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The Prognostic Impact of Dynamic Change in Neutrophil to Lymphocyte Ratio in Patients with Acute Pulmonary Embolism

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Aim: It is unclear whether temporal changes in neutrophil to lymphocyte ratio (NLR) are associated with total mortality in acute pulmonary embolism (APE). We investigated the value of dynamic monitoring of NLR for the prognosis in patients with APE.
Methods: We retrospectively analyzed 214 consecutive APE patients. The patients were divided into two groups: survivors or non-survivors. The neutrophil count, lymphocyte count and NLR were obtained at admission and 72 hours. The difference between the 2 measurements was considered as the NLR change (ΔNLR). The end point of the study was total mortality at 30-day follow-up.
Results: During follow-up, there were 30 deaths (14%). ΔNLR was higher in non-survivors than survivors survivors (5.22 [0.62-7.76] vs -0.71 [-2.28-0.76], P < .001). In multivariate analysis, the ΔNLR was found to be a significant predictor of 30-day mortality (OR: 1.059, 95% CI:1.021-1.098, p=0.002). For 30-day mortality, the area under the curve (AUC) of Simplified Pulmonary Embolism Severity Index (sPESI) score was 0.719 (95% CI:0.630-0.809, p < 0.001). When ΔNLR was added to sPESI score, the AUC was 0.841 (95% CI: 0.769-0.913, difference p = 0.0008, Fig.1). Morever, the addition of ΔNLR to sPESI score was associated with a significant net reclassification improvement estimated at 68.9% (p < 0.001) and an integrated discrimination improvement of 0.108 (p = 0.0046).
Conclusion: Our findings show that an increase in NLR after admission was independently associated with total mortality in patients with APE.
Keywords: Neutrophil to Lymphocyte Ratio, Inflammation, Pulmonary Embolism, Mortality.

Akut Pulmoner Embolili Hastalarda Nötrofil Lenfosit Oranındaki Dinamik Değişimin Prognostik Etkisi

Amaç: Nötrofil lenfosit oranındaki (NLR) geçici değişikliklerin akut pulmoner embolide (APE) toplam mortalite ile ilişkili olup olmadığı belirsizdir. APE'li hastalarda prognoz için NLR'nin dinamik monitorizasyonunun değerini araştırdık.
Gereç ve Yöntem: 214 ardışık APE hastasını retrospektif olarak analiz ettik. Hastalar iki gruba ayrıldı: hayatta kalanlar ve ölenler. Nötrofil sayısı, lenfosit sayısı ve NLR girişte ve 72. Saatteki değerleri alındı. 2 ölçüm arasındaki fark NLR değişimi (ΔNLR) olarak kabul edildi. Çalışmanın son noktası 30 günlük takipteki toplam mortalite idi.
Bulgular: Takip süresince 30 ölüm (%14) vardı. ΔNLR, hayatta kalanlarda ölenlere göre daha yüksekti (5.22 [0.62-7.76] ve -0.71 [-2.28-0.76], p <.001). Çok değişkenli analizde, ΔNLR 30 günlük mortalitenin anlamlı bir öngördürücüsüydü. (OR: 1.059, %95 CI: 1.021-1.098, p = 0.002). 30 günlük mortalite için, Basitleştirilmiş Pulmoner Emboli Şiddet İndeksi (sPESI) skorunun eğri altındaki alanı (AUC) 0.719'du (%95 CI: 0.630-0.809, p <0.001). SPESI skoruna ΔNLR eklendiğinde, AUC 0.841'dir (%95 CI: 0.769-0.913, fark p = 0.0008, Şekil 1). Dahası, sPESI skoruna ΔNLR eklenmesi, %68.9 (p <0.001) ve entegre bir ayrımcılık iyileşmesi 0.108 (p = 0.0046) olarak tahmin edilen önemli bir net yeniden sınıflandırma iyileştirmesi ile ilişkilendirilmiştir.
Sonuç: Bulgularımız, başvuru sonrası NLR'deki artışın APE'li hastalarda toplam mortalite ile bağımsız olarak ilişkili olduğunu göstermektedir.
Anahtar Kelimeler: Nötrofil Lenfosit Oranı, İnflamasyon, Pulmoner Emboli, Mortalite.

