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Evaluation of hemogram parameters in patients with deep vein thrombosis and pulmonary thromboembolism

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Abstract

Deep vein thrombosis (DVT) and pulmonary embolism is defined as venous thromboembolism (VTE). Deep vein thrombosis is the most common in lower extremity veins, it is seen in the upper extremity veins, more rarely. In this study we aimed to research the values of NLR, PLR, PCT and PDW in DVT and pulmonary thromboembolism (PET). Our study is the only study in which these parameters are examined together. Patients' gender, age, pulmonary embolism history, medications used, hospitalization history and hemogram values are recorded. Extremity involvement findings, neutrophil lymphocyte ratio (NLR), platelet lymphocyte ratio (PLR), plateletcrit (PCT) and platelet distribution width (PDW) is recorded. The mean age of patients was 60±19.83. Eigtheen (10.2%) of the patients had a history of recurrent deep vein thrombosis. 30 (16.9%) of the patients with deep vein thrombosis have pulmonary thromboembolism. While 94 (53.1%) patients with deep vein thrombosis had left lower extremity involvement, 39 (22%) had right lower extremity involvement. 52 (29.4%) patients were hospitalized, and 81(60,9%) patients were followed up outpatient. 44 (33.1%) patients had warfarin treatment, and 89 (%66.9) patients had DMAH treatment. NLR, PLR, PDW, PCT were 5.84 (min0.35- max 0.10), 181.26±144.14, 12.31±2.82, 0.25 (min0.00-max0.50) respectively in DVT, 7.32 (min 0.35-max34.5), 184.97±130.06, 11.93±1.95, 0.22 (min0.08-max0.39) respectively in PTE. In the light of the data obtained, we believe that hemogram parameters are appropriate markers for the prediction of DVT and PTE patients and/or inflammatory response during DVT and PTE. However, there is a need for more comprehensive studies on the course of the disease and the value of these markers.

Keywords: Hemogram parameters. deep vein thrombosis, pulmonary thromboembolism

Introduction

Deep vein thrombosis (DVT) and pulmonary embolism is defined as venous thromboembolism (VTE). Deep vein thrombosis is the most common in lower extremity veins, it is seen in the upper extremity veins, more rarely [1,2]. The incidence of DVT has been reported in the general population at 5 cases per 10000 per year [1,3]. The incidence of venous thromboembolism (VTE) is approximately 25% higher with the addition of pulmonary embolism (PE) events [1]. Three main causes of DVT pathogenetic mechanism has been defined. This mechanism, known as the Virchow triad, consists of vascular endothelial damage, decrease in venous blood flow (venous stasis) and hypercoagulopathy [4]. It is known that PE is common in patients with lower extremity DVT. Several studies have reported that approximately 30% and 40% of patients with DVT have high-probability pulmonary scintigraphy or CT findings suggestive of clinically silent PE, but prevalences of up to 66% have been reported. The prevalence of clinically silent PE in patients diagnosed with DVT increases with age and is higher in patients with proximal DVT than in patients with calf DVT [1].

Platelets also play a role in pathogenesis of deep vein thrombosis. Platelet function plays a key role in deep vein thrombosis. Neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), plateletcrit (PCT) and platelet distribution width (PDW) can be easily obtained from routine laboratory studies and provides important information on systemic inflammation status [5]. Complex interactions between inflammatory and coagulation factors play a role in the pathophysiology of vascular diseases and can lead to thromboembolic complications. In previous studies, NLR, PLR and PCT values were examined in patients with deep vein thrombosis [6,7,8]. In this study we aimed to research the values of NLR, PLR, PCT and PDW in DVT and pulmonary

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thromboembolism (PET). Our study is the only study in which these parameters are examined together.

Materials and Methods

Our study was retrospective and patients over 18 years of age who came to the Emergency Department of Muğla Sıtkı Koçman University Training and Research Hospital between January 2016 and December 2020 are included in the study. Ethics Committee Received from Muğla Sıtkı Koçman University Health Sciences Ethics Committee on 14.04.2021 (No:210050).

