International Journal of Medicine Research
ISSN: 2455-7404; Impact Factor: RJIF 5.42
Received: 03-01-2021; Accepted: 19-01-2021; Published: 08-03-2021
www.medicinesjournal.com
Volume 6; Issue 1; 2021; Page No. 45-48

Prognostic role of neutrophil–lymphocyte ratio for hospital mortality in patients with Acute exacerbation of chronic obstructive pulmonary disease

Abhilash KN[1], Prakash Rao[2], Anushree B Nambiar[1]
[1] Junior Resident, Department of General Medicine, KVG Medical College and Hospital, Sullia, Karnataka, India
[2] Professor, Department of General Medicine, KVG Medical College and Hospital, Sullia, Karnataka, India

Abstract
Background and objectives: Acute exacerbation of chronic obstructive pulmonary disease (AECOPD) is one of the leading causes of hospitalization and is associated with considerable mortality, for which clinicians are seeking useful and easily obtained biomarkers for prognostic evaluation. This study aimed to determine the potential role of the neutrophil–lymphocyte ratio (NLR) as prognostic markers for hospital mortality in patients with AECOPD.
Methods: We included 50 patients with AECOPD in this retrospective study. Clinical characteristics, NLR, serum levels of C-reactive protein (CRP) and other data were collected. Relationships between NLR and CRP were evaluated by Pearson's correlation test.
Results: Mean levels of NLR of all patients with AECOPD were 8.02±8. NLR levels correlated with serum CRP levels (P=0.05). The overall hospital mortality rate was 16%. Levels of NLR were significantly higher among non-survivors compared to survivors of AECOPD (both P=0.05).
Conclusion: NLR levels increased in non-survivor patients with AECOPD, and the NLR may be simple and useful prognostic marker for hospital mortality in patients with AECOPD. More studies should be carried out to confirm our findings.

Keywords: acute exacerbation of chronic obstructive pulmonary disease, neutrophil–lymphocyte ratio, hospital mortality, prognosis

Introduction

Chronic obstructive pulmonary disease (COPD) is a common chronic airway inflammatory disease characterized by persistent respiratory symptoms and airflow limitation [1]. COPD is associated, worldwide, with high morbidity and mortality. In India, the overall prevalence of COPD was 6.5 to 7.7% in residents based on a cross-sectional survey [2]. COPD was the third leading cause of mortality in 2011 [3]. Acute exacerbation of COPD (AECOPD) is associated with an acute worsening of respiratory symptoms that result in additional therapy[1]. AECOPD has an independent and significant negative influence on the prognosis of patients with COPD, it increases the frequency of further severe exacerbations, reduces health status and physical activity, speeds the decline of lung function, increases mortality, and places great economic burden on patients – with both high direct and in-direct medical costs [4, 6]. AECOPD is one of the leading causes of hospitalization, and contributes significantly to mortality among patients with COPD [7]. Considering the important role of AECOPD in the prognosis of patients with COPD, early and accurate individual mortality risk assessment during exacerbation is of critical importance for clinical management, and is helpful for optimal allocation of limited medical resources. Clinicians are seeking clinically meaningful predictors of mortality following AECOPD admission, especially for biomarkers which can be easily obtained upon admission [8].

AECOPD is associated with increased systemic and airway inflammation, and enhanced inflammation worsens clinical symptoms and decreases lung function of patients, necessitating hospitalized treatment [9, 10]. The neutrophil–lymphocyte ratio (NLR) is an marker of inflammatory status, representing both the neutrophil and lymphocyte counts [11, 12] NLR is an indicators of general immune response to various stress stimuli, and play an important role in the prognostic evaluation of a series of diseases, including malignant cancers, myocardial infarction, community-acquired pneumonia, and acute pulmonary embolism [13, 16]. However, limited data have been presented on the relationship between NLR and clinical outcomes of hospitalized patients with AECOPD. This study sought to investigate the prognostic role of NLR on in-hospital mortality of patients with AECOPD.

Methods

Patients with AECOPD who were admitted to referral hospital in South Karnataka from july 2018 to March 2020 were studied retrospectively with the Following Inclusion Criteria. 1) primary diagnosis of AECOPD, defined as an acute worsening of respiratory symptoms such as dyspnea, cough, or sputum purulence severe enough to warrant hospital admission;[1] 2) a COPD diagnosis supported by spirometric data of airflow obstruction even with broncho-dilator (forced expiratory volume in 1 second [FEV1]/forced vital capacity [FVC], 0.70) when clinically stable at least for 3 months;[1] and 3) age 40 years and above, and admitted from their primary residence.