INTRODUCTION

Acute pulmonary embolism (APE) is one of the most prevalent acute cardiovascular disease that frequently caused by venous tromboembolism following ischemic heart disease and stroke (Raja et al., 2015). It is characterized by high mortality and high morbidity due to delayed diagnosis, misdiagnosis or missed diagnosis (Konstantinides et al., 2014). The short-term prognosis of APE depends on the initial hemodynamic status of patients and its underlying disease (Goldhaber et al., 1999; Aujesky et al., 2005). Morever, the presence of right ventricular dysfunction (RVD), high levels of brain natriuretic peptide (BNP), N-terminal–proBNP (NT-proBNP), and myocardial injury with increased cardiac troponins are associated with increased risk of short-term death from APE (Cecilia Becattini et al., 2007; Klok et al., 2008; Sanchez et al., 2008). Therefore, the prognostic tools has a pivotal role in risk classification of patients with APE.

In recent studies, growing evidences points towards the role of inflammation in the pathophysiology of APE (Venetz et al., 2013, Watts et al., 2008). Venetz et al. have found that increased counts of white blood cell (WBC) might be an independent prognostic indicator in patients with APE (Venetz et al., 2013). Soylu et al. indicated that the neutrophil to lymphocyte ratio (NLR) as a systemic inflammatory marker may be a predictor which reflects short term mortality in patients with APE (Soylu et al., 2016).

However, in a recent study conducted by Park et al. demonstrated that the total counts of leucocytes and its subtypes such as neutrophil and lymphocyte counts and the neutrophil and lymphocyte ratio (NLR) are unstable in the acute phase of critical illness and their alteration might be predict short term mortality due to the disease (Park et al., 2013).

In light of these studies, we aimed to investigate whether the dynamic changes of NLR may predict the short-term mortality in patients with APE.

MATERIAL AND METHODS

Study population

A retrospective study was conducted in Balikesir State Hospital and Balikesir University. Overall, 230 consequtive patients with APE were included in the study poplation between June 2008 and June 2015. Patients who had one of the following conditions were excluded from the study: Patients who had any other disorder such as major trauma with limiting the estimated life expectancy to less than one month, any hematological, infectious and inflammatory diseases, serious renal and liver disease, the length of hospital stay < 72 hours, deaths within first 72 hours and missing data. Also, patients who took medicine suh as immunosuppressant and anti-inflammatory drugs were excluded from the study. According to these criteria 16 of 230 patients were excluded from the study.

The remaining 214 patients were divided into two groups as survivors (n=184) and non-survivors (n=30) based on 30-day total mortality. The groups were compared the clinical and laboratory findings. The median ages of patients were comperable between the groups and all patients was included into the studied population were aged between 20 and 90 years.

Data regarding demographic and clinical properties and laboratory parameters were collected from hospital records. In this retrospective study, we received permission from the ethics committee to use patient data registered at our hospital.

Definitions

The 30-day mortality was defined as death from any cause within the 30 days during the follow-up period. According to the current guideline, diagnostic criteria of the APE was defined as ascertained with a combination of the following criteria: transthoracic echocardiographic findings confirming APE, lower limb venous ultrasonography findings interpreted as positive for deep venous thrombosis, presence of radiological criteria of acute PE on CTPA within 30 days after the beginning of shortness of breath or chest pain (Konstantinides et al., 2014).

Hypertension (HT) was defined as the use of antihypertensive drugs or systolic blood pressure (SBP) ≥ 140 mmHg and/or a diastolic blood pressure (DBP) ≥ 90 mmHg, diabetes mellitus (DM) was defined as use of antidiabetic drugs or fasting plasma glucose levels of > 7 mmol/L. The term of cancer was defined as active cancer disease and/or cancer in patients' history. Major bleeding was defined as a decline in hemoglobin level of 20 g per litre or more or transfusion of two or more units of red blood cells. Syncope was defined as a transient, self-limited loss of consciousness due to transient global cerebral hypoperfusion characterized by rapid onset, short duration, and spontaneous complete recovery (Moya, 2009). All patients' simplified pulmonary embolism severity index (sPESI) scores (which includes age, heart rate, systolic blood pressure, arterial oxyhemoglobin saturation, presence of cancer, chronic heart failure, and chronic pulmonary disease) were calculated for clinical risk stratification (Konstantinides et al., 2014). The myocardial necrosis was defined as cardiac troponin (cTnI) elevation > 0.06 ng/ml.

