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RESEARCH

THE PROGNOSTIC ROLE OF NEUTROPHIL-TO-LYMPHOCYTE AND PLATELET-TO-LYMPHOCYTE RATIOS IN PATIENTS WITH ASPIRATION PNEUMONIA

Abstract

Introduction: Aspiration pneumonia is difficult to diagnose, and it has a high mortality rate. In this study, the prognostic values of neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) and their association with intensive care unit (ICU) admission and mortality were investigated in patients with aspiration pneumonia.

Materials and Method: Between November 2016 and December 2018, 162 patients aged>40 years, with no immunosuppression or malignancy, and hospitalized with a diagnosis of aspiration pneumonia were included in this retrospective study. The patients were divided into two groups: those with and without ICU admission. In addition, the patients were divided into two groups: those who died and recovered. NLR and PLR ratios were compared between groups.

Results: Among the 162 patients, 87 (54%) were male and 75 (46%) were female, 72 patients were administered to the ICU, and 28 died. NLRs in patients admitted to the ICU (13.88±10.83) compared with those who were not admitted (10.5±10.07) and NLRs in patients who died (14.91±9.41) compared with those who recovered (11.4±10.67) were significantly high ($p<0.05$). There was no significant difference between the groups for PLRs ($p>0.05$). The NLR cutoff value was determined as 8, and sensitivity and specificity for admission to the ICU was 68.25% and 58.89%, respectively (AUC, 0.62), whereas sensitivity and specificity for mortality were 67.86% and 54.48%, respectively (AUC, 0.658).

Conclusion: NLR has a prognostic value in predicting ICU admission and mortality in patients with aspiration pneumonia.

Keywords: Aspiration pneumonia; Neutrophil; Lymphocyte; Platelet; Mortality; Intensive care unit.

ARAŞTIRMA

ASPİRASYON PNÖMONİLİ HASTALARDA NÖTROFİL LENFOSİT ORANI VE PLATELET LENFOSİT ORANININ PROGNOZ İLE İLİŞKİSİ

Öz

Giriş: Aspirasyon pnömonisi, tanısı zor, mortalitesi yüksek bir hastalıktır. Bu çalışmada, aspirasyon pnömonili hastalarda, nötrofil lenfosit oranı (NLO) ve platelet lenfosit oranının (PLO), yoğun bakıma giriş ve mortalite ile ilişkili prognostik değerinin incelenmesi amaçlanmıştır.

Gereç ve Yöntem: Kasım 2016-Aralık 2018 tarihleri arasında başvuran, 40 yaş üzerinde, immünsüpresyonu ve malignitesi olmayan, aspirasyon pnömonisi tanısı konularak hastaneye yatırılan 162 hasta retrospektif olarak çalışmaya alındı. Hastalar yoğun bakıma yatış ve ex olmalarına göre iki ayrı gruba ayrıldı, bu gruplarda NLO ve PLO oranları karşılaştırıldı.

Bulgular: 162 hastanın 87'si (%54) erkek, 75'i (%46) kadındı. 72 hasta yoğun bakıma alınırken, 28 hasta öldü. NLO seviyeleri yoğun bakıma giren hastalarda (13.88±10.83), girmeyenlere (10.5±10.07) göre; ölen hastalarda (14.91±9.41), ölmeyenlere göre (11.4±10.67) istatistiksel olarak anlamlı yüksek saptandı ($p<0.05$). PLO seviyeleri açısından, gruplar arasında istatistiksel olarak anlamlı farklılık saptanmadı ($p>0.05$). NLO cut-off değeri 8 olarak saptanmış olup, yoğun bakıma giriş için sensitivite ve spesifitesi %68.25 ve %58,89 (AUC:0.62); mortalite için sensitivite ve spesifitesi %67.86 ve %54.48 saptandı (AUC:0,658).

Sonuç: Aspirasyon pnömonisi hastaların, NLO'nın yoğun bakıma giriş ve mortaliteyi öngörmede prognostik değeri olduğu saptandı.

Anahtar Sözcükler: Aspirasyon pnömonisi; Nötrofil; Lenfosit; Platelet; Mortalite; Yoğun Bakım.

