Postprint of a Retrospective Study on Clinical Characteristics of Patients with Acute Pulmonary Embolism and Thrombocytopenia

Authors: Wuchao Wang, Liu Siqi, Liu Qianqian, Zhu Jihong, Jihong Zhu

Date: 2023-12-06T00:00:00+00:00

Abstract

Background Acute pulmonary embolism (APE) is a severe cardiovascular disease. In recent years, the detection rate of patients with APE complicated by thrombocytopenia has been continuously increasing. These patients face dual problems of thrombosis and bleeding. Current research mainly consists of successful case reports, and there exists a research gap in clinical assessment and treatment protocols.

Objective To investigate the clinical characteristics and prognosis of patients with APE complicated by thrombocytopenia, and to provide a basis for clinical diagnosis and treatment.

Methods Twenty-one patients with APE complicated by thrombocytopenia who presented to the Emergency Department of Peking University People' s Hospital between January 2015 and January 2020 were enrolled as study subjects. Patients were divided into a severe bleeding group (7 cases) and a mild/no bleeding group (14 cases) according to their bleeding status; they were divided into a multiple-site thrombosis group (7 cases) and a pulmonary artery thrombosis group (14 cases) based on whether they had thrombosis in sites other than the pulmonary artery; and they were divided into a death group (5 cases) and a survival group (16 cases) according to patient mortality. Clinical data were collected and compared between groups.

Results This study enrolled a total of 21 patients with APE complicated by thrombocytopenia, including 7 males and 14 females, with a mean age of (63.2$±$18.9) years. Analysis of patient etiologies revealed 5 cases of immune thrombocytopenic purpura, 4 cases of antiphospholipid antibody syndrome, 3 cases of eosinophilia, 2 cases of drug-related thrombocytopenia, 2 cases of systemic lupus erythematosus, 2 cases of tumor-related thrombocytopenia, and 3 cases of unknown etiology. Nineteen patients received anticoagulation

therapy. The pulmonary artery thrombosis group had higher fibrinogen and fibrinogen/albumin ratio than the multiple-site thrombosis group (P<0.05). The severe bleeding group had lower male proportion and mean platelet volume, and higher multiple-site thrombosis proportion and neutrophil/lymphocyte ratio than the mild/no bleeding group (P<0.05). The death group had lower anticoagulation therapy proportion and platelet count, and higher heart rate, mean platelet volume/platelet ratio, and tumor-related thrombocytopenia proportion than the survival group (P<0.05).

Conclusion Patients with APE complicated by thrombocytopenia are at risk for multiple thrombotic events. Anticoagulation therapy helps improve clinical prognosis. Initiating anticoagulation therapy based on platelet count shows no significant correlation with severe bleeding events. Platelet count, platelet-related parameters, and other coagulation-related parameters are helpful for assessing thrombus burden, bleeding risk, and clinical prognosis.

Full Text

Abstract

Background: Acute pulmonary embolism (APE) is a serious cardiovascular disease. In recent years, the detection rate of APE patients with concurrent thrombocytopenia has been increasing, presenting a dual challenge of thrombosis and bleeding. Current research consists primarily of successful case reports, leaving a significant gap in clinical evaluation and treatment protocols.

Objective: To investigate the clinical characteristics and prognosis of APE patients complicated with thrombocytopenia, providing evidence for clinical diagnosis and treatment.

Methods: We enrolled 21 APE patients with thrombocytopenia who presented to the Emergency Department of Peking University People' s Hospital between January 2015 and January 2020. Patients were stratified into a severe bleeding group (n=7) and a mild/no bleeding group (n=14) based on bleeding severity; into a multiple-site thrombosis group (n=7) and a pulmonary artery thrombosis group (n=14) based on the presence of thrombosis at sites other than the pulmonary artery; and into a death group (n=5) and a survival group (n=16) based on in-hospital mortality. Clinical data were collected and compared between groups.