Echocardiography and Computed Tomography Imaging

A complete echocardiographic study was performed with Vivid 3 system (General Electric, made in Norway) during the initial evaluation of the patients. Right ventricular (RV) dimensions were measured from apical four-chamber view in diastole at mid-ventricular level. Systolic pulmonary arterial pressure (sPAP) was calculated by adding trans-tricuspid pressure gradient to mean right atrial pressure estimated from inferior vena cava diameter and motion during respiration as follows: mean right atrial pressure was estimated to be 5 mm Hg if there was complete collapse of a normal diameter inferior vena cava during inspiration; 10 mm Hg if a normal diameter inferior vena cava collapse was > 50%; 15 mm Hg if a dilated inferior vena cava collapsed by > 50% with inspiration; and 20 mm Hg if there was no visible collapse of a dilated inferior vena cava with inspiration (Jae, 2009). The CTPA was performed in the radiology clinic, using pulmonary embolism protocol (field of view: 35 cm, section thickness: 3 mm, contrast agent volume: 135 mL, contrast material injection rate: 4 mL/sec). Diagnosis of acute PE was established in case of a complete or partial luminal filling defect in the main pulmonary artery or its branches. RVD in echocardiography or CTPA was defined as right

ventricular enlargement (end diastolic lateral-septal diameter divided by end-diastolic left ventricular lateral-septal diameter > 0.9)(Konstantinides et al., 2014).

Laboratory analysis

Blood counts were measured from blood samples taken after the patient admission to emergency service or before APE diagnosis, and at 72h after admission for NLR. Dynamic change of NLR (ΔNLR) was defined as NLR at 72 hours minus NLR at admission. Blood samples for blood count were collected into commercially available EDTA tubes. Plasma samples were collected into tubes containing 0.106 M tri-sodium citrate (9/1). Samples were centrifuged for routine testing and analysis was performed within 1h after sampling. Complete blood count and platelet count was made by using a Coulter LH 780 Hematology Analyzer (Beckman Coulter Ireland, Inc., Galway, Ireland). Biochemical measurements were performed using Siemens Healthcare Diagnostic Products kits and calibrators (Marburg, Germany). The peak level of cardiac troponin I was measured.

Medications

18% of the patients were treated with a thrombolytic treatment (tissue plasminogen activator or streptokinase). Low-molecular weight heparin (LMWH) was given subcutaneously at weight-adjusted doses monitoring after the diagnosis of APE was ascertained. Intravenous unfractionated heparin (UFH) or subcutaneous LMWH was used after the thrombolytic treatment. Warfarin therapy was given to patients without active cancer on the day of admission except for the cases treated with thrombolytic who had warfarin treatment 24 hours after the therapy. Patients who received warfarin treatment were discharged with appropriate INR levels. In patients with cancer, weight-adjusted LMWH was prescribed at discharge.

Statistical analysis

Continuous variables were presented as means±SD or medians with inter-quartile ranges (IQR), whereas categoric variables were described as numbers and percentages. The differences between the two groups were compared using the chi-square test for categorical variables and Student's ttests or Mann Whitney U test for continuous variables. The relationship between ΔNLR and other demographic/biochemical parameters was assessed with pearson correlation test. We performed univariate and multivariate Cox regression analyses to asses the relation between ΔNLR and 30-day total mortality. Receiver operating characteristic curve analysis (ROC) was used to evaluate the predictive value of sPESI, and sPESI plus ΔNLR. The comparison of ROC curves of ΔNLR and sPESI plus ΔNLR was calculated using DeLong's test. Morever, the increased discriminative value after the addition of ΔNLR to sPESI score was also estimated using the Net Reclassification Improvement (NRI) and Integrated Discrimination Improvement(Pencina et al., 2011). The 30-day total mortality was estimated by the Kaplan-Meier method according to ΔNLR, and the curves were compared with the log-rank test. Statistical analysis was performed using the Statistical Package for Social Sciences, version 16 (SPSS Inc., Chicago, IL, USA. All tests were two-sided; a $p< 0.05$ was considered significant.