INTRODUCTION

Aspiration is defined as inhalation of the oropharyngeal and gastric contents into the larynx and lower respiratory tract. After aspiration, different diseases develop depending on the content of the aspirated material, amount of aspiration, and response of host. In young patients, aspiration pneumonitis (Mendelson's syndrome) develops because of aspiration of sterile gastric contents, but aspiration pneumonia develops in elderly patients because of aspiration of oropharyngeal material with bacterial colonization (1). The most common risk factors in elderly patients are impaired clearance, decreased cough reflex, and poor oropharyngeal secretion control (2). As the diagnostic criteria for aspiration pneumonia cannot be clearly established, a heterogeneous patient population is included in studies. It is reported that 5%–15% of community-acquired pneumonia are aspiration pneumonia (3). In another study, the incidence of aspiration pneumonia in patients with hospitalized community-acquired pneumonia ranged from 8.7% to 60.1% (4). Mortality was found to be three-fold higher in aspiration pneumonia (29.4%–11.6%) than in other forms of pneumonia (5). White blood cells (WBC) play an important role in the systemic inflammatory response triggered by infection. Due to endotoxemia, circulating neutrophils increase and lymphocyte count decreases (6). Zahorec R. et al. have published the first study reporting that the neutrophil-to-lymphocyte ratio (NLR) can be used as a marker for systemic infection (7). Another study has determined that NLR is more effective as an indicator of bacteremia than the classical parameters such as WBC, neutrophil count, and C-reactive protein (CRP) levels (8). Similarly, the platelet-to-lymphocyte ratio (PLR) has also been recognized as a useful marker of systemic inflammation (9).

The present study investigated the prognostic values of NLR and PLR and their association with intensive care unit (ICU) admission and mortality in patients diagnosed with aspiration pneumonia.

MATERIALS AND METHOD

Between November 2016 and December 2018, 162 patients diagnosed with aspiration pneumonia, hospitalized at Sultan Abdulhamid Han Training and Research Hospital, and were older than 40 years of age without immunosuppression and malignancy, were retrospectively included in the study. Informed consent was waived because of the retrospective nature of the study. This study was approved by the Ethics Committee of the Umraniye Training and Research Hospital (172/04.09.2019). The patients were divided into two groups: those with and without ICU admission. In addition, the patients were divided into two separate groups: those who died and recovered. The diagnosis of aspiration pneumonia was made according to the criteria described below:

a) New emerging radiographic infiltration suggestive of pneumonia,

b) Symptoms and signs of lower respiratory tract infection (one major criterion: cough, expectoration, fever>38 °C or<35.5 °C; two minor criteria: pleuritic chest pain, dyspnea, delirium, increased alveolar–arterial gradient, WBC>12000/mm^3, and/or left shift or leukopenia<3000/mm^3),

c) Presence of aspiration risk factors (confusion, swallowing reflex deterioration, diagnostic aspiration, gastroesophageal junction disorder, pharyngeal anatomical abnormalities) (2).

Age, sex, WBC, neutrophils, lymphocytes, platelets, CRP, room air saturation (SpO_2), radiological findings (single lobe, multilobar, and accompanying pleurisy presence), length of hospital stay, admission to the ICU during treatment, and mortality (survival or death) data were collected. NLR and PLR were calculated.

CRP levels were measured with full automated immunoturbidimetric method using Archem Diagnostics (Istanbul-Turkey) kit by Abbott Architect C-16000 Clinical Chemistry Analyzer (California-USA). The WBC count, neutrophil and

lymphocyte counts were determined on BC-6800 Hematology Analyzer (Mindray Corporation, China).

Descriptive analyses (frequency distributions, percentage, mean, standard deviation, and 95% confidence intervals) were used as statistical methods in analyzing the research data. Data were analyzed using the Chi-square test for normally distributed data, and the Mann–Whitney U test was used when the data was not normally distributed. Pearson's correlation coefficient, cutoff point, ROC curve, and sensitivity analysis were used to evaluate the relationships. The cutoff point for the hospitalization period was found using the K-means cluster method. The results were evaluated at 95% confidence interval and $p<0.05$ significance level. In the analysis of the data, the PSPP [PSPP is free software; you can redistribute it and/or modify it under the terms of the GNU General Public License as published by the Free Software Foundation, either version 3 of the license or (at your option) any later version] and Microsoft Excel computer programs were used.

