. Through comparison of hospital stays, high-level CRP cases and mortality in NLR >7.3 group and NLR <7.3 group, we further proved the relationship between high-level NLR and inflammatory response degree and poor prognosis.

In conclusion, NLR was the high risk factors of in-hospital death in elderly AECOPD patients, early NLR level detection had a certain significance to the evaluation for short-term prognosis of elderly AECOPD patients and guide treatment. In this paper, due to monocentric cases, fewer sample size, further discussion on the basis of enlarging sample size was necessary.

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