Ethic approval

The study was approved by the Balikesir University School of Medicine Local Ethics Committee (2019/160), and the protocols of the study were in accordance with the Helsinki Committee requirements. Informed consents were obtained from all participants.

RESULTS

Baseline characteristics

Baseline characteristics of the study population were summarized in Table 1. Non-survivor patients had significantly higher prevalence of cancer compared with survivors' patients (40 % vs 19%, p=0.010). They had also higher percentage of sPESI score ≥ 1 (100 % vs 79 %, p=0.004). RVD was more frequent in non-survivor patients than those of survivor (93 % vs 57%, p< 0.001). Major bleeding complication was observed in one patients in the non-survivor group.

Laboratory parameters

Laboratory parameters of patients in the survivor and non-survivor group were presented in Table 2. On admission, the neutrophil counts were higher in non-survivors than those survivors, but lmphocyte counts were comparable between the two groups (Table 2). The NLR was significantly higher in non-survivors at 72 hours after admission than those survivors [4.05 (2.63-6.33) vs. 14.18 (9.42- 17.71), p <0.001]. ΔNLR was significantly higher in non-survivors than those survivors (5.22 [0.62-7.76] vs -0.71 [-2.28-0.76], p<0.001). Also, ΔNLR was positively correlated with age, sPESI score, heart rate, RV/LV ratio (Table 3). Whereas it had a negative correlation with systolic blood pressure (r= -0.301, p < 0.001).

Clinical outcomes and ΔNLR

The percentage of 30-day death was 14% in our study population. Multivariate analysis was demonstrated that the RVD, sPESI, thrombolytic treatment, INR, and ΔNLR were independent predictors of mortality in patients with APE (Table 4).

Table 1. Clinical characteristics

Variables	Survivors (n = 184)	Non-survivors (n = 30)	p
Age, years	61 ± 18	68 ± 17	0.052
Gender (female / male)	102 / 82	14 / 16	0.371
History of cancer, n (%)	35 (19)	12 (40)	0.010
Hypertension, n (%)	62 (34)	10 (33)	0.969
Diabetes Mellitus, n (%)	27 (15)	6 (20)	0.454
COPD, n (%)	21 (11)	4 (13)	0.761
Deep vein thrombosis, n (%)	58 (32)	9 (35)	0.808
History of Stroke/TIA, n (%)	24 (13)	4 (14)	0.920
Heart failure, n (%)	12 (7)	1 (3)	0.498
CAD, n (%)	22 (12)	1 (3)	0.170
Recently surgery, n (%)	66 (36)	9 (30)	0.532
Hypoxia[#], n (%)	103 (56)	23 (77)	0.033
Syncope, n (%)	11 (6)	1 (3)	0.559
Systolic blood pressure, mmHg	116 ± 21	102 ± 28	0.003
Heart rate, beats/min	95 ± 22	112 ± 26	0.001
sPAP, mmHg	47 ± 19	48 ± 17	0.835
Thrombolytic treatment, n (%)	38 (21)	2 (7)	0.067
LVEF (%)	58 ± 7	58 ± 4	0.833
RV/LV ratio	0.99 ± 0.19	1.10 ± 0.19	0.017
RV dysfunction	102 (57)	25 (93)	< 0.001
sPESI ≥ 1, n (%)	146 (79)	30 (100)	0.006

CAD: coronary artery disease; COPD: chronic obstructive pulmonary disease; TIA: transient ischemic attack. sPAP: systolic pulmonary arterial pressure; LVEF: left ventricular ejection fraction; RV: right venricular, sPESI: simplified pulmonary embolism severity index.
[#] Hypoxia was defined as arterial oxyhaemoglobin saturation <90%.

