Paradigm Academic Press
Journal of Innovations in Medical Research
ISSN 2788-7022
APR. 2025 VOL.4, NO.2

Research Advances of Risk Prediction Methods for Acute Pulmonary Embolism in Patients with Lower Extremities Deep Venous Thrombosis

Yue Zhang[1]

[1] Department of Radiology, The First Affiliated Hospital of Chongqing Medical University, Chongqing 400016, China

Correspondence: Yue Zhang, Department of Radiology, The First Affiliated Hospital of Chongqing Medical University, Chongqing 400016, China.

doi:10.63593/JIMR.2788-7022.2025.04.011

Abstract

Lower extremity deep venous thrombosis (LEDVT) is a disease of venous return disorder caused by abnormal blood agglutination in lower extremity deep vein. In recent years, the incidence of DVT is increasing gradually and the age of onset tends to be younger. One of the primary hazards associated with LEDVT is pulmonary embolism (PE) resulting from thrombus dislodgement. Once pulmonary embolism occurs, the prognosis is frequently poor; in severe cases, it can pose a significant threat to the patient's life. Consequently, early detection and prompt diagnosis of pulmonary embolism are crucial for enhancing patient outcomes and mitigating the risk of mortality. There is sound evidence supporting the use of several methods to enhance the diagnosis and predict the risk of PE. Therefore, the review aims to provide a comprehensive overview of the literature concerning diagnostic methods for PE.

Keywords: lower extremity deep venous thrombosis, pulmonary embolism, biomarkers

1. Introduction

Deep venous thrombosis (DVT) is a common disease characterized by the abnormal coagulation of blood within deep veins, resulting in impaired venous return. This condition frequently occurs in the lower extremities (Heit JA, 2015; Krutman M, Wolosker N, Kuzniec S, et al., 2013). The dislodgement of DVT can lead to pulmonary embolism (PE) (Khan, F., et al., 2021). As an acute and severe illness with a high mortality rate, PE has a 30-day mortality rate ranging from 2.4% to 11% (Ho ATN, Bellamy N & Naydenov SK., 2021) and has emerged as the third leading cause of cardiovascular-related deaths (Schaefer JK, Jacobs B, Wakefield TW, et al., 2017). From the perspective of physiopathology, DVT is intricately linked to PE. DVT serves as the primary source of thrombi that can lead to PE, while PE represents one of the most severe complications arising from DVT. Given this inherent connection, DVT and PE are collectively termed venous thromboembolism (VTE), which essentially reflects different manifestations of the same underlying disease at various stages (Stevens, S.M., et al., 2021). Due to the absence of typical clinical symptoms and signs, PE often results in delayed diagnosis, missed diagnosis, or misdiagnosis. Therefore, early assessment of the risk of acute PE in patients with LEDVT is essential for developing appropriate treatment strategies and improving patient prognosis. Based on a comprehensive review of the current methodologies for predicting the risk of PE, including clinical scoring systems, biomarkers, imaging technologies, and artificial intelligence, this paper provides an in-depth analysis of the advantages and limitations associated with these various approaches, and aims to predict the risk of acute PE accurately to facilitate hierarchical management of patients and effectively enhance patient prognosis.

2. Clinical Scoring System

2.1 Wells Score

As a widely used PE risk assessment tool in clinical practice, Wells score builds a standardized hierarchical prediction model by systematically integrating clinical symptoms, signs and risk factors of patients. According to the score results, the risk of PE occurrence in patients was divided into three grades: low risk (0-1 points), medium risk (2-6 points) and high risk (≥7 points), which provided an objective basis for clinical decision-making (Wells PS, Anderson DR, Rodger M, et al., 2000). The scoring system is both straightforward and practical; however, it does possess certain limitations. Firstly, the final criterion in the scoring framework states that "Alternative diagnosis is less likely than pulmonary embolism." This criterion is highly subjective and lacks objective quantitative measures. Secondly, the scoring standards are applicable to all populations, which may introduce bias in risk stratification among high-risk patients with LEDVT, thereby impacting the accuracy of clinical decision-making.

2.2 Simplified Wells Score

The simplified Wells score is a simplified version of the Wells score, designed to improve the convenience and usability of clinical evaluations. This adaptation reduces the emphasis on the subjective criterion "Alternative diagnosis is less likely than pulmonary embolism" found in the Wells score, while retaining six objective indicators (with each item assigned a value of 1 point). The simplified Wells score categorizes patients into two distinct risk levels: low risk (⩽1 point) and high risk (⩾2 points). Esiene et al. demonstrated that the sensitivity of the simplified Wells scoring system surpasses that of other assessment tools, including the Wells score (Esiene A, Tochie J N, Metogo J a M, et al., 2019). Given that the Wells score is significantly influenced by the clinician's experience and requires a lengthy evaluation process, the simplified Wells score is often preferred in situations where physicians are inexperienced or in emergency.

2.3 Geneva Score

The Geneva score is a widely utilized tool for predicting PE, primarily based on objective clinical indicators. This reliance on measurable data minimizes the influence of subjective judgment, thereby enhancing both the consistency and repeatability of the scoring system.

2.4 Revised Geneva Score

The revised Geneva score is obtained by eliminating some variables on the basis of the Geneva score. Compared with the Geneva score system, the revised Geneva score is simpler in application and faster in calculation, which can effectively help clinicians to initially judge the risk of PE occurrence in patients. Bertoletti et al. demonstrated that the revised Geneva score is an effective tool for screening patients at very low risk of adverse events, thereby enabling them to benefit from outpatient treatment (Subramaniam RM, Mandrekar J, Blair D, et al., 2009).

3. Biomarkers

3.1 D-Dimer and D-Dimer/Fibrinogen

D-dimer is a specific degradation product resulting from the fibrinolytic breakdown of fibrin and has emerged as a crucial biological marker for PE due to its significant role in the coagulation-fibrinolytic system. Previous studies have demonstrated that a negative D-dimer test can effectively exclude VTE, leading to its widespread application in clinical practice (Khan, F., et al., 2021; Stevens, S.M., et al., 2021; Wells PS, Anderson DR, Rodger M, et al., 2000).

In recent years, the D-dimer/fibrinogen ratio (D/F ratio) has emerged as a promising biomarker with significant potential for application in the diagnosis of PE (Gkana A, Papadopoulou A, Mermiri M, et al., 2022). Kucher et al. conducted a prospective study involving 191 outpatients suspected of PE. They found that fibrinogen levels were decreased in patients diagnosed with PE, while the D/F ratio was significantly elevated. Notably, a D/F ratio value greater than 1000 demonstrated high specificity for the diagnosis of acute PE (Kucher N, Kohler HP, Dornhöfer T, et al., 2003). Similarly, Kara et al. reported that the D/F ratio in patients with PE was markedly higher than that observed in the control group, and its diagnostic specificity surpassed that of D-dimer detection alone (Kara H, Bayir A, Degirmenci S, Kayis SA, et al., 2014). However, a prospective study involving 40 patients with PE revealed no significant reduction in fibrinogen levels among those with positive D-dimer test (Calvo-Romero JM., 2004). In summary, while the D/F value demonstrates certain potential applications in the diagnosis of PE, most existing studies are based on small sample cohorts and lack external validation. Furthermore, both D-dimer and D/F ratio are elevated in patients with LEDVT, making it challenging to further stratify the risk of PE occurrence within this specific patient population. Consequently, significant challenges remain for its clinical implementation.

3.2 MicroRNAs

MicroRNAs (