Results: Among the 21 APE patients with thrombocytopenia, 7 were male and 14 were female, with a mean age of (63.2$±$18.9) years. Etiological analysis revealed 5 cases of immune thrombocytopenic purpura, 4 cases of antiphospholipid syndrome, 3 cases of eosinophilia, 2 cases of drug-related thrombocytopenia, 2 cases of systemic lupus erythematosus, 2 cases of tumor-related thrombocytopenia, and 3 cases of unknown etiology. Nineteen patients received anticoagulation therapy. The pulmonary artery thrombosis group exhibited significantly higher fibrinogen (FIB) and fibrinogen-to-albumin ratio (FAR) com-

pared to the multiple-site thrombosis group (P<0.05). The severe bleeding group had lower male proportion and mean platelet volume (MPV), but higher multiple-site thrombosis proportion and neutrophil-to-lymphocyte ratio (NLR) compared to the mild/no bleeding group (P<0.05). The death group showed lower anticoagulation therapy proportion and platelet count, but higher heart rate, MPV-to-platelet ratio (MPR), and tumor-related thrombocytopenia proportion compared to the survival group (P<0.05).

Conclusion: APE patients with thrombocytopenia face a high risk of multiple thrombotic events. Anticoagulation therapy helps improve clinical prognosis, and its implementation based on platelet count shows no significant correlation with severe bleeding events. Platelet count, platelet-related parameters, and other coagulation-related indicators are valuable for assessing thrombus burden, bleeding risk, and clinical prognosis.

Keywords: pulmonary embolism; thrombocytopenia; prognosis; retrospective study

1.4 Statistical Methods

Data analysis was performed using SPSS 25.0 statistical software. Normally distributed continuous variables were expressed as mean±standard deviation ($\bar{x}\pm s$) and compared between groups using independent samples t-test. Non-normally distributed continuous variables were expressed as median (interquartile range) [M(P25, P75)] and compared using Mann-Whitney U test. Categorical variables were expressed as percentages and compared using Fisher' s exact test. A P-value <0.05 was considered statistically significant.

2.1 Patient Characteristics

This study included 21 APE patients with thrombocytopenia, comprising 7 males and 14 females with a mean age of (63.2$±$18.9) years. Etiological analysis revealed immune thrombocytopenic purpura in 5 cases, antiphospholipid syndrome in 4 cases, eosinophilia in 3 cases, drug-related thrombocytopenia in 2 cases, systemic lupus erythematosus in 2 cases, tumor-related thrombocytopenia in 2 cases, and unknown etiology in 3 cases. Nineteen patients received anticoagulation therapy, including 12 who received standard-dose low molecular weight heparin and 7 who received half-dose low molecular weight heparin or unfractionated heparin. Seven patients had multiple-site thrombosis, 7 experienced severe bleeding, and 5 died in hospital (including 2 who did not receive anticoagulation therapy).

2.2 Comparison Between Multiple-Site Thrombosis and Pulmonary Artery Thrombosis Groups

The pulmonary artery thrombosis group showed significantly higher fibrinogen (FIB) and fibrinogen-to-albumin ratio (FAR) compared to the multiple-site

thrombosis group (P<0.05). No statistically significant differences were observed between the groups in terms of gender, age, platelet count (PLT), mean platelet volume (MPV), international normalized ratio (INR), activated partial thromboplastin time (APTT), creatinine (Cr), total bilirubin (TBil), serum albumin (ALB), MPV-to-platelet ratio (MPR), neutrophil-to-lymphocyte ratio (NLR), proportion of critically ill patients, or etiology (P>0.05) .

This study found that 85.7% (18/21) of APE patients with thrombocytopenia had identifiable etiologies, suggesting that APE with thrombocytopenia is likely caused by underlying diseases. Therefore, further etiological investigation is warranted in these patients. While PLT and MPV showed no significant correlation with multiple-site thrombotic events, FIB and FAR levels were associated with such events, with lower levels observed in patients with multiple-site thrombosis, likely due to platelet consumption during thrombus formation.

Research has confirmed that elevated fibrinogen promotes fibrin formation, increasing thrombus strength and stability while enhancing resistance to fibrinolysis, and is associated with cardiovascular disease and both arterial and venous thrombosis. Fibrinogen levels may show dynamic evolution during different disease stages, initially rising then falling. In cases of excessive thrombus burden, consumptive hypofibrinogenemia may occur. Albumin directly or indirectly inhibits platelet activation and thrombus formation, suppressing fibrinogen activation and reducing fibrin aggregation. FAR is considered a marker for various pre-thrombotic conditions such as ST-elevation myocardial infarction and chronic venous insufficiency. Therefore, we believe that fibrinogen is associated with high thrombotic risk and thrombus burden, while albumin has a protective effect. FIB and FAR can help clinicians assess the risk of multiple-site thrombotic events in APE patients with thrombocytopenia.