Table 2. Laboratory findings of the study population

Variables	Survivors (n = 184)	Non-survivors (n = 30)	p
Neutrophils $_{adm}$ (x10^9/L)	8.4 ± 3.3	10.7 ± 3.8	0.001
Neutrophils $_{72h}$ (x10^9/L)	6.8 ± 2.9	11.7 ± 4.9	< 0.001
Lymphocytes $_{adm}$ (x10^9/L) *	1.60 (1.15-2.30)	1.19 (0.84-2.01)	0.108
Lmyphocytes $_{72h}$ (x10^9/L) *	1.51 (1.09-2.11)	0.95 (0.54-1.28)	< 0.001
NRL*adm	4.82 (2.95-7.40)	8.90 (5.70-12.60)	0.003
NLR*$_{72h}$	4.05 (2.63-6.33)	14.18 (9.42- 17.71)	< 0.001
ΔNLR	-0.71 (-2.28-0.76)	5.22 (0.62-7.76)	< 0.001
Haemoglobin (g/ dL)	12.4 ± 3.1	11.8 ± 2	0.331
Glucose, mg/dl	152 ± 70	156 ± 69	0.818
Creatinine, mg/dl*	0.83 (0.70-1.10)	0.84 (0.66-1.56)	0.975
D-dimer (mg/dl) *	1978 (946-4288)	2576 (1051-5647)	0.369
Troponin	0.067 (0.016-0.31)	0.09 (0.045-0.65)	0.324

NRL: neutrophil to lymphocyte ratio; RDW: red cell distribution width; adm: admission.
* Comparison was made using Mann-Whitney *U* test at *P* <0.05 and these values were described by median with inter-quartile range (25th and 75th percentile).

Table 3. Linear association between ΔNLR and other variables

Variables	r	p
Age, years	0.201	0.003
Systolic blood pressure, mmHg	-0.301	< 0.001
Heart rate, beats/min	0.223	0.001
RV/LV ratio	0.210	0.008
INR	0.109	0.118
sPESI score	0.290	< 0.001
c TnI levels	0.192	0.023

ΔNLR: neutrophil to lymphocyte ratio difference between at 72 hour and admission; RV/LV: right ventricular end-diastolic diameter ratio left ventricular diameter; INR: international normalized ratio; sPESI: simplified pulmonary embolism severity index; cTnI: cardiac troponin I.

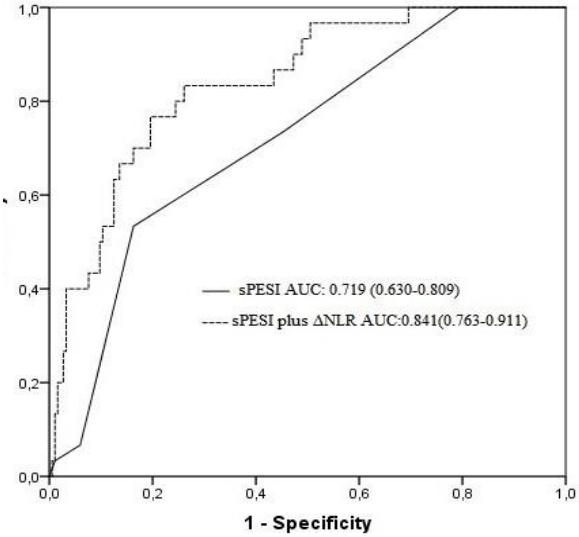
Table 4. Predictors of total mortality in univariate and multivariate analysis

Variables	Univariate		Multivariate	
	OR (95% CI)	p	OR (95% CI)	p
Age (years)[#]	1.023 (1.000-1.047)	0.055		
Cancer [#]	2.560 (1.233-5.318)	0.012		
Hypoxia[#]	2.405 (1.032-5.605)	0.042		
RVD	8.443 (1.999-35.649)	< 0.001	8.609 (1.984-37.364)	0.004
NLR_{adm}	1.092 (1.035-1.053)	0.001	1.055 (0.981-1.134)	0.152
NLR_{72h}	1.060 (1.039-1.080)	< 0.001		
ΔNLR	1.072 (1.044-1.101)	< 0.001	1.059 (1.021-1.098)	0.002
Systolic blood pressure < 90 mmHG[#]	2.746 (1.285-5.867)	0.009		
Heart rate > 100/min[#]	2.193 (1.072-4.487)	0.032		
Thrombolytic treatment	0.294 (0.070-1.234)	0.094	0.105 (0.018-0.604)	0.012
sPESI score	1.699 (1.233-2.233)	< 0.001	1.466 (1.006-2.136)	0.046
INR	3.771 (1.711-8.311)	0.001	5.205 (1.736-15.612)	0.003

OR: odds ratio; CI: confidence interval; RVD: right ventricular dysfunction; NLR: neutrophil to lymphocyte ratio; adm: admission; sPESI: simplified pulmonary embolism severity index; INR: international normalized ratio, ΔNLR: difference between NLR_{adm} and NLR_{72h}.
[#]Systolic blood pressure, heart rate, cancer history, hypoxia, and age were not entered to the multivariate model as this parameters are included in the simplified pulmonary embolism severity index.