RESULTS

A total of 162 patients were included in this study. The mean age of the patients admitted to the ICU was 81.60±9.99 years. Among the 162 patients, 72 were admitted to the ICU during hospitalization or treatment period and 28 died there.

Comparison of patients who were admitted and not admitted to the ICU

The mean age of the patients who were treated and not treated in the ICU was 82.19±8.02 and 81.13±11.34 years, respectively. There was no statistically significant difference between the two groups in terms of age ($p>0.05$). Overall, 37of the 87 male patients and 35 of the 75 female patients were admitted to the ICU, and no statistically significant difference was found between the groups in terms of sex ($p>0.05$). Similarly, no statistically significant difference was found between the groups in terms of WBC, neutrophils, lymphocytes, platelets, PLR, and radiological findings ($p>0.05$). Among 119 patients, 70 were hypoxic at the time of admission to the hospital and 2 of the remaining 43 non-hypoxic patients were admitted to the ICU. Significant differences were noted between the two groups in terms of hypoxia ($p<0.05$). The mean NLR in patients who were admitted and not admitted to the ICU was 13.83±10.83 and 10.5±10.07, respectively, and the difference was significant ($p<0.05$). The mean CRP levels were found to be 133.94±80.15 in patients admitted to the ICU and 102.91±63.88 in patients who were not admitted to the ICU, and the difference between the groups was significant ($p<0.05$). The length of hospital stay was 24.25±19.92 days for patients admitted to the ICU and 9.66±4.67 days for patients not admitted to the ICU; this difference was also significant ($p<0.05$) (Table 1).

Comparison of patients who died and recovered

The mean ages of the patients who died was 82.04±9.11 years and of those who did not die was 81.51±10.19 years. There were no significant differences between the groups in terms of age ($p>0.05$). Overall, 10 of the 87 male patients and 18 of the 75 female patients died. There was a statistically significant difference between the two groups in terms of sex ($p<0.05$). No statistically significant difference was found between the groups in terms of WBC, neutrophils, lymphocytes, PLR, CRP, and radiological findings ($p>0.05$). Among 119 patients who were hypoxic upon admission, 28 died; none of the remaining 43 non-hypoxic patients upon admission died, and the difference between the groups was significant ($p<0.05$). The mean platelet count was 206.22±100.1 in the mortality group and 248.55±91.39 in the survival group, and the difference was significant ($p<0.05$). The mean NLR was 14.91±9.41 in the mortality groups and 11.4±10.67 in the survival group, and the difference between the groups was

Table 1. Clinical baseline characteristics and infection markers in subgroups of patients admitted and not admitted to the ICU.

Clinical characteristics		No ICU admission (n=90)	ICU admission (n=72)	p
Sex	Male	50 (55.56%)	37 (51.39%)	0.59
	Female	40 (44.44%)	35 (48.61%)	
SpO_2	Hypoxia	49 (54.44%)	70 (97.22%)	0.0001
	Normal	41 (45.56%)	2 (2.78%)	
Radiologic findings	Multilobar	56 (62.22%)	35 (48.61%)	0.097
	Multilobar + PE	25 (27.78%)	33 (45.83%)	
	Single Lobe	5 (5.56%)	3 (4.17%)	
	Single Lobe + PE	4 (4.44%)	1 (1.39%)	
Age (year)		81.13±11.34	82.19±8.02	0.503
WBC (x 103/µL)		11.58±5.26	12.7±5.65	0.192
Platelet		238.97±87.74	244.06±101.86	0.734
Neutrophils		9.6±5.1	10.8±5.18	0.140
Lymphocytes		1.29±0.84	1 11±0.72	0.135
NLR		10.5±10.07	13 88±10.83	0.042
PLR		246.86±185.32	308.89±246.9	0.079
CRP		102.91±63.88	133.94±80.15	0.007
Hospital LOS (days)		9.66±4.67	24.25±19.92	0.0001

Note: Data are presented as mean±Standard deviation (SD)

Abbreviations: PE, pleural effusion; WBC, white blood cell; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; CRP, C-reactive protein; LOS, length of stay.

significant ($p<0.05$). The length of hospital stay was 32.14±26.98 days in patients who died and 12.8±8.8 days in patients who recovered, and this difference was significant ($p<0.05$) (Table 2).

