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MEDICAL SCIENCES / DAHİLİ TIP BİLİMLERİ

# Diagnostic Value of Mean Platelet Volume and Platelet Distrubition Width for Massive Pulmonary Embolism in Emergency Care

## Acil Serviste Masif Pulmoner Emboli Tanısı için Trombosit Dağılım Genişliği ve Ortalama Trombosit Hacminin Tanısal Değeri

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## Abstract

**Objectives:** Massive pulmonary embolism is a life-threatening condition mostly seen in the emergency setting. Early diagnosis and treatment decrease the risk of mortality. Apart from imaging tests, increased blood levels of several parameters were shown to be helpful to identify these patients. We aimed to determine the diagnostic value of mean platelet volume and platelet distribution width for the diagnosis of acute massive pulmonary embolism.

**Materials and Methods:** We retrospectively reviewed the medical records of patients who were admitted to the emergency department from January 2012 to January 2016. Patients who had a diagnosis of massive pulmonary embolism confirmed by computed tomography pulmonary angiography were included. Blood samples were drawn at admission. Transthoracic echocardiography was performed to evaluate right ventricular size and function. Age and sex matched patients who were admitted to the emergency department with any diagnosis other than pulmonary embolism were enrolled as a control group.

**Results:** Eighty patients met the inclusion criteria and age and sex matched 80 patients were enrolled as a control group. The mean platelet volume and platelet distribution width were significantly higher in patients with massive pulmonary embolism compared to control group [10.1±0.1 fL vs 7.9±0.1 fL p<0.001, 17 (15.5-18.8) vs 13.6 (12.3-15.9) p<0.001 respectively]. Platelet distribution width had the most powerful diagnostic value among other parameters including the mean platelet volume, D-dimer and pro-BNP (area under the curve=0.998, p<0.001).

**Conclusion:** Massive pulmonary embolism is a thromboembolic disease associated with high mortality. Platelet distribution width and mean platelet volume are simple parameters of complete blood count that can be used to increase predictive value of previously validated tests when used concomitantly. They may also help to select patients who will undergo imaging.

**Key Words:** Massive Pulmonary Embolism, Platelet Distribution Width, Mean Platelet Volume

## Öz

**Amaç:** Masif pulmoner emboli çoğunlukla acil serviste karşılaşılan hayatı tehdit eden bir durumdur. Erken tanı ve tedavi ölüm riskini azaltır. Görüntüleme tetkikleri dışında artmış kan seviyesindeki bazı birkaç parametrenin bu hastaları ayırt etmede yardımcı olduğu gösterilmiştir. Biz çalışmamızda, masif pulmoner emboli tanısında trombosit dağılım genişliği ve ortalama trombosit hacminin tanısal değerini tespit etmeyi amaçladık.

**Gereç ve Yöntem:** Ocak 2012 ile Ocak 2016 yılları arasında acil servise başvuran hastaların kayıtları geriye dönük olarak incelendi. Bilgisayarlı tomografi pulmoner anjiyografi ile tanısı doğrulanmış masif pulmoner emboli hastaları çalışmaya dahil edildi. Tam kan sayımı, D-dimer, pro-BNP

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ve troponin I testleri için kan örnekleri ilk başvuruda alındı. Sağ ventrikül boyutu ve fonksiyonunun değerlendirilmesi için hastalara ekokardiyografi yapıldı. Yaş ve cinsiyet eşleşmesi yöntemi ile kontrol grubu çalışmaya alındı.

**Bulgular:** Toplam 80 hasta çalışma kriterlerine uydu ve bu hastalarla yaş ve cinsiyet olarak eşleşmiş 80 kontrol hastası ayrıca çalışmaya dahil edildi. Ortalama trombosit hacmi ve trombosit dağılım genişliği anlamlı olarak masif pulmoner emboli tanısı almış hastalarda kontrol grubuna göre yüksek bulundu [10,1±0,1 fL, 7,9±0,1 fL p<0,001, 17 (15,5-18,8) 13,6 (12,3-15,9) p<0,001 sırasıyla]. Trombosit dağılım genişliğinin ortalama trombosit hacmi, D-dimer, pro-BNP dahil parametreler içerisinde en güçlü tanısal değere sahip olduğu tespit edildi (eğri altında kalan alan=0,998, p<0,001).