2.3 Comparison Between Severe Bleeding and Mild/No Bleeding Groups

The severe bleeding group had a lower male proportion and MPV, but a higher proportion of multiple-site thrombosis and NLR compared to the mild/no bleeding group (P<0.05). No statistically significant differences were observed in age, anticoagulation therapy, PLT, INR, FIB, APTT, Cr, TBil, ALB, MPR, FAR, proportion of critically ill patients, or etiology between the two groups (P>0.05) .

Severe bleeding was defined as a hemoglobin decrease $ $20 g/L and/or requirement for $ $2 units of blood transfusion, while mild/no bleeding was defined as not meeting these criteria.

This study found that among APE patients with thrombocytopenia, those with severe bleeding had higher proportions of females and multiple-site thrombotic events, lower admission MPV, and higher NLR. However, admission PLT, INR, APTT, FIB, and anticoagulation therapy showed no significant correlation with severe bleeding. Studies have shown that MPV reflects platelet function to some

extent; under physiological conditions, MPV is inversely proportional to PLT to maintain constant platelet mass. Increased MPV indicates release of large, newly generated platelets into circulation. MPV is associated with hemostasis and thrombosis and helps assess hemostatic status even in thrombocytopenic patients. MPV correlates with platelet activation, inflammatory processes, and thrombus formation. Therefore, platelet function may influence the occurrence of severe bleeding events.

APE severity is associated with inflammatory status, and NLR, an easily obtainable parameter from routine blood tests, can assess inflammatory status and is associated with APE prognosis. NLR can affect fibrinogen, factor VII, and factor VIII levels. PLT and MPV play important roles in evaluating thrombosis and inflammatory responses and are associated with inflammatory processes. Platelet-neutrophil interactions contribute to thrombus formation. Therefore, we believe that severe bleeding risk in APE patients with thrombocytopenia may be associated with multiple-site thrombosis, platelet quality, and inflammatory status. Screening for multiple-site thrombotic events and monitoring MPV and NLR may help predict severe bleeding.

No difference in anticoagulation therapy was observed between the severe bleeding and mild/no bleeding groups, suggesting that anticoagulation can be administered to APE patients with thrombocytopenia under effective monitoring without significantly increasing severe bleeding risk.

2.4 Comparison Between Death and Survival Groups

The death group had lower anticoagulation therapy proportion and PLT, but higher heart rate, MPR, and tumor-related thrombocytopenia proportion compared to the survival group ($P<0.05$). No statistically significant differences were observed in gender, age, multiple-site thrombosis proportion, systolic blood pressure, respiratory rate, follow-up platelet count, MPV, NLR, FAR, or proportion of critically ill patients between the two groups ($P>0.05$) .

This study suggests that tumor-related thrombocytopenia and lack of anticoagulation therapy are associated with higher in-hospital mortality. The death group had higher admission heart rate, lower PLT, higher MPR, and lower post-treatment PLT. Research has shown that critically ill patients can develop thrombocytopenia with increased MPV, and that PLT and MPV can predict mortality risk in ICU patients. The prognostic value of MPR has been confirmed in numerous studies; elevated MPR predicts early mortality risk in severe sepsis and is associated with prognosis in acute myocardial infarction, post-myocardial infarction stroke, and venous thromboembolism. Yardan et al. confirmed that MPR correlates with right heart function and disease severity in APE patients, with decreased MPR indicating lower risk, consistent with our findings. Therefore, we believe that APE patients with thrombocytopenia should receive active anticoagulation therapy to improve prognosis. Tumor-related APE with thrombocytopenia carries a poor prognosis, and monitoring PLT and MPR may help

further assess clinical outcomes.

Limitations

This study has several limitations. First, it is a single-center retrospective study with a small sample size. Second, single-timepoint measurements may not fully reflect patients'disease status. Prospective studies are needed to further evaluate the predictive value of MPV, MPR, and FAR in APE patients with thrombocytopenia.

Conclusion

In conclusion, APE patients with thrombocytopenia have a high incidence of multiple-site thrombotic events. Patients with multiple-site thrombosis have lower FIB and FAR levels, while those with severe bleeding have lower MPV and higher NLR. APE patients with thrombocytopenia should receive active anticoagulation therapy. In-hospital mortality is not significantly associated with multiple-site thrombosis or severe bleeding events. Screening for underlying diseases and evaluating platelet-related parameters along with other coagulation and inflammatory markers such as FIB and FAR can help predict thrombotic events, bleeding risk, and clinical prognosis.