Patients' gender, age, comorbidity, pulmonary embolism history, medications used, hospitalization history and hemogram values are recorded. Patients are diagnosed with clinical symptoms and Doppler ultrasonography. Patients who had leg swelling, pain, difference in diameter, immobile patients and who underwent USG in the emergency clinic and found DVT in USG findings were included in the study. Patients with DVT and diagnosed pulmonary embolism with CT Angio are included ın to the study, retrospectively. The control group are generated of healthy volunteers with similar age and gender distribution who coming for checkup to internal medicine policlinic. Healthy volunteers will be selected from individuals who do not have any comorbid diseases who apply to internal medicine policlinic. Extremity involvement findings, neutrophyl lymphocyte ratio (NLR), platelet lymphocyte ratio (PLR), plateletcrit (PCT) and platelet distribution width (PDW) will be recorded. The study exclusion criterias are patients with chronic inflammatory disease, cancer patients, using steroids, active infection, blood disease, and pregnant women.

All data obtained from the study were recorded in the standard program "Statistical Package for Social Sciences for Windows 20" and evaluated. Frequency analysis was done, to check whether the distribution is normal when comparing between groups.

Kolmogorov-Smirnov test was performed for Numerical variables with normal distribution were summarized as mean ± SD (standard deviation), variables with non-normal distribution as median (min-max), and categorical variables as numbers and percentages. Parametric test (Indipendent samples test and posthocTukey test) was applied to data with normal distribution, and non-parametric test (Mann-Whitney U test and Kruskal-Wallis Test) was applied for data where distribution was not normal. Cumulative survival rate was calculated using the Kaplan-Meier method, and survival differences between groups were compared using the Mantel-Cox log-rank test. To determine the variables associated with in-hospital mortality, the data were evaluated by Multivariate logistic regression analysis. It was planned to perform the ROC Curve test and find the AUC areas and specificity sensitivity values.

Results

There were 177 patients participating in the study with leg pain. There were 133 patients of these 177 patients who presented to the emergency room with the diagnosis of deep vein thrombosis between January 2016 and December 2020. The control group consisted of 44 patients. The mean age of patients was 60±19.83. 90(%50,8) patients were male, 87(%49.2) patients were female. Eigtheen (10.2%) of the patients had a history of recurrent deep vein thrombosis. 30(16.9%) of the patients with deep vein thrombosis have pulmonary thromboembolism. While 94(53.1%) patients with deep vein thrombosis had left lower extremity involvement, 39 (22%) had right lower extremity involvement. 22 (12.4%) patients had femoral vein involvement, 15 (8.5%) pateints had popliteal involvement, 62 (35%) patients had femorapopliteal involvement 5(2.8%) patients had iliac involvement. 52(29.4%) patients were hospitalized, and 81(60,9%) patients were followed up outpatient. 44(33.1%) patients had warfarin treatment, and 89 (%66.9) patients had DMAH treatment. The mean platelet, PDW, PCT were 241.75±80.59, 12.46±2.57, 0.24±0.08 respectively. The demographic characteristics of the patients are given in table 1.

When we divided the patients into patients with deep vein thrombosis and the control group, statistical significance was observed in terms of PDW NEU, LYMP, NLR, PLR (p<0.001).