**Sonuç:** Masif pulmoner emboli, yüksek ölüm riski ile ilişkili bir tromboembolik hastalıktır. Trombosit dağılım genişliği ve ortalama trombosit hacmi, tam kan sayımının basit bir parçası olup daha önceden geçerliliği kabul edilmiş testlerle beraber kullanıldığında onların tanı koydurucu gücünü artırır. Görüntüleme testine gidecek hastaları tespit etmeye yardımcı olabilir.

**Anahtar Kelimeler:** Masif Pulmoner Emboli, Trombosit Dağılım Genişliği, Ortalama Trombosit Hacmi

## Introduction

Acute pulmonary embolism (PE) is a venous thromboembolic disease which can be stratified into low risk, submassive and massive with increasing mortality. Massive PE accounts for 5% of all PE-related admissions (1). In the presence of circulatory shock, defined as a sustained arterial blood pressure <90 mmHg with manifestations of organ hypoperfusion, the mortality rate from PE may be 45% or higher even with anticoagulation and fibrinolytic treatment (2). Major contributor to mortality in massive PE is the failure of timely and accurate diagnosis (3,4). Elevated D-dimer, pro-brain natriuretic peptide (BNP) and troponin I with clinical findings can raise the suspicion of acute PE. However they are not specific so if there is no contraindication, computed tomographic pulmonary angiography (CTPA) is performed for the diagnosis (5,6). There are several limitations of CTPA including contrast use and radiation. Availability can also be limited and compared to blood tests it has higher cost and needs expertise. So in the emergency setting, it is crucial to select these patients. Platelet (PLT) distribution width (PDW) and mean platelet volume (MPV) are components of complete blood count which are readily available and increase in the thromboembolic disorders (7). In our study, we aimed to determine the diagnostic value of PDW and MPV in patients with massive PE.

## Materials and Methods

All patients who were admitted to the Emergency Department (ED) of a tertiary care Süreyyapaşa Chest Diseases and Thoracic Surgery Training Hospital from January 2012 to January 2016 were reviewed from medical records retrospectively. The patients who were diagnosed with massive PE and confirmed by CTPA were included into the study. All of them presented with shock and had echocardiographic findings of right ventricular dysfunction. Shock was defined as systemic blood pressure ≤90 mmHg or a reduction of 40 mmHg in systolic blood pressure from baseline for at least 30 minutes. Patients who were younger than 18 yrs old, had acute coronary syndrome, end stage renal failure, end stage chronic liver failure, hematological diseases, chronic pulmonary hypertension, chronic inflammatory diseases, diabetes mellitus, cancer, hypothyroidism, pregnancy, use of anticoagulation drugs were excluded. Eighty patients met the inclusion criteria. Age and sex matched 80 patients who were hypotensive and/or in low cardiac output state associated with cardiogenic shock, septic shock, decompansated heart failure etc admitted to ED were enrolled as a control group. All patients in the control group had negative CTPA. The study protocol was approved by the local ethics commitee. Informed consent was not sought due to the retrospective nature of the study.

Transthoracic echocardiography (Vivid 7, GE Vingmed Ultrasound; Horten, Norway) using 2.5 MHz phased-array transducer was performed by a cardiologist for the assesment of right ventricle (RV) dysfunction with the patients in the left lateral decubitis position, on the same day of diagnosis of massive PE. All parameters were measured according to the recommendations of the American Society of Echocardiography (8). Patients with at least one of the following findings were diagnosed as having RV dysfunction: RV hypokinesis (asymmetrical or delayed contraction, usually in the RV base), paradoxical septal systolic motion or RV dilatation (end-diastolic diameter >30 mm or right-to-left ventricular end-diastolic diameter ratio ≥1 in an apical 4-chamber view) (9). All patients underwent CTPA using a 64-row multiple detector computed tomography scanner (LightSpeed VCT; GE Healthcare, Waukesha, WI). The imaging result of each patient was reported based on the consensus of 2 radiological technicians who were blinded to the plasma results.