References

[2] WENDELBOE A M, RASKOB G E. Global burden of thrombosis: epidemiologic aspects[J]. Circ Res, 2016, 118(9): 1340-1347. DOI: 10.1161/CIRCRESAHA.115.306841.

[3] GARCÍA-SANZ M T, PENA-ÁLVAREZ C, LÓPEZ-LANDEIRO P, et al. Symptoms, location and prognosis of pulmonary embolism[J]. Rev Port Pneumol, 2014, 20(4): 194-199. DOI: 10.1016/j.rppneu.2013.09.006.

[4] JIMÉNEZ D, MIGUEL-DÍEZ J D, GUIJARRO R, et al. Trends in the management and outcomes of acute pulmonary embolism: analysis from the RIETE registry[J]. J Am Coll Cardiol, 2016, 67(2): 162-170. DOI: 10.1016/j.jacc.2015.10.060.

[5] DE WIT K, LINKINS L A. Challenging anticoagulation cases: a case of acute pulmonary embolism in a patient with chronic thrombocytopenia[J]. Thromb Res, 2021, 198: 83-85. DOI: 10.1016/j.thromres.2020.11.035.

[6] SARPATWARI A, BENNETT D, LOGIE J W, et al. Thromboembolic events among adult patients with primary immune thrombocytopenia in the United Kingdom General Practice Research Database[J]. Haematologica, 2010, 95(7): 1167-1175. DOI: 10.3324/haematol.2009.018390.

[7] KHANAL N, BOCIEK R G, CHEN B J, et al. Venous thromboembolism in patients with hematologic malignancy and thrombocytopenia[J]. Am J Hematol, 2016, 91(11): E468-E472. DOI: 10.1002/ajh.24526.

[8] MA L B, DENG G, WANG M. Research status of thromboembolic disease in systemic lupus erythematosus[J]. Chinese Journal of Rheumatology, 2010, 14(9): 641-644. DOI: 10.3760/cma.j.issn.1007-7480.2010.09.016.

[9] GU C Y, WANG Z Y. Mechanisms of thrombosis and current treatment status in patients with thrombocytopenia[J]. International Journal of Blood Transfusion and Hematology, 2021, 44(3): 185-190. DOI: 10.3760/cma.j.cn511693-20200917-00209.

[11] KOPOLOVIC I, LEE A Y Y, WU C. Management and outcomes of cancer-associated venous thromboembolism in patients with concomitant thrombocytopenia: a retrospective cohort study[J]. Ann Hematol, 2015, 94(2): 329-336. DOI: 10.1007/s00277-014-2198-6.

[12] SAMUELSON BANNOW B T, LEE A, KHORANA A A, et al. Management of cancer-associated thrombosis in patients with thrombocytopenia: guidance from the SSC of the ISTH[J]. J Thromb Haemost, 2018, 16(6): 1246-1249. DOI: 10.1111/jth.14015.

[13] CAMPBELL P M, IPPOLITI C, PARMAR S. Safety of anticoagulation in thrombocytopenic patients with hematologic malignancies: a case series[J]. J Oncol Pharm Pract, 2017, 23(3): 220-225. DOI: 10.1177/1078155216631407.

[14] ZANINETTI C, THIELE T. Anticoagulation in patients with platelet disorders[J]. Hamostaseologie, 2021, 41(2): 112-119. DOI: 10.1055/a-1344-7279.

[15] MARSHALL J C, COOK D J, CHRISTOU N V, et al. Multiple organ dysfunction score: a reliable descriptor of a complex clinical outcome[J]. Crit Care Med, 1995, 23(10): 1638-1652. DOI: 10.1097/00003246-199510000-00007.

[16] SCHULMAN S, KEARON C, SUBCOMMITTEE ON CONTROL OF ANTICOAGULATION OF THE SCIENTIFIC AND STANDARDIZATION COMMITTEE OF THE INTERNATIONAL SOCIETY ON THROMBOSIS AND HAEMOSTASIS. Definition of major bleeding in clinical investigations of antihemostatic medicinal products in non-surgical patients[J]. J Thromb Haemost, 2005, 3(4): 692-694. DOI: 10.1111/j.1538-7836.2005.01204.x.