There was a significant positive correlation between CRP and NLR ($r=0.18$; $p<0.05$). There was no statistically significant relationship between CRP and PLR ($r=-0.03$; $p>0.05$) (Table 3, Figure 1).

Table 2. Clinical baseline characteristics and infection markers in patients who died and recovered.

Clinical characteristics		Recovered (n=134)	Died (n=28)	p
Sex	Male	77 (57.46%)	10 (35.71%)	0.036
	Female	57 (42.54%)	18 (64.29%)	
SpO_2	Hypoxia	91 (67.91%)	28 (100%)	0.0001
	Normal	43 (32.09%)	0 (0%)	
Radiologic findings	Multilobar	78 (58.21%)	13 (46.43%)	0.62
	Multilobar + PE	45 (33.58%)	13 (46.43%)	
	Single lobe	7 (5.22%)	1 (3.57%)	
	Single lobe + PE	4 (2.99%)	1 (3.57%)	
Age (years)		81.51±10.19	82.04±9.11	0.68
WBC ($\times 10^3/\mu L$)		11.79±5.28	13.44±6.13	0.27
Platelet		248.55±91.39	206.22±100.1	0.04
Neutrophils		9.85±5.05	11.5±5.51	0.15
Lymphocytes		1.25±0.82	1.02±0.64	0.13
NLR		11.4±10.67	14.91±9.41	0.009
PLR		276.1±222.43	266.46±188.19	0.80
CRP		112.92±72.1	134.79±75.83	0.14
Hospital LOS (days)		12.8±8.8	32.14±26.98	00001

Note: Data are presented as mean±Standard deviation (SD)

Abbreviations: PE, pleural effusion; WBC, white blood cell count; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; CRP, C-reactive protein; LOS, length of stay.

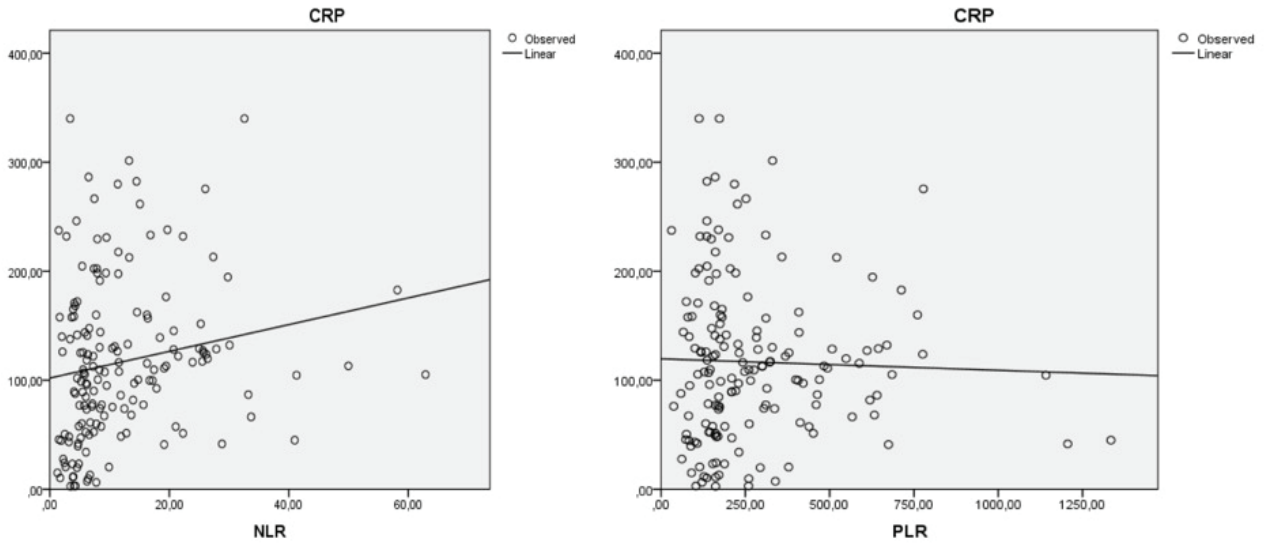
Table 3. .Correlations of the NLR and PLR with CRP