Venous peripheral blood samples were drawn from all patients on admission. Blood samples for measurement of PLT indexes were taken into standardized tubes containing dipotassium ethylenedi-nitrilotetraacetic acid and analyzed in an automated blood cell counter (SYSMEX XS-1000i; SYSMEX Corporation, Kobe, Japan) immediately as per standard protocol. The reference values for PLT, MPV, PDW, white blood cell, neutrophil, and lymphocyte are 150 to 440x109/L, 7.4 to 11 fL, 9 to 17, 4 to 10x109/L, 1.4 to 6.2x109/L and 1.2 to 3.1x109/L respectively. Plasma D-dimer levels were measured by an immuno turbidimetric assay (ACL TOP; Instrumentation Laboratory, Fullerton, CA). The normal value of D-dimer is

0.0 to 0.5 µ/mL. Other indicators were detected at the same time, including pro-BNP, troponin I, red blood cell count (RBC), hemoglobin (Hgb), C-reactive protein and serum creatinine. According to our laboratory, the reference values are 0 to 125 pg/m, 0.0 to 0.04 ng/mL, 3.5 to 5.7x1012/L, 12 to 17g/dL, 0 to 5 mg/dL, 0.6 to 1.3 mg/dL, respectively. All assays were performed by laboratory technicians who were blinded to the CTPA results.

### Statistical Analysis

Descriptive statistics were reported, including mean, standard deviation, median, minimum value, maximum value and percentage. For the continuous dependent variables Student's t-test or Mann-Whitney U test was used for comparisons between two groups, depending on whether the dependent variable follows a normal distribution. For the categorical dependent variables Pearson chi-squared test was used for testing the independence. Receiver operating characteristic (ROC) curves were analyzed to assess the optimal cut-off values of the influence factors. Optimal cut-off values were calculated by using the maximum Youden's index. Sensitivity, specificity, negative predictive value (NPV), and positive predictive value (PPV) were calculated for the chosen cut-off values. The probability of a Type I error (alpha) was chosen as 5% (two-tailed) in all tests. Statistical Analysis was performed using the "Statistical Package for Social Sciences (SPSS) v17.0" (SPSS for Windows version 17.0, Chicago, IL, USA - September 2012 license number:1093910, Baskent University).

## Results

Baseline clinical and laboratory characteristics of the patients were shown in Table 1. The mean age was 66±16 and 53% of the patients were female. There was significant differences between the groups in terms of hypertension, deep venous thrombosis, chronic obstructive pulmonary disease. On the other hand smoking status, Hb and neutrophil/lymphocyte ratio were similar in both groups. All of the patients with massive pulmonary PE were administered a thrombolytic drug and 55% of them died. RBC and PLT count were significantly lower in patients with massive PE compared to control group [3650 (450-5650) vs 3792.125±811.97, p<0.001, 212.5 (165-475x10$^3$) vs 293.5 (132-550x103, p<0.001) respectively]. On contrary, serum pro-BNP, D-dimer and troponin I level were significantly higher in patients with massive PE compared to control (p<0.05). PDW in patients with massive PE was 17 (15.5-18.8) versus 13.6 (12.3-15.9) in control group and MPV in patients with massive PE was 10.1±0.1 versus 7.9±0.1 in control group. The difference was significant for both parameters (p<0.001) (Table 1).