[17] MACHLUS K R, CARDENAS J C, CHURCH F C, et al. Causal relationship between hyperfibrinogenemia, thrombosis, and resistance to thrombolysis in mice[J]. Blood, 2011, 117(18): 4953-4963. DOI: 10.1182/blood-2010-11-316885.

[18] KARAHAN O, ACET H, ERTAŞ F, et al. The relationship between fibrinogen to albumin ratio and severity of coronary artery disease in patients with STEMI[J]. Am J Emerg Med, 2016, 34(6): 1037-1042. DOI: 10.1016/j.ajem.2016.03.003.

[19] KARAHAN O, YAVUZ C, KANKILIC N, et al. Simple blood tests as predictive markers of disease severity and clinical condition in patients with venous insufficiency[J]. Blood Coagul Fibrinolysis, 2016, 27(6): 684-690. DOI: 10.1097/MBC.0000000000000478.

[20] GUCLU H, OZAL S A, PELITLI GURLU V, et al. Increased fibrinogen to albumin ratio in ischemic retinal vein occlusions[J]. Eur J Ophthalmol, 2017, 27(6): 735-739. DOI: 10.5301/ejo.5000942.

[21] XIE H X, WANG M S, PAN J Y, et al. Changes in fibrinolytic function and antithrombin activity in hemorrhagic shock models[J]. Laboratory Medicine, 2007, 22(4): 469-471. DOI: 10.3969/j.issn.1673-8640.2007.04.031.

[22] WADA H, MATSUMOTO T, YAMASHITA Y. Diagnosis and treatment of disseminated intravascular coagulation (DIC) according to four DIC guidelines[J]. J Intensive Care, 2014, 2(1): 15. DOI: 10.1186/2052-0492-2-15.

[23] ACHARYA P, JAKOBLEFF W A, FOREST S J, et al. Fibrinogen albumin ratio and ischemic stroke during venoarterial extracorporeal membrane oxygenation[J]. ASAIO J, 2020, 66(3): 277-282. DOI: 10.1097/MAT.0000000000000992.

[24] PAAR M, ROSSMANN C, NUSSHOLD C, et al. Anticoagulant action of low, physiologic, and high albumin levels in whole blood[J]. PLoS One, 2017, 12(8): e0182997. DOI: 10.1371/journal.pone.0182997.

[25] THOMPSON C B, JAKUBOWSKI J A. The pathophysiology and clinical relevance of platelet heterogeneity[J]. Blood, 1988, 72(1): 1-8. DOI: 10.1182/blood.v72.1.1.bloodjournal7211.

[26] TAMELYTĖ E, VAIČEKAUSKIENĖ G, DAGYS A, et al. Early blood biomarkers to improve sepsis/bacteremia diagnostics in pediatric emergency settings[J]. Medicina, 2019, 55(4): 99. DOI: 10.3390/medicina55040099.

[27] YIN W Y, SHEN Y, ZHANG L H. Application value of PLT, MPV, PCT and PDW in diagnosis of idiopathic thrombocytopenic purpura[J]. Chinese Journal of Laboratory Diagnosis, 2017, 21(3): 420-422. DOI: 10.3969/j.issn.1007-4287.2017.03.014.

[28] CIL H, YAVUZ C, ISLAMOGLU Y, et al. Platelet count and mean platelet volume in patients with in-hospital deep venous thrombosis[J]. Clin Appl Thromb Hemost, 2012, 18(6): 650-653. DOI: 10.1177/1076029611435838.

[29] NTOLIOS P, PAPANAS N, NENA E, et al. Mean platelet volume as a surrogate marker for platelet activation in patients with idiopathic pulmonary fibrosis[J]. Clin Appl Thromb Hemost, 2016, 22(4): 346-350. DOI: 10.1177/1076029615618023.

[30] SCHWERTZ H, KÖSTER S, KAHR W H A, et al. Anucleate platelets generate progeny[J]. Blood, 2010, 115(18): 3801-3809. DOI: 10.1182/blood-2009-08-239558.

[31] PAPANAS N, MIKHAILIDIS D P. Mean platelet volume: a predictor of mortality in diabetic and non-diabetic patients with STEMI?[J]. J Diabetes Complications, 2014, 28(5): 581-582. DOI: 10.1016/j.jdiacomp.2014.05.004.