Table 1. The demographic characteristics of the patients with deep vein thrombosis

	DVT n=133 (75%)	Control n=44 (25%)	Total n=177 (100%)	P
Age (years old±SD)	64.10±18.85	48.15±17.98	60.14±19.83	p≥0.001
Platelet (180-370x10^3/µL)	245.33±88.22	230.95±50.37	241.75±80.55	p≥0.001
PDW (9.9-15.4 fL)	12.31±2.82	12.94±1.47	12.46±2.57	p<0.001
Neutrophil (1.56-6.13x10^3/µL)	7.40±4.85	3.67±1.12	6.47±4.18	p<0.001
Lymphocyte (1.18-3.74x10^3/µL)	1.97±0.98	2.08±0.67	2.05±0.75	p<0.001
NLR	5.84 (min 0.35-60.10)	1.70 (min 0.53-3.63)	4.08 (0.35-60.10)	p<0.001
PLR	181.26±144.14	110.95±44.53	163.78±130.36	p<0.001
PCT	0.25 (min 0.00-max 0.50)	0.24 (0.18-0.33)	0.24 (0.00-0.50)	p<0.001

DVT: deep venous thrombosus. **PDW:** platelet distribution width. **NLR:** neutrophil lymphocyte ratio. **PLR:** platelet lymphocyte ratio. **PCT:** plateletcrit

As lymp decreases, as Neu, NLR and PLR increases, the possibility of deep vein thrombosis was observed in patients. When we classified the patients as who had pulmonary thromboembolism and who did not, it was seen that patients with pulmonary thromboembolism, were statistically significant with NLR (p<0.001) Table 2. Pulmonary thromboembolism was observed more frequently as neu and NLR increased and lymp decreased. Pulmonary thromboembolism was observed more frequently in patients with recurrent deep vein thrombosis attack, hospitalized patients with left lower extremity involvement.

According to Roc analysis, neu, lymp, NLR, PLR was determined to be 0.791 (95% Cl 0.726-0.855), 0.694 (95% Cl 0.617-0.771), 0.820 (95% Cl 0.759-0.880), 0.689 (95% CI 0.609-0.759) respectively (Figure 1).

Table 2. Comparison of patients with and without pulmonary thromboembolism

	Without PTE n=103 (77.44%)	With PTE n=30(22.56%)	Total n=133 (100%)	P
Age (years old±SD)	63.68±18.73	65.50±19.52	64.10±18.85	p≥0.001
Platelet (180-370x10^3/µL)	252.32±88.58	221.33±84.02	245.39±88.12	p≥0.001
PDW (9.9-15.4 fL)	12.42±3.03	11.93±1.95	12.31±2.82	p≥0.001
Neutrophil (1.56-6.13x10^3/µL)	7.15±4.12	8.27±4.58	7.40±4.68	p≥0.001
Lymphocyte (1.18-3.74x10^3/µL)	1.94 (min 0.30-13.50)	2.04 (min 0.38-18.40)	1.97 (min 0.30-18.40)	p≥0.001
NLR	5.41 (min 0.57-60.10)	7.32 (min 0.35-34.5)	5.84 (min 0.35-60.10)	p≥0.001
PLR	180.18±148.34	184.97±130.06	181.26±144.14	p≥0.001
PCT	0.25 (min 0.00-max 0.50)	0.22 (0.08-0.39)	0.25 (0.00-0.50)	p≥0.001

DVT: deep venous thrombosus. **PDW:** platelet distribution width. **NLR:** neutrophil lymphocyte ratio. **PLR:** platelet lymphocyte ratio. **PCT:** plateletcrit

