NEW INFLAMMATORY PARAMETERS TO PREDICT IN-HOSPITAL PROGRESSION OF ACUTE PULMONARY EMBOLISM

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ABSTRACT

Background: Mechanical and inflammatory alterations are linked to the progression of hemodynamic instability in normotensive patients with Acute Pulmonary Embolism (APE).

Objective: This study aimed to evaluate the ability of some new inflammatory parameters to predict the outcome of normotensive APE patients in an In-hospital setting.

Patients and Methods: This prospective cohort study included 62 normotensive patients diagnosed as acute pulmonary embolism by CTPA. Neutrophil-Lymphocyte ratio (NLR) and Platelet-Lymphocyte ratio (PLR) were estimated during hospital stay. According to outcome they were divided in two groups. The indices were compared in both groups.

Conclusions: NLR and PLR are useful tools independently or combined to identify normotensive patients with APE to predict short-term poor outcome.

Keywords: Pulmonary Embolism; Neutrophils; Lymphocytes; Platelets; Troponin; Adverse Events; Haemodynamic Instability.

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Introduction

Venous thromboembolism (VTE) or pulmonary embolism (PE) is the third most common cause of cardiovascular death. Its incidence has been rising over the years. [(1)]. APE may cause a large number of deaths within a few hours after the onset of symptoms [(2)].

Patients with PE may vary in severity from extremely sick to stable, with a very diverse clinical appearance. Guidelines distinguish patients at low, moderate, and high risk. Patient risk categorization will affect how treatments are administered. Hemodynamic instability, obstructive shock, chronic arterial hypotension that is unresponsive to therapy and cardiac arrest are linked to high-risk PE [(3)]. New studies are reporting the importance and diagnostic potential of inflammatory response in APE [(4)].

In addition, inflammatory biomarkers are useful due to their accessibility, speed of study, and suitability for everyday application. During the clinical course of APE, platelets and leukocytes release more procoagulatory and pro-inflammatory substances [(5)].

An increased platelet activation and neutrophils recruitment during APE have been associated with short-term mortality and poor prognosis [(6)]. On the other hand, lymphocyte count decreases because of the increased adrenaline and glucocorticoid response [(7)].

The present study aimed to investigate the prognostic value of NLR and PLR in the in-hospital course and progression of normotensive patients with acute pulmonary embolism.

Patients and Methods

This prospective cohort study was carried out in cardiology department, Faculty of medicine, Zagazig university hospitals & cardiology department, Alahrar Teaching Hospital,Zagazig.

75 patients consecutively admitted with the diagnosis of acute PE.

Inclusion criteria

The diagnosis of acute PE confirmed by contrast enhanced computed tomographic pulmonary angiography (CTPA). Only patients with systolic blood pressure (BP) of at least 90 mmHg without hemodynamic support were included in the study.

Exclusion criteria:

Patients with an active cancer, sepsis, and known inflammatory and autoimmune diseases.

Clinical Assessment:

After excluding 13 patients who met the exclusion criteria or whose data were missing, 62 patients of both genders were analyzed in the present study. All Patients were subjected to:

- Complete history taking: Factors such as age, history of heart attack, high blood pressure, diabetes, and other cardiac diseases.
- Clinical evaluation: Measurements of BP, HR, basal rales, and body mass index.
- Laboratory investigations: cardiac enzymes (troponin, CK-MB), Complete blood count were taken at admission.
- Twelve lead surface ECG.
- Echocardiography: a full study was done to each patient

All patients were treated according to ESC guidelines and were followed up during hospital stay for development of any adverse events which were as follows:

- **Death**: PE related death was confirmed shortly after a clinically severe PE or in the absence of an alternative diagnosis.
- **Resuscitated cardiac arrest:** Cardiac arrest was defined as the need for cardiopulmonary resuscitation.
- **Development of hemodynamic instability** (cardiogenic shock or need of hemodynamic support, need of systemic rescue thrombolysis): Development of hemodynamic instability was defined as the occurrence of cardiogenic shock defined as sustained reduction of systolic blood pressure < 90 mmHg for at least 15 min or requiring pressor support, or a systolic BP drop ≥ 40 mmHg for >15 min, not caused by new-onset arrhythmia, hypovolemia, or sepsis.
- **Need of systemic rescue thrombolysis** was defined as escalation of therapy due to hemodynamic instability and was established at the indication of the attending physician or on call physician.