For patients with multiple hospital admissions, only the first admission was recorded. A patient was excluded from the study if AECOPD was not the primary diagnosis, or had other acute events such as acute myocardial infarction, or the patient had other end-stage diseases. The treatment plan for each patient was not influenced by participation in current study.

Data collection

Demographic and clinical data were collected from all subjects, including: age, gender, smoking history, lung function test results (FEV1, FEV1%Pred, FVC, and FEV1/FVC), arterial blood gas on admission (SpO2, PaO2, PaCO2, and pH value), serum C-reactive protein (CRP) levels, complete haemogram on admission before antibiotic treatment (white blood cell, platelets, neutrophils, lymphocytes;) length of hospital stay, and in-hospital mortality.

Statistical analysis

Data are represented as mean ± standard deviation. Categorical data are represented as frequencies and percentages. Differences between the survivor and non-survivor groups were compared by chi-squared test for categorical variables and an unpaired *t*-test for continuous variables. In addition, we assessed the ability of two- or three-marker combinations to predict in-hospital mortality with methods recommended by Creaney *et al*. [17] Data on NLR, and CRP were transformed with the natural logarithm and then standardized relative to controls; a logistic regression to predict AECOPD death/alive status was used to determine the weight given to each standardized marker. Data analysis was conducted using SPSS 18.0 for Windows. The level of significance for all statistical tests was set as a two-sided *P*-value of 0.05.

Results

Characteristics of included subjects

During the above study period 80 patients had symptoms of COPD out of which 50 patients with AECOPD met our inclusion criteria and were included in this study. There were 39 men and 11 women, and the mean age was 61 years.; the mean FEV1% predicted value was 56%, suggesting most patients presented with moderate airflow limitation. Overall, 45 (90%) patients with AECOPD underwent a chest X-ray or chest CT scan examination. The mean length of hospitalization was 15 days, and 8 patients died during hospitalization, corresponding to an in-hospital mortality of 16%. The clinical characteristics, lung function data, and main laboratory findings of survivors and non-survivors are listed in Table 1.

Table 1: Clinical summary of patients with AECOPD

Clinical characteristic	Overall (n=50)	Survivor (n=42)	Non-survivor (n=8)	*P*-value
Age (year)	61±10	60±10	67±10	,0.001
Gender, n (%)				
Male	39 (78%)	34 (81%)	5 (63%)	0.831
Female	11 (22%)	08 (19%)	3 (37%)	
Smoking status, n (%)				
Current/ever smoker	38(76%)	33(78%)	6 (75%)	0.928
Never smoker	12 (24%)	09 (22%)	2 (25%)	0.535
FEV1 (L)	1.33±0.5	1.35±0.6	1.18±0.4	0.117
FEV1%Pred (%)	56.12±21.4	56.97±21.7	50.01±18.2	0.065
FVC (L)	2.32±0.8	2.37±0.8	1.99±0.6	0.007
FEV1/FVC (%)	53.54±11.7	53.74±11.7	52.08±11.7	0.421
SpO2 (%)	95.67±6.4	95.87±6.5	94.22±5.3	0.143
PaO2 (mmHg)	86.62±31.2	87.06±29.5	82.47±42.1	0.514
PaCO2 (mmHg)	46.47±15.9	45.64±15.1	52.41±19.8	0.015
pHvalue	7.40±0.06	7.41±0.06	7.36±0.08	<0.001
WBC (×10*9/L)	8.45±4.3	8.05±3.7	11.63±6.6	<0.001
Platelet (×10*9/L)	192.95±90.9	192.60±90.8	180.05±92.5	0.397
Neutrophils (×10*9/L)	6.49±4.2	5.98±3.6	10.16±6.2	<0.001
Lymphocytes (×10*9/L)	1.20±0.6	1.25±0.6	0.87±0.6	<0.001
NLR	8.02±8.7	7.08±8.19	16.61±10.1	<0.001
CRP (mg/L)	65.22±14.4	59.22±19.2	90.76±10.2	<0.001
Hospital LOS(day)	15±9	15±11	15±8	0.642

Note: Data presented as mean ± SD.

Abbreviations: AECOPD, acute exacerbation of chronic obstructive pulmonary disease; CRP, C-reactive protein; FEV1, forced expiratory volume in one second; FVC, forced vital capacity; GOLD, Global Initiative for Chronic Obstructive Lung Disease; LOS, length of stay; NLR, neutrophil–lymphocyte ratio; WBC, white blood cell;

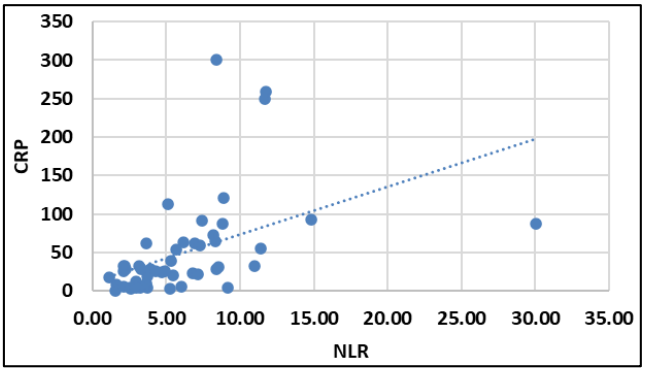

Fig 1: correlations of the NLR with CRP.