MPV, PDW, Troponin I, D-dimer and pro-BNP were analyzed with ROC curves. The results indicated that area under the curve (AUC) of PDW was larger than the AUC of troponin I and pro-BNP [0.998, 95% confidence interval (CI) 0.995-1.00; p<0.001 vs 0.972, 95% CI 0.951-0.994; p<0.001 vs 0.985, 95% CI 0.967-

**Table 1: Comparison of the clinical and laboratory characteristics of the groups**

| Index | MPE (n=80) | Control (n=80) | p-value |
|---|---|---|---|
| **Age (yrs)** | 66±16 | 66±16 | 0.98 |
| **Female, n (%)** | 42 (53%) | 42 (53%) | - |
| **HT, n (%)** | 53 (66%) | 28 (35%) | <0.001 |
| **Smoking, n (%)** | 39 (49%) | 34 (43%) | 0.427 |
| **DVT, n (%)** | 40 (50%) | 14 (18%) | <0.001 |
| **COPD, n (%)** | 38 (48%) | 23 (29%) | 0.015 |
| **sPAP (mmHg)** | 65 (35-90) | 38 (25-55) | <0.001 |
| **RBC ($10^{12}$/L)** | 3.65 (2.45-5.65) | 3.79 (2.81-8.97) | <0.001 |
| **Hb (g/dL)** | 11.3 (8-15.6) | 11.7±2 | 0.098 |
| **PLT ($10^9$/L)** | 212.5 (165-475x10$^3$) | 293.5 (132-550x103) | <0.001 |
| **PDW** | 17 (15.5-18.8) | 13.6 (12.3-15.9) | <0.001 |
| **MPV (fL)** | 10.1±0.1 | 7.9±0.1 | <0.001 |
| **Troponin I (ng/mL)** | 2 (0.08-5.3) | 0.02 (0.01-2.2) | <0.001 |
| **D-dimer (µ/mL)** | 5 (0.3-15) | 2.6 (0.4-8.8) | <0.001 |
| **proBNP (pg/mL)** | 1840 (350-16,618) | 115.5 (25-2570) | <0.001 |
| **Creatinine (mg/dL)** | 0.94 (0.3-1.8) | 0.8 (0.1-1.4) | 0.004 |
| **CRP (mg/dL)** | 151 (31.7-450) | 9.6 (2.2-148) | <0.001 |
| **Trombolytic treatment, n (%)** | 80 (100%) | 0 (0%) | <0.001 |
| **Dead, n (%)** | 44 (55%) | 0 (0%) | <0.001 |

COPD: Chronic obstructive pulmonary disease, CRP: C-reactive protein, DVT: Deep venous thrombosis, Hb: Hemoglobin, HT: Hypertension, MPV: Mean platelet volume, PDW: Platelet distribution width, PLT: Platelet, pro-BNP: Pro-brain natriuretic peptide, RBC: Red blood cell, sPAP: Systolic pulmonary artery pressure

1.000; p<0.001 respectively]. The AUC of MPV was larger than the AUC of D-dimer (0.955, 95% CI 0.924-0.986; p<0.001 vs 0.797, 95% CI 0.727-0.868; p<0.001) (Table 2 and Figure 1). Taking the maximum Youden's index (sensitivity+specificity-1) as standard, the optimal cut-off values were assessed. Sensitivity, spesificity, NPV and PPV were calculated for the chosen cut-off values. When the cut-off value was set at 16.07, PDW had a sensitivity of 96.2%, NPV of 97.6%, specificity of 100% and PPV of 100%, MPV had a sensitivity of 89.7%, NPV of 93.1%, specificity of 90% and PPV of 85.3% when the cut-off value was set at 8.8 (Table 3).