All patients Laboratory Indices were compared between groups of patients with and without adverse events, and those parameters that differed significantly between groups were evaluated regarding their predictive power in multivariate analysis.

Statistical analysis

All data were collected, tabulated and statistically analyzed using statistical package of special science SPSS version 22 (SPSS Inc. Chicago, IL, U.S.A) in consultation with a medical statistician from the epidemiology department of Zagazig university. Paired t-test was used to compare between two dependent groups of normally distributed variables. Chi square test ($\chi 2$) and

fisher exact was used to calculated difference between qualitative variables. Regression analysis of different parameters associated with low performance of 6MWT. Roc Curve analysis of Blood Pressure and low performance of 6MWT. All statistical comparison were two tailed with significance level of p-value ≤ 0.05 indicates significant, p- value <0.001 indicates highly significant difference while p-value > 0.05 indicates non-significant difference.

Results

A number of 80 patients were admitted with the diagnosis of APE. 75 normotensive patients were included and after final evaluation and application of exclusion criteria, 62 Patients were included in our study. Adverse outcome (including haemodynamic instability, need of rescue thrombolysis, in-hospital death and cardiac arrest) was present in 11 patients (17.74%).11 patients developed haemodynamic instability(17.74%), all of them required rescue thrombolysis (17.74%), PE related death was registered in 2 patients (6.45%) and resuscitated cardiac arrest occurred in 3 patients (4.83%). Laboratory parameters including NLR and PLR to predict PE-related adverse events, including mortality, cardiac arrest, hemodynamic instability, need of rescue thrombolysis during hospitalization were directly compared in 62 normotensive patients with acute PE Multiple logistic regression demonstrated that NLR, PLR could be used as predictors for AE **(Table 1,2)**. Multiple logistic regression demonstrated that NLR, PLR could be used as predictors for AE **(Table 3)**.

Table (1): Baseline characters of included patients

	mean	SD
Age	58.76	12.638
	N	**%**
Gender		
Male	35	56.5
Female	27	43.5
Adverse Events	11	17.7
In-Hospital Death	2	3.2
Resuscitated Cardiac Arrest	3	4.8
Haemodynamic Instability	11	17.7
Rescue Thrombolysis	11	17.7

Table (2): laboratory examinations

	Total	**Without AE**	**With AE**	**P value**
NLR	**2.815[1.87, 4.28]**	**2.47 [1.79, 3.63]**	**4.75 [3.75, 5.8]**	**.000**
PLR	**121.11[98.913, 182.84]**	**105.88 [97.13, 162.72]**	**193.25 [158.67, 207.5]**	**.001**

Table (3): Risk factors for AE

	B	**S.E.**	**Exp(B)**	**95% C.I.for EXP(B)**		**P value**
NLR	**1.226**	**.415**	**3.407**	**1.511**	**7.684**	**.003**
PLR	**0.022**	**.007**	**1.023**	**1.008**	**1.038**	**.003**

NLR was the highest sensitive parameter with sensitivity of 100% and relatively low specificity (74.5%). AUC = 0.840 (95% CI 0.793 to 0.960, *p*< .0001). PLR showed significant value of predicting AE with AUC= .834 (95%CI 0.718 to 0.917,***p*** <.0001). PLR was 90.9% sensitive and 74.5% specific for AE **(Table 4,**

Fig. 1&2).

Table (4): Accuracy of predictors with AE

Adverse outcomes	AUC	95% CI	Cut-off	Sensitivity	Specificity	Youden index J	P value
NLR	0.897	0.793 to 0.960	>3.47	100%	74.51%	0.7451	**<0.0001**
PLR	0.834	0.718 to 0.917	>147.19	90.91%	74.51%	0.6542	**<0.0001**