In ROC analysis, a ΔNLR value of 0.66 had 77% sensitivity and 75 % specificity for prediction of 30-day mortality (AUC = 0.805, p <0.001) (Figure 1). A ΔNLR level> 0.66 (OR 4.78, 95 % CI1.82–12.52; P = 0.001) remained significantly associated with 30-day mortality after adjusting for RVD, sPESI, thrombolytic treatment, and INR. For 30-day mortality, the AUC of sPESI score was 0.719 (95% CI:0.630-0.809, p < 0.001). When ΔNLR was added to sPESI score, the AUC was 0.841 (95% CI: 0.769-0.913, difference p = 0.0008, Fig.1).

Figure 1. Receiver operating characteristics (ROC) curves of sPESI and sPESI plus ΔNLR for 30-day mortality.



Morever, the addition of ΔNLR to sPESI score was associated with a significant net reclassification improvement estimated at 68.9% (p < 0.001) and an integrated discrimination improvement of 0.108 (p = 0.0046) (Table 5).

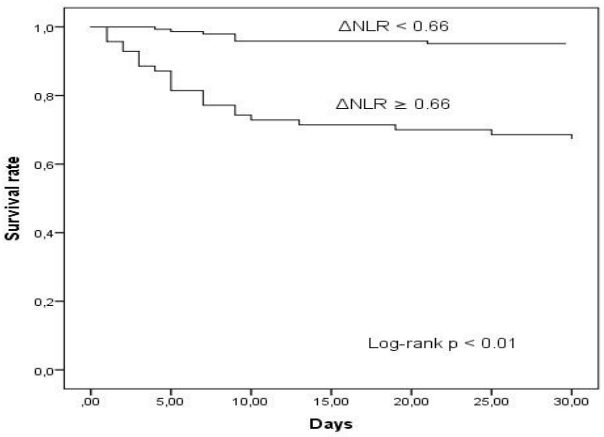
Table 5. Statistics for model improvement with the addition of ΔNLR

		p
Continous NRI	68.9%	p< 0.001
IDI statistics	0.108	p = 0.0046
AUC		
sPESI	0.719	p < 0.001
sPESI plus ΔNLR	0.841	p < 0.001
Difference p		0.0008

sPESI: simplified pulmonary embolism severity index, ΔNLR: dynamic change in neutrophil to lymphocyte ratio, NRI:Net Reclassification Index, IDI: integrated discrimination index.

Kaplan-Meier survival analysis curves revealed 30-day total mortality was higher in patients with high ΔNLR than for those with low ΔNLR (Figure 2).

Figure 2: Kaplan-Meier survival curve according to ΔNLR



DISCUSSION

In the present study, we investigated clinical importance of dynamic monitoring of NLR for the prediction of the prognosis in patients with APE. Importantly, we found that the NLR is a dynamic variable, and its change is associated with 30-day total mortality in patients with APE. Morever, the best discriminating value of the ΔNLR for 30-day mortality was 0.66, which was associated with an 4.78 - fold increased risk for 30-day mortality in these patients. These results indicated that dynamic monitorization of NLR may give further information related to mortality of the patients with APE. To the best of our knowledge, this is the first study to investigate the association between dynamic changes of NLR and prognosis of patients with APE. APE is defined as a form of venous thromboembolism (VTE). It is a common disease that can cause mortality. The clinical presentation of APE is variable and often nonspecific making the diagnosis challenging. The evaluation of patients with suspected APE should be efficient so that patients can be diagnosed and therapy administered quickly to reduce the risk of associated morbidity and mortality.