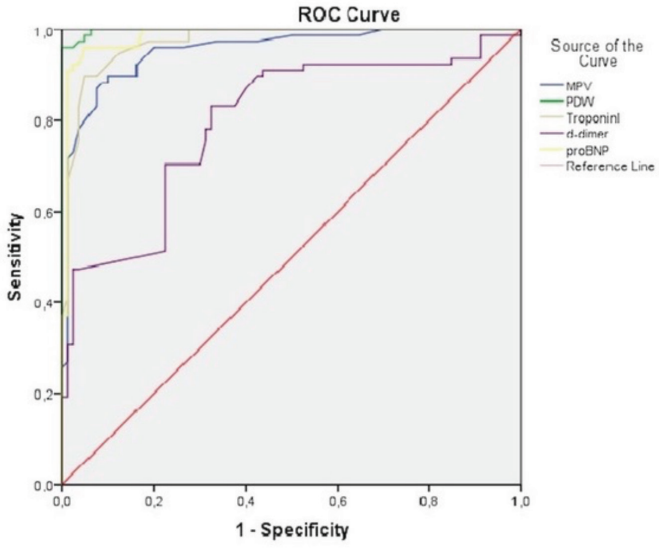


**Figure 1:** Comparison of ROC curves of MPV, PDW, Troponin I, D-dimer and pro-BNP

MPV: Mean platelet volume, PDW: Platelet distribution width, pro-BNP: Pro-brain natriuretic peptide, ROC: Receiver operating characteristic

## Discussion

Massive PE is one of the diseases encountered in the ED that has a high mortality rate. Definitive diagnosis is sometimes challenging and takes time. There are several markers including pro-BNP, troponin I and D-dimer that may help to differentiate this disease from others. However these markers are not specific yet their sensitivity is also limited. Transthoracic echocardiography and CTPA are also important imaging tools for risk stratification as well as diagnosis but they have also limitations. Both testes are more expensive compared to the blood tests and experts can only perform and interpret them. Radiation exposure is another limitation of CTPA. It is also contraindicated for patients with chronic renal disease. For this reason, rapid, easy and cheap blood tests with a high sensitivity and specificity are needed in ED to select the patients who will undergo these imaging tests before definitive diagnosis. In our study, we aimed to determine the diagnostic value of readily available blood markers in ED.

There are several studies that have found that troponin I increases in patients with PE and correlates well with right ventricular overload and dilatation (10,11). However patients with acute myocardial infarction or heart failure also present with high serum troponin levels to ED and may have variable degree of RV overload. Pro-BNP is another important nonspecific marker that we currently use to rule out acute heart failure in ED. In our study, we found that troponin I is as specific as pro-BNP but less sensitive for diagnosis of massive PE. In addition, it has been shown that both of them are associated with a higher risk of all cause mortality and death attributed to the PE (12,13).

**Table 2: The AUC of ROC curves of MPV, PDW, Troponin I, D-dimer and pro-BNP**

| Index | AUC | Std. error | p-value | 95% CI |
|---|---|---|---|---|
| MPV | 0.955 | 0.016 | <0.001 | 0.924-0.986 |
| PDW | 0.998 | 0.001 | <0.001 | 0.995-1.000 |
| Troponin I | 0.972 | 0.011 | <0.001 | 0.951-0.994 |
| d-dimer | 0.797 | 0.036 | <0.001 | 0.727-0.868 |
| Pro-BNP | 0.985 | 0.009 | <0.001 | 0.967-1.000 |

MPV: Mean platelet volume, PDW: Platelet distribution width, pro-BNP: Pro-brain natriuretic peptide, AUC: Area under the curve, ROC: Receiver operating characteristic, CI: Confidence interval, Std.: Standard

**Table 3: Performance characteristics of MPV, PDW, Troponin I, D-dimer and pro-BNP**

| Index | Cut-off value | The maximum Youden's index | Sensitivity | Specificity | PPV | NPV |
|---|---|---|---|---|---|---|
| MPV | 8.8 | 0.797 | 89.7 (%) | 90.0 (%) | 85.3 (%) | 93.1 (%) |
| PDW | 16 | 0.962 | 96.2 (%) | 100.0 (%) | 100.0 (%) | 97.6 (%) |
| Troponin I | 0.65 | 0.847 | 89.7 (%) | 95.0 (%) | 92.0 (%) | 93.5 (%) |
| D-dimer | 3.65 | 0.508 | 83.3 (%) | 67.5 (%) | 62.3 (%) | 86.2 (%) |
| Pro-BNP | 615 | 0.912 | 96.2 (%) | 95.0 (%) | 92.5 (%) | 97.5 (%) |