[32] KAMISLI O, KAMISLI S, KABLAN Y, et al. The prognostic value of an increased mean platelet volume and platelet distribution width in the early

phase of cerebral venous sinus thrombosis[J]. Clin Appl Thromb Hemost, 2013, 19(1): 29-32. DOI: 10.1177/1076029612453196.

[33] MARCHENA YGLESIAS P J, NIETO RODRÍGUEZ J A, SERRANO MARTÍNEZ S, et al. Acute-phase reactants and markers of inflammation in venous thromboembolic disease: correlation with clinical and evolution parameters[J]. An Med Interna, 2006, 23(3): 105-110. DOI: 10.4321/s0212-71992006000300005.

[34] WANG Q, MA J F, JIANG Z Y, et al. Prognostic value of neutrophil-to-lymphocyte ratio and platelet-to-lymphocyte ratio in acute pulmonary embolism: a systematic review and meta-analysis[J]. Int Angiol, 2018, 37(1): 4-11. DOI: 10.23736/S0392-9590.17.03848-2.

[35] BOVILL E G, BILD D E, HEISS G, et al. White blood cell counts in persons aged 65 years or more from the Cardiovascular Health Study. Correlations with baseline clinical and demographic characteristics[J]. Am J Epidemiol, 1996, 143(11): 1107-1115. DOI: 10.1093/oxfordjournals.aje.a008687.

[36] BALTA S, DEMıRKOL S, KUCUK U. The platelet lymphocyte ratio may be useful inflammatory indicator in clinical practice[J]. Hemodial Int, 2013, 17(4): 668-669. DOI: 10.1111/hdi.12058.

[37] SREERAMKUMAR V, ADROVER J M, BALLESTEROS I, et al. Neutrophils scan for activated platelets to initiate inflammation[J]. Science, 2014, 346(6214): 1234-1238. DOI: 10.1126/science.1256478.

[38] LIU Z G, LI X X, ZHANG M P, et al. The role of Mean Platelet Volume/platelet count Ratio and Neutrophil to Lymphocyte Ratio on risk of Febrile Seizure[J]. Sci Rep, 2018, 8(1): 15123. DOI: 10.1038/s41598-018-33373-3.

[39] FARAH R, NSEIR W, KAGANSKY D, et al. The role of neutrophil-lymphocyte ratio, and mean platelet volume in detecting patients with acute venous thromboembolism[J]. J Clin Lab Anal, 2020, 34(1): e23010. DOI: 10.1002/jcla.23010.

[40] DURAN M, ULUDAĞ Ö. Can platelet count and mean platelet volume and red cell distribution width be used as a prognostic factor for mortality in intensive care unit?[J]. Cureus, 2020, 12(11): e11630. DOI: 10.7759/cureus.11630.

[41] OH G H, CHUNG S P, PARK Y S, et al. Mean platelet volume to platelet count ratio as a promising predictor of early mortality in severe sepsis[J]. Shock, 2017, 47(3): 323-330. DOI: 10.1097/SHK.0000000000000718.

[42] BOLAT I, AKGUL O, CAKMAK H A, et al. The prognostic value of admission mean platelet volume to platelet count ratio in patients with ST-segment elevation myocardial infarction undergoing primary percutaneous coronary intervention[J]. Kardiol Pol, 2016, 74(4): 346-355. DOI: 10.5603/KP.a2015.0179.

[43] GUENANCIA C, HACHET O, STAMBOUL K, et al. Incremental predictive value of mean platelet volume/platelet count ratio in in-hospital

stroke after acute myocardial infarction[J]. Platelets, 2017, 28(1): 54-59. DOI: 10.1080/09537104.2016.1203397.

[44] HAN J S, PARK T S, CHO S Y, et al. Increased mean platelet volume and mean platelet volume/platelet count ratio in Korean patients with deep vein thrombosis[J]. Platelets, 2013, 24(8): 590-593. DOI: 10.3109/09537104.2012.748187.

[45] YARDAN T, MERIC M, KATI C, et al. Mean platelet volume and mean platelet volume/platelet count ratio in risk stratification of pulmonary embolism[J]. Medicina, 2016, 52(2): 110-115. DOI: 10.1016/j.medici.2016.03.001.

Note: Figure translations are in progress. See original paper for figures.