Inflammation plays a key role in the underlying molecular and cellular mechanism of APE (Bakirci et al., 2015). Inflammatory poccess in APE patients interacts with several common pathways including the activation of coagulation, inhibition of fibrinolysis and anticoagulant process leading to thrombotic events (Bakirci et al., 2015; Begieneman et al., 2008; Iwadate et al., 2003). It is known that the platelets, leukocytes, and endothelial cells are pivotal role in all these processes. Hemostasis and thrombosis are related processes involving the coagulation system, platelets, endothelial cells, and the vascular wall.

In APE patients, the neutrophil influx occurs between in 6 and 18 h in the inflammatory phase of the disease and it returns to baseline between in 4 and 7 days after APE(Watts et al., 2008). Previous studies have revealed that APE leads to myocyte lysis of right ventricle (RV) and infiltration of RV by inflammatory cells, such as neutrophil, macrophage and lymphocyte(Watts et al., 2008; Iwadate et al., 2001). In addition, recent studies have shown that presence of infiltration of inflammatory cells might increase the damage in RV(Watts et al., 2008). On the other hand, previous studies have shown that there are various biomarker alterations including myeloperoxidase and CRP, related to inflammatory condition in patients with APE (Nordenholz et al., 2008; Kline et al., 2008). Moreover in some recent studies have demonstrated that presence of RV dysfunction and cardiac damage which can be detected by increased levels of cardiac troponins correlated with prognosis of the disease (Binder et al., 2005; Scridon et al., 2005;Mitchell et al., 2008; C Becattini, 2008; Jiménez Castro et al., 2008; Gallotta et al., 2008). In the present study, we found that the values of ΔNLR was positively correlated with cTnI levels in our study population. It is known that the NLR is a newly introduced inflammatory marker, which reflect the balance between neutrophil count to lymphocytes count. Previous studies have indicated that increased value of NLR may be associated with severity of inflammation (Başer et al., 2017). Zahorec showed that the severity of the clinical course was correlated with NLR and the author concluded that the NLR is an easily measurable parameter to show severity of injury in the body (Zahorec R, 2001). Moreover, Nordenholz et al. have indicated that NLR may be exhibit temporal variation in patient with ischemic stroke (Nordenholz et al., 2008). Compatible with these results, we found that the NLR is a dynamic variable, and its change is associated with 30-day total mortality in patients with APE. These changes in the value of NLR might be related to the stimulation of bone marrow which causes many different cell production and release to the circulation, leukocyte margination, and migration of the leukocyte into the damaged tissue. The changes in the value of NLR might be also related to decreases in the circulating levels of lymphocytes counts during the acute stress events.

Li et al. demonstrated that increase in the value of NLR may be associated with adverse clinical outcomes before the PCI. They have demonstrated that increased value of NLR and its changes may reflect mortaliy and morbidity in many disease (Li et al., 2017). Park et al. found that the NLR value within 24 hours after hospital admission was an independent marker for the prediction of mortality in STEMI patients who underwent PCI (Park et al., 2013). In our study, we found that the neutrophil counts tend to be decrease at 72 h after hospital admission in survivors group. Whereas the neutrophil counts did not decrease at 72h in non-survivors patients. Morever, lymphocyte count decreased in both survivors and non-survivors group at 72 h after hospital admission. However, this decrease was greater in non-survivors group than those who lived. To date, the sPESI score is the most commonly used and validated score in APE patients and it may accurately identify a low-risk in patients with APE(Konstantinides et al., 2014)(Jiménez et al., 2010). In our study, we indicated that the NLR value was positively correlated with sPESI score in our study population. The main limitations of this study concerns its retrospective study design and its relatively small population size. Also, systemic thrombolysis was not administered in some patients suffering from haemodynamic instability because of contraindications to thrombolysis. Moreover, we did not evaluate the extent of cancer and treatments such as chemotheraphy. We did not measure conventional pro-inflammatory markers like CRP, IL-6 or thromboxane A2 and analyze the correlation of these parameters with the ΔNLR.

CONCLUSION

In patients with APE, ΔNLR was an independent predictor which was related to 30-day mortality. This parameter may identify the PE patients at high risk for early mortality. In this study, adding ΔNLR to sPESI score seemed to have a contributive role in predicting 30-day all-cause mortality and may provide more precise risk categorization. Thus, such patients who had a higher ΔNLR may need more close monitoring. However, further studies are needed to implement it into clinical practice in patients with APE.

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