MPV: Mean platelet volume, PDW: Platelet distribution width, pro-BNP: Pro-brain natriuretic peptide, NPV: Negative predictive value, PPV: Positive predictive value

During normal haemostasis, collagen is exposed from subendothelial space when there is damage to the endothelial surface. Circulating PLTs interact with collagen and von Willebrand factor via glycoproteins (GPVI and GPIb/V/IX) that leads to more PLT activation and adhesion at the damage site. Activated PLTs aggregate by secreting mediators such as thromboxane A2, adenosine diphosphate, seratonin as well as by producing thrombin. Thrombin mediates fibrin formation and activation of clotting cascade. Acute PE is usually a consequence of deep vein thrombosis and plaletlet activation plays a major role as we previously described (14). The size of the PLTs vary and larger ones are more reactive, have greater tendency to be involved in the thrombus formation and more resistant to inhibition with aspirin and clopidogrel (15,16). MPV is an indicator of activated PLTs and PDW is another PLT parameter indicates variation in size. These are routinely assessed parameters of complete blood count that are shown to be associated with PLT activitation (17-19). Yardan et al. (20) showed that patients with PE and RV dysfunction had significantly higher MPV levels than patients without RV dysfunction. The sensitivity was 53.3% and specificity was 68.5% at a cut-off of 7.85 fL. They also found that systolic pulmonary artery pressure was positively correlated with MPV. In our study, MPV was found to have a sensitivity of 89.7% and speficity of 90% at a cut-off of 8.8 fL. We specifically investigated the diagnostic value of MPV in patients with massive PE so we did not include the patients with submassive PE and low-risk PE in our cohort, additionally we had control group.

In another study (21), MPV was found to have a sensitivity of 88.7% and specificity of 50% at a cut-off of 8.45 fL. Higher specificity was found in our study due to the higher cut-off value. However based on our study, PDW had the highest sensitivity and specificity compared to MPV and D-dimer to diagnose massive PE. As our knowledge, there is not any other study investigating these parameters specially in patients with massive PE. Günay et al. (22) showed that MPV and PDW were positively correlated with level of obstruction in pulmonary vascular bed in patients with acute PE.

### Study Limitations

One of the limitation of our study is single center and retrospective nature. Nonetheless, it provides crucial clinical information due to the specific patient groups. It was designed in the emergency setting so the results need to be tested in other settings like inpatient and post-op care. Due to lack of documentation, we do not have the number of patients that were already taking antiplatelet drugs as part of their treatment plan. Since there is a possible interaction with the test results, this needs to be further investigated. Threshold for abnormal values of blood markers may vary depending on the centers so this variety may make the assessment challenging. Secondly, the study was undertaken using only massive PE patients and the results were not generalized. These results may be helpful for the physicians during the management of the patients with acute massive PE.

## Conclusion

Acute massive PE is a life-threatening condition diagnosed by several blood markers and imaging tests. This study shows that PDW and MPV have higher diagnostic value compared to traditional blood markers and may help in diagnosis and patient selection who will undergo CTPA thus allowing them timely appropriate treatment.

### Ethics

**Ethics Committee Approval:** The Başkent University Medicine and Health Sciences Research Board approved this retrospective study protocol (Approval no: KA16/80, Date: 01.03.2016).

**Informed Consent:** Informed consent was not sought due to the retrospective nature of the study.

**Peer-reviewed:** Externally peer-reviewed.

### Authorship Contributions

Concept: D.O., E.T., Design: D.O., E.T., Data Collection and Processing: E.T., Analysis or Interpretation: D.O., E.T., Literature Search: D.O., Writing: D.O., Y.Z., E.T.