		NLR	PLR
CRP	r*	0.176*	−0.031
	p	0.025	0.695
	N	162	162

*Pearson's correlation

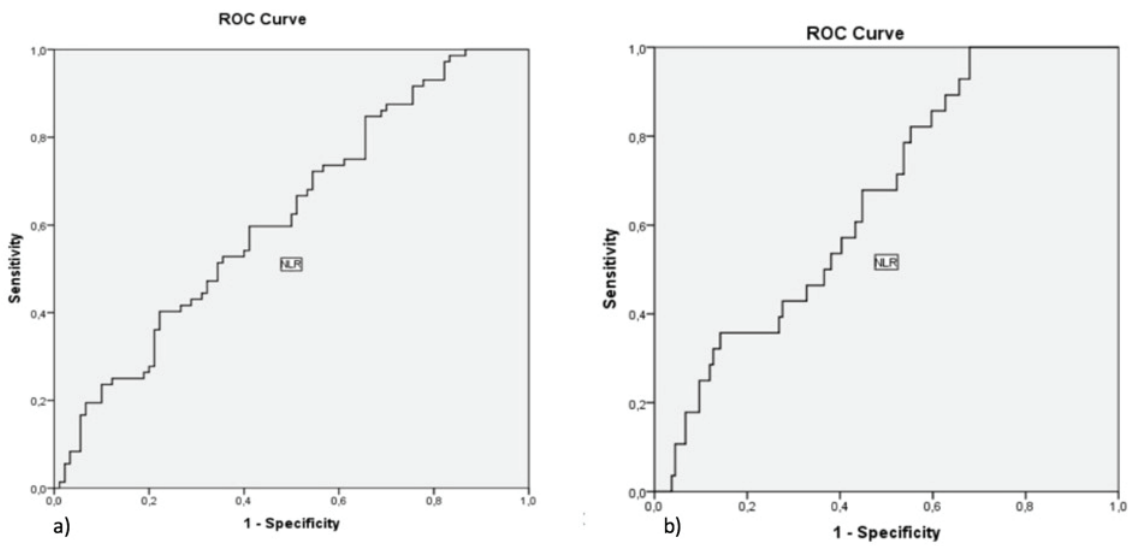
Abbreviations: NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; CRP, C-reactive protein; N, number.

Figure 1. Correlations of the NLR and PLR with CRP.



Distinguishing the characteristic of NLR values according to the patient's ICU admission and mortality status was investigated through the ROC curve. NLR was found to be a significant distinctive variable ($AUC_{mortality}$=0.66 and $AUC_{ICU\ admission}$=0.62) (Figure 2).

Figure 2. ROC curves of the NLR ICU admission (a) and for predicting mortality (b).



NLR cutoff values were calculated with ROC curve. The NLR cutoff was 8 for both patients admitted to the ICU and those who died (Table 4).

Table 4. Prognostic accuracy of the NLR.

NLR	Cutoff	Sensitivity	Specificity	PPV	NPV	AUC	p
ICU admission	8	68.25	58.89	53.75	72.6	0.62	0.009
Mortality	8	67.86	54.48	23.75	89.02	0.658	0.009

Abbreviations: NLR, neutrophil-to-lymphocyte ratio; ICU, intensive care unit; PPV, positive predictive value; NPV, negative predictive value; AUC, area under the curve.

The NLR and PLR of patients hospitalized for>10 days and patients hospitalized for<10 days were compared. There was no significant difference in terms of NLR and PLR (p>0.05) (Table 5).

Table 5. Prognostic accuracy of the NLR and PLR for predicting the length of hospital stay

Hospital LOS	≤ 10 days	> 10 days	p
NLR	12.48±11.12	11.65±10.1	0.72
PLR	269.27±215.29	278.26±218.28	0.93

Abbreviations: LOS, length of stay; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio.

DISCUSSION

The diagnosis of aspiration pneumonia is difficult because it can be confused with other types of pneumonia and it has a high mortality (10, 11). CRP, WBC, and neutrophil counts are still the most commonly used infection markers (12). Although procalcitonin, proadrenomedullin (proADM), urokinase-type plasminogen activator receptor (suPAR), and several cytokines have been studied as new infection markers, they are costly and have not yet been widely used (13, 14). The advantage of NLR and PLR is that they are calculated using the parameters in the whole blood count, which are currently used and are more cost-effective. NLR was first mentioned in 1985 by Varenko luS et al. (15). NLR and PLR have been used as prognostic parameters in predicting mortality in many oncological diseases as well as in cardiovascular and autoimmune diseases (15-19).