NLR levels

The mean NLR levels across all patients with AECOPD were 8.02. NLR levels correlated positively with serum CRP levels (P=0.001), As shown in Table 1, levels of NLR were significantly higher among patients who died in hospital than among those who survived (both P,0.05).

Discussion

AECOPD is an acute event during the clinical course of COPD, and is significantly associated with the clinical outcomes of patients with COPD by worsening clinical symptoms, declining lung function, and increasing mortality.[18] Identifying a simple and reliable biomarker that can accurately assess the mortality risk during AECOPD hospitalization is of great importance for the management of patients and rational allocation of medical resources. In this study, we found that NLR levels correlated with CRP – a systemic inflammation maker – in patients with AECOPD, and NLR levels were higher in non-survivors than in survivors who were patients with AECOPD; the NLR plays a valuable role in predicting the in-hospital mortality of patients with AECOPD.

COPD is associated with both enhanced airway and systemic inflammation and, during states of exacerbation, the severity of inflammation is significantly increased [19], and may stimulate the increase of the NLR, which may be used as markers of inflammation and as prognostic markers for patients with AECOPD. CRP is a classical inflammatory maker, and has been used to evaluate the systemic inflammation and prognosis of patients with COPD [20]. In our study, we observed that serum CRP levels were significantly increased in non-survivor patients with AECOPD. Taylan *et al*. reported that increased NLR is as useful as CRP in the evaluation of elevated inflammation in AECOPD, and the NLR is useful for the early identification of potential acute exacerbations in patients with COPD who have normal levels of traditional markers [21]. The NLR is a straightforward and valuable biomarker of AECOPD that may contribute as a predictor for respiratory hospitalization in patients with COPD [22]. In this study, we observed that levels of NLR were increased in patients with AECOPD and correlated positively with CRP levels, and NLR levels were higher in non-survivors than in survivor patients with AECOPD. The results suggest that the NLR is useful as a prognostic biomarker for hospital mortality in patients with AECOPD. In addition, two studies supported that elevated NLR may be associated with long-term mortality in patients with COPD [23, 24]. Thus, the NLR plays multiple roles in AECOPD as a predictor of hospitalization, inflammation evaluation, and in-hospital/long-term mortality, and is helpful in the clinical management of patients with AECOPD.

Our study suggests that the NLR is a simple and useful biomarker for predicting in-hospital mortality in patients with AECOPD, as routine blood testing is available and affordable for each patient with AECOPD; the clinic utility of the NLR may be superior to that of other markers, which may need specific equipment or reagent. However, there were several limitations in our study. Our result in this study was from a single medical center, and it should be verified in larger studies with multiple centers and with different ethnic groups. More studies are needed to build a more definite conclusion on the prognostic accuracy of NLR in patients with AECOPD for both short- and long-term mortality. Second, future work should examine how the predictive power of the NLR relates to infection, to determine their ability of discriminating bacterial from nonbacterial AECOPD. Further studies with larger patient series are required to highlight the clinical significance of the NLR in the responses of patients with AECOPD to antibiotic therapy and further exacerbations.

Conclusion

This study shows in hospital mortality were high among patient with increased levels of NLR, and the NLR is a simple, promising prognostic marker for assessing in-hospital mortality in patients with AECOPD. These findings justify further work into the role of the NLR in comprehensive management of patients with AECOPD.