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## References

1. Kucher N, Goldhaber SZ. Management of massive pulmonary embolism. Circulation. 2005;112:e28-32.
2. Lin BW, Schreiber DH, Liu G, et al. Therapy and outcomes in massive pulmonary embolism from the Emergency Medicine Pulmonary Embolism in the Real World Registry. Am J Emerg Med. 2012;30:1774-1781.
3. Busse LW, Vourlekis JS. Submassive pulmonary embolism. Crit Care Clin. 2014;30:447-473.
4. Shujaat A, Shapiro JM, Eden E. Utilization of CT Pulmonary Angiography in Suspected Pulmonary Embolism in a Major Urban Emergency Department. Pulm Med. 2013;2013:915213.
5. Marshall PS, Mathews KS, Siegel MD. Diagnosis and management of life-threatening pulmonary embolism. J Intensive Care Med. 2011;26:275-294.
6. Levin D, Seo JB, Kiely DG, et al. Triage for suspected acute Pulmonary Embolism: Think before opening Pandora's Box. Eur J Radiol. 2015;84:1202-1211.
7. Sunnetcioglu A, Sertogullarindan B, Ozbay B, et al. Assessments of the associations of thrombus localization with accompanying disorders, risk factors, D-dimer levels, and the red cell distribution width in pulmonary embolism. Clinics (Sao Paulo). 2015;70:441-445.

8. Schiller NB, Shah PM, Crawford M, et al. Recommendations for quantitation of the left ventricle by two-dimensional echocardiography. American Society of Echocardiography Committee on Standards, Subcommittee on Quantitation of Two-Dimensional Echocardiograms. J Am Soc Echocardiogr. 1989;2:358-367.
9. Golpe R, Pérez-de-Llano LA, Castro-Añón O, et al. Right ventricle dysfunction and pulmonary hypertension in hemodynamically stable pulmonary embolism. Respir Med. 2010;104:1370-1376.
10. Amorim S, Dias P, Rodrigues RA, et al. Troponin I as a marker of right ventricular dysfunction and severity of pulmonary embolism. Rev Port Cardiol. 2006;25:181-186.
11. Mehta NJ, Jani K, Khan IA. Clinical usefulness and prognostic value of elevated cardiac troponin I levels in acute pulmonary embolism. Am Heart J. 2003;145:821-825.
12. Konstantinides S, Geibel A, Olschewski M, et al. Importance of cardiac troponins I and T in risk stratification of patients with acute pulmonary embolism. Circulation. 2002;106:1263-1268.
13. Coutance G, Le Page O, Lo T, Hamon M. Prognostic value of brain natriuretic peptide in acute pulmonary embolism. Crit Care. 2008;12:R109.
14. Frisbie JH. An animal model for venous thrombosis and spontaneous pulmonary embolism. Spinal Cord. 2005;43:635-639.
15. Koupenova M, Kehrel BE, Corkrey HA, et al. Thrombosis and platelets: an update. Eur Heart J. 2017;38:785-791.
16. Martin JF, Trowbridge EA, Salmon G, et al. The biological significance of platelet volume: its relationship to bleeding time, platelet thromboxane B2 production and megakaryocyte nuclear DNA concentration. Thromb Res. 1983;32:443-460.
17. Kostrubiec M, Łabyk A, Pedowska-Włoszek J, et al. Mean platelet volume predicts early death in acute pulmonary embolism. Heart. 2010;96:460-465.
18. Park Y, Schoene N, Harris W. Mean platelet volume as an indicator of platelet activation: methodological issues. Platelets. 2002;13:301-306.
19. Vagdatli E, Gounari E, Lazaridou E, et al. Platelet distribution width: a simple, practical and specific marker of activation of coagulation. Hippokratia. 2010;14:28-32.
20. Yardan T, Meric M, Kati C, et al. Mean platelet volume and mean platelet volume/platelet count ratio in risk stratification of pulmonary embolism. Medicina (Kaunas). 2016;52:110-115.
21. Huang J, Chen Y, Cai Z, et al. Diagnostic value of platelet indexes for pulmonary embolism. Am J Emerg Med. 2015;33:760-763.
22. Günay E, Sarinc Ulasli S, Kacar E, et al. Can platelet indices predict obstruction level of pulmonary vascular bed in patients with acute pulmonary embolism? Clin Respir J. 2014;8:33-40.