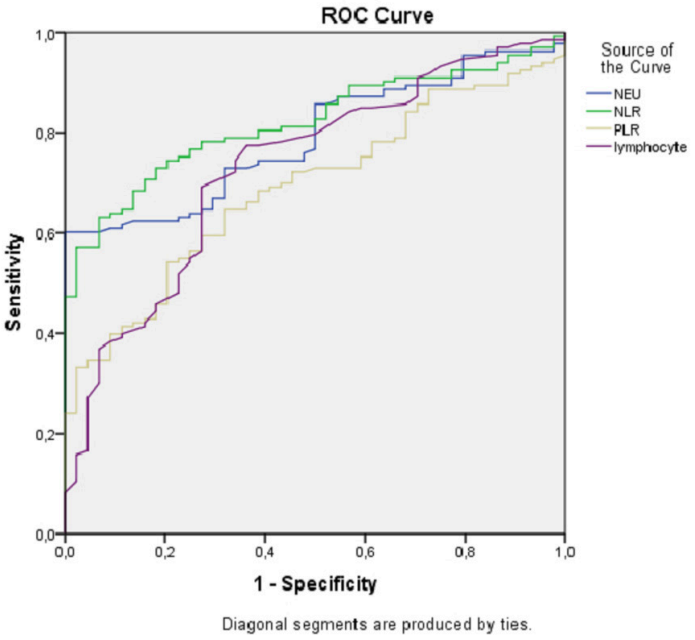

Figure 1. ROC analysis of Neu, NLR, PLR, lymphocyte

Discussion

DVT is still a common disease with serious morbidity and mortality if early diagnosis and treatment is not performed. Today, despite all advanced Technologies and approaches, it is a serious disease that causes pulmonary embolism, venous gangrene, chronic venous insufficiency and postthrombotic syndromes [2]. Although the incidence of DVT has been reported as 0.11% in the American and European population, it may vary with various factors (eg, gender, age, race, environmental factors) [2]. The recurrence rate is reported as 30% according to the analysis in developed countries [2]. Most of the studies have focused on the diagnosis and treatment of DVT and prevention from DVT. Although study participants were concerned with the natüre or treatment of DVT, they generally considered the end point of itself or of complications after treatment. DVT quality of life should also be considered. Quality of life includes a wide range of concepts from mortality and morbidity, guiding us in therapeutic efficacy [9].

The relationship between thrombosis and inflammatory response is significant and important. Inflammatory cells are linked by adhesion molecules, cytokines, and procoagulant microparticles in a cascade of events. A good understanding of the basic markers of thrombogenesis and thrombus resolution is extremely important in the prevention and acute treatment of venous thrombosis [9]. When the role of neutrophils in the DVT model created in a study on mice was examined, it was observed that DNA chromatins released from these inflammatory agents played an active role in the aggregation of thrombus, and it was suggested that understanding this mechanism wouldshedlight on the development of new group drugs in the treatment of DVT [10]. We observed statistical significance in hematologic parameters which PDW NEU, LYMP, NLR, PLR according to control group in our study.

The PLR value, which has recently started to attract attention in the literature, has been reported by Ertaş et al. [11] to see metastasis and the inflammatory response to it in cancer cases. Although there is a relationship between DVT, VTE, coronary artery disease and many inflammatory markers (eg IL-6, IL-8, P-Selectin, TNF-α and CRP etc.) We also investigated the importance of the role of PLR in this inflammatory process, and as a result, we observed that there was significant difference in cases with DVT. No relationship was found in the study of Çalışkan et al [12].

In the study of Gülen et al., NLR and MPV values were examined before and after treatment in patients with pulmonary embolism. NLR, MPV values were found to decrease statistically significantly after treatment [13]. In the other study when survival and mortality rates were compared in patients with pulmonary embolism, a significant correlation was found between mortality and neutrophil-lymphocyte ratio and mean platelet volume [14]. In the study by Akyıl et al., NLR was found to be a predictor of long-term mortality in pulmonary embolism [15].

Conclusion

In our study, we observed that the hematological markers of patients with DVT were significantly higher than the control group. When we looked at the Roc analysis, we observed that neu, lymp, NLR, PLR values in hematological parameters were associated with DVT. Future studies will help explain the relationship between hemogram parameters and DVT. In the light of the data obtained, we believe that hemogram parameters are appropriate markers for the prediction of DVT. However, there is a need for more comprehensive studies on the course of the disease and the value of these markers.

Conflict of interests
The authors declare that there is no conflict of interest in the study.

Financial Disclosure
The authors declare that they have received no financial support for the study.

Ethical approval

Ethics Committee Received from Muğla Sıtkı Koçman University Health Sciences Ethics Committee on 14.04.2021 (No:210050).

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