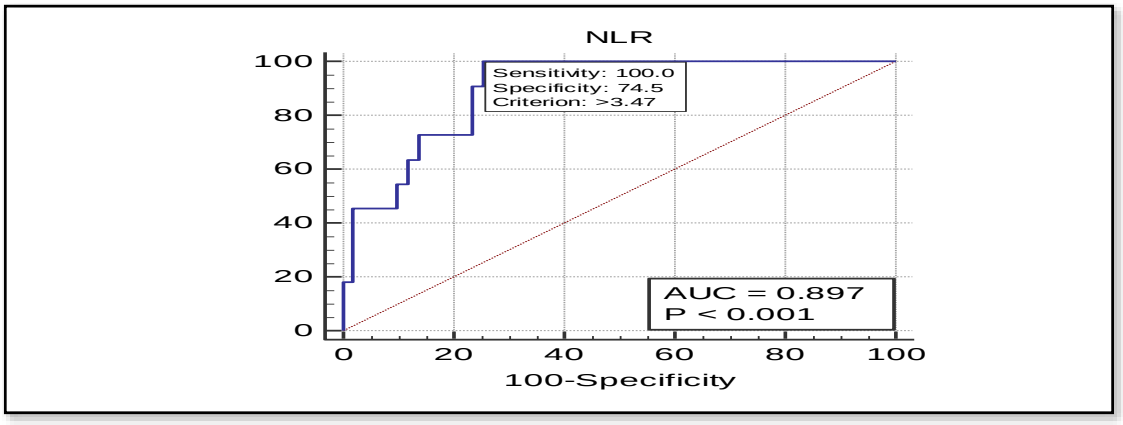

Figure (1): ROC curve for the accuracy of NLR in the prediction of adverse events

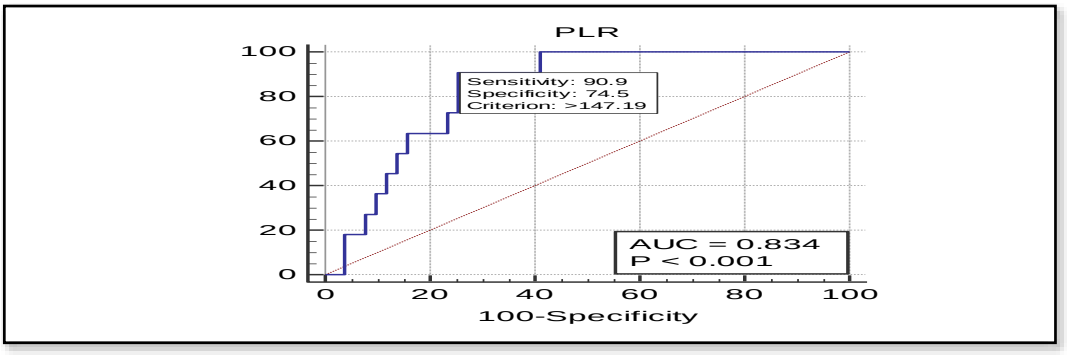

Figure (2): ROC curve for the accuracy of PLR in the prediction of adverse events.

Discussion

The present study showed that some laboratory parameters could strongly predict acute pulmonary embolism course and outcome. Main results of this study showed that NLR and PLR could each be an independent predictor of in-hospital adverse outcome of acute pulmonary embolism.

There is a good evidence of an association between the pathophysiology of venous thromboembolism (VTE) and Tissue factors released by inflammatory cytokines contribute to the progression of thrombosis [(8)].

Actually the use of inflammatory markers has been linked to vast cardiovascular diseases including coronaries [(9)].Tissue factors released as a response to inflammatory cascade or as a direct injury by mechanical strain such as troponin [(10-11)].

In the current study NLR was the most sensitive parameter to expect AE with a sensitivity of 100%. However, its specificity was relatively lower in comparison with LVOT VTI (74.51% specificity). The cut off value of NLR was >3.47 with (95CI 0.793 to 0.960, p< .0001). On the other hand, PLR showed sensitivity of 90.91% and specificity of 74.51% with (AUC=0.834, 95CI 0.718 to 0.917, p=0.0001). the cut-off value for AE was >147.19.

Among both groups there was significant difference in the mean value of both NLR and PLR, where mean NLR for AE group was 4.75 while being 2.47 in the group without adverse events. Regarding PLR, the mean value in AE group was 193.25 and in the group with no adverse events it was 105.88.

Conclusion

Our results suggest that NLR and PLR are useful tools independently or combined to identify normotensive patients with APE to predict short-term poor outcome.

Further studies on a larger scale should be performed to establish the accurate relationship of these parameters and outcome and possibility of a change of management plan in these patients.

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