References

1. Vogelmeier CF, Criner GJ, Martinez FJ, *et al*. Global strategy for the diagnosis, management, and prevention of chronic obstructive lung disease 2017 report. GOLD executive summary. Am J Respir Crit Care Med. 2017; 195(5):557-582.
2. McKay, Ailsa J *et al*. Prevalence of COPD in India: a systematic review." Primary Care Respiratory Journal. 2012; 21(3):313-321.
3. Hoyert DL, Xu JQ. Deaths: preliminary data for 2011. Natl Vital Stat Rep. 2012; 61(6):1-65.
4. Soler-Cataluña JJ, Martínez-García MA, Román Sánchez P, Salcedo E, Navarro M, Ochando R *et al*. Severe acute exacerbations and mortality in patients with chronic obstructive pulmonary disease. Thorax. 2005; 60(11):925-931.
5. Wedzicha JA, Singh R, Mackay AJ. Acute COPD exacerbations. Clin Chest Med 2014; 35(1):157-163.
6. Ozkaya S, Findik S, Atici AG. The costs of hospitalization in patients with acute exacerbation of chronic obstructive pulmonary disease. Clinicoecon Outcomes Res. 2011; 3:15-18.
7. Lima FV, Yen TY, Patel JK. Trends in in-hospital outcomes among adults hospitalized with exacerbation of chronic obstructive pulmonary disease. COPD. 2015; 12(6):636-642.
8. Singanayagam A, Schembri S, Chalmers JD. Predictors of mortality in hospitalized adults with acute exacerbation of chronic obstructive pulmonary disease. Ann Am Thorac Soc. 2013; 10(2):81-89.
9. Zhou X, Li Q, Zhou X. Exacerbation of chronic obstructive pulmonary disease. Cell Biochem Biophys. 2015; 73(2):349-355.
10. Groenewegen KH, Postma DS, Hop WC, Wielders PL, Schlösser NJ, Wouters EF *et al*. COSMIC Study Group. Increased systemic inflammation is a risk factor for COPD exacerbations. Chest. 2008; 133(2):350-357.
11. Faria SS, Fernandes PC Jr, Silva MJ, *et al*. The neutrophil-to-lymphocyte ratio: a narrative review. Ecancermedicalscience. 2016; 10:702.
12. Yang W, Wang X, Zhang W *et al*. Neutrophil-lymphocyte ratio and platelet-lymphocyte ratio are 2 new inflammatory markers associated with pulmonary involvement and disease activity in patients with dermatomyositis. Clin Chim Acta. 2017; 465:11-16.
13. Templeton AJ, McNamara MG, Šeruga B *et al*. Prognostic role of neutrophil-to-lymphocyte ratio in solid tumors: a systematic review and meta-analysis. J Natl Cancer Inst. 2014; 106(6):dju124.
14. Yang T, Wan C, Wang H *et al*. The prognostic and risk-

stratified value of neutrophil–lymphocyte count ratio in Chinese patients with community-acquired pneumonia. Eur J Inflamm. 2017; 15(1):22-27.
15. de Jager CP, Wever PC, Gemen EF *et al*. The neutrophil-lymphocyte count ratio in patients with community-acquired pneumonia. PLoS One. 2012; 7(10):e46561.
16. Karataş MB, İpek G, Onuk T *et al*. Assessment of prognostic value of neutrophil to lymphocyte ratio and platelet to lymphocyte ratio in patients with pulmonary embolism. Acta Cardiol Sin. 2016; 32(3):313-320.
17. Creaney J, Yeoman D, Musk AW, de Klerk N, Skates SJ, Robinson BW. Plasma versus serum levels of osteopontin and mesothelin in patients with malignant mesothelioma – which is best? Lung Cancer. 2011;74(1):55-60.
18. Rodríguez-Roisin R. COPD exacerbations.5: management. Thorax. 2006; 61(6):535-544.
19. Gan WQ, Man SF, Senthilselvan A, Sin DD. Association between chronic obstructive pulmonary disease and systemic inflammation: a systematic review and a meta-analysis. Thorax. 2004; 59(7):574-580.
20. Leuzzi G, Galeone C, Taverna F, Suatoni P, Morelli D, Pastorino U, *et al*. C-reactive protein level predicts mortality in COPD: a systematic review and meta-analysis. Eur Respir Rev. 2017; 26(143):160070.
21. Taylan M, Demir M, Kaya H *et al*. Alterations of the neutrophil-lymphocyte ratio during the period of stable and acute exacerbation of chronic obstructive pulmonary disease patients. Clin Respir J. 2017; 11(3):311-317.
22. Lee SJ, Lee HR, Lee TW *et al*. Usefulness of neutrophil to lymphocyte ratio in patients with chronic obstructive pulmonary disease: a prospective observational study. Korean J Intern Med. 2016; 31(5):891-898.
23. Sørensen AK, Holmgaard DB, Mygind LH, Johansen J, Pedersen C. Neutrophil-to-lymphocyte ratio, calprotectin and YKL-40 in patients with chronic obstructive pulmonary disease: correlations and 5-year mortality – a cohort study. J Inflamm (Lond). 2015; 12:20.
24. Xiong W, Xu M, Zhao Y, Wu X, Pudasaini B, Liu JM, *et al*. Can we predict the prognosis of COPD with a routine blood test? Int J Chron Obstruct Pulmon Dis. 2017; 12:615-625.