In this study, we investigated the prognostic value of NLR and PLR in aspiration pneumonia. To the best of our knowledge, this is the first study to evaluate NLR and PLR in aspiration pneumonia. Lee JH et al. have reported that NLR and PLR have prognostic importance for predicting ICU admission in patients with pneumonia (20). Yoon NB et al. have found that NLR can support tuberculosis when the cutoff value is lower than 7 in the differentiation of patients with bacterial community-acquired pneumonia and tuberculosis (21). De Jager PC et al. have found that the prognostic value for predicting hospitalization, ICU admission, and mortality was higher for of NLR than for other infection parameters in patients with pneumonia admitted to the emergency room (6). In the same study, the NLR cutoff value was determined to be 10, which was higher in patients who were hospitalized for>10 days (6).

In our study, the NLR cutoff value was 8; sensitivity and specificity for ICU admission were 68.25% and 58.89%, respectively (AUC, 0.62); sensitivity and specificity for mortality were 67.86% and 54.48%, respectively (AUC, 0.658), and the difference was significant ($p<0.05$). However, NLR did not have significant prognostic value in predicting the length of hospital stay in our study ($p>0.05$).

Yao C et al. have reported that both NLR and PLR have a prognostic role in chronic obstructive pulmonary disease acute exacerbation mortality (22). In the same study, a linear correlation was found between NLR and CRP, but no correlation was found between PLR and CRP (22).

In our study, NLR was significant in predicting mortality in aspiration pneumonia, whereas PLR had no prognostic significance in predicting both ICU admission and mortality. Similarly, a linear correlation was found between NLR and CRP, whereas no linear correlation was found between PLR and CRP. In our study, PLR was higher in patients admitted to the ICU than in those who were not admitted, but the difference was not significant ($p=0.079$). On the other hand, PLR was higher in the survival group than the mortality group. In addition, the platelet counts were significantly lower in the mortality group than the survival group.

According to Anderson R et al., this can be explained by the fact that patients with pneumonia sometimes develop thrombocytosis or thrombocytopenia (23); therefore, PLR was possibly insignificant in predicting mortality in our study.

This study had some limitations. First, this is primarily a single-center retrospective study and should be supported by prospective studies. Second, no comparison of NLR with new infection markers (such as procalcitonin and proadrenomedullin, etc.) has been made. Third, the data on the microbiological results of patients were not used in the study.

In conclusion, the prognostic value of NLR and PLR in patients with aspiration pneumonia for predicting ICU admission and mortality was investigated. NLR has a prognostic value in predicting ICU admission and mortality in patients with aspiration pneumonia, but PLR had no prognostic significance. We believe that NLR can be used, in addition to other prognostic criteria, in patients diagnosed with aspiration pneumonia with high mortality.

CONFLICTS OF INTEREST

The authors of this article state that they have no conflict of interest.

REFERENCES

1. Marik PE. Aspiration pneumonitis and aspiration pneumonia. N Engl J Med 2001;344(9):665-71. (PMID:11228282).
2. El-Solh AA, Pietrantoni C, Bhat A, et al. Microbiology of severe aspiration pneumonia in institutionalized elderly. Am J Respir Crit Care Med 2003;167(12):1650-4. (PMID:12689848).
3. Mandell LA, Niederman MS. Aspiration Pneumonia. N Engl J Med 2019;380(7):651-63. (PMID:30763196).
4. Papadopoulos D, Bader I, Gkioxari E, et al. Microbiology and prognosis assessment of hospitalized patients with aspiration pneumonia: a single-center prospective cohort study. Infez Med 2018;26(2):103-14. (PMID:29932081).
5. Lindenauer PK, Strait KM, Grady JN, et al. Variation in the Diagnosis of Aspiration Pneumonia and Association with Hospital Pneumonia Outcomes. Ann Am Thorac Soc 2018;15(5):562-9. (PMID:29298090).
6. 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. (PMID:23049706).
7. Zahorec R. Ratio of neutrophil to lymphocyte counts—rapid and simple parameter of systemic inflammation

and stress in critically ill. Bratisl Lek Listy 2001;102(1):5-14. (PMID:11723675).

8. de Jager CP, van Wijk PT, Mathoera RB, de Jongh-Leuvenink J, van der Poll T, Wever PC. Lymphocytopenia and neutrophil-lymphocyte count ratio predict bacteremia better than conventional infection markers in an emergency care unit. Crit Care 2010;14(5):R192. (PMID:21034463).
9. 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. Clim Chim Acta 2017;465:11-16. (PMID:27965019).
10. Mandell LA, Niederman MS. Aspiration Pneumonia. N Engl J Med 2019;380(7):651-63. (PMID:30763196).
11. Lindenauer PK, Strait KM, Grady JN, et al. Variation in the Diagnosis of Aspiration Pneumonia and Association with Hospital Pneumonia Outcomes. Ann Am Thorac Soc 2018;15(5):562-9. (PMID:29298090).
12. Ticinesi A, Lauretani F, Nouvenne A, et al. C-reactive protein (CRP) measurement in geriatric patients hospitalized for acute infection. Eur J Intern Med 2017;37:7-12. (PMID:27594414).
13. Li Q, Wang BS, Yang L, Peng C, Ma LB, Chai C. Assessment of adrenomedullin and proadrenomedullin as predictors of mortality in septic patients: A systematic review and meta-analysis. Med Intensiva 2018;42(7):416-24. (PMID:29246418).
14. Suberviola B, Castellanos-Ortega A, Ruiz Ruiz A, Lopez-Hoyos M, Santibañez M. Hospital mortality prognostication in sepsis using the new biomarkers suPAR and proADM in a single determination on ICU admission. Intensive Care Med 2013;39(11):1945-52. (PMID:23949703).
15. Varenko IuS, Lekakh VA, Shidlovskaia MP. Significance of the ratio of blood lymphocytes to polymorphonuclear neutrophils in pneumonia and bronchitis patients. Vrach Delo 1985; (8): 102-3. (PMID:4072096).
16. Kabir T, Ye M, Mohd Noor NA, Woon W, Junnarkar SP, Shelat VG. Preoperative Neutrophil-to-Lymphocyte Ratio plus Platelet-to-Lymphocyte Ratio predicts the outcomes after curative resection for hepatocellular carcinoma. Int J Hepatol 2019; 2019:4239463. (PMID:31065387).
17. Soylu K, Gedikli Ö, Dagasan G, et al. Neutrophil-to-lymphocyte ratio predicts coronary artery lesion complexity and mortality after non-ST-segment elevation acute coronary syndrome. Rev Port Cardiol 2015;34(7-8): 465-71. (PMID:26164277).
18. Paliogiannis P, Satta R, Deligia G, et al. Associations between the neutrophil-to-lymphocyte and the platelet-to-lymphocyte ratios and the presence and severity of psoriasis: a systematic review and meta-analysis. Clin Exp Med 2019;19(1):37-45. (PMID:30478648).
19. Erre GL, Paliogiannis P, Castagna F, et al. Meta-analysis of neutrophil-to-lymphocyte and platelet-to-lymphocyte ratio in rheumatoid arthritis. Eur J Clin Invest 2019;49(1):e13037. (PMID:31316204).
20. Lee JH, Song S, Yoon SY, Lim CS, Song JW, Kim HS. Neutrophil to lymphocyte ratio and platelet to lymphocyte ratio as diagnostic markers for pneumonia severity. Br J Biomed Sci 2016;73(3):140-2. (PMID:27723441).
21. Yoon NB, Son C, Um SJ. Role of the neutrophil lymphocyte count ratio in the differential diagnosis between pulmonary tuberculosis and bacterial community-acquired pneumonia. Ann Lab Med 2013;33(2):105-10. (PMID:23482854).
22. Yao C, Liu X, Tang Z. Prognostic role of neutrophil-lymphocyte ratio and platelet-lymphocyte ratio for hospital mortality in patients with AECOPD. Int J Chron Obstruct Pulmon Dis 2017;12:2285-90. (PMID:28814856).
23. Anderson R, Feldman C. Review manuscript: Mechanisms of platelet activation by the pneumococcus and the role of platelets in community-acquired pneumonia. J Infect 2017: 75(6): 473-85. (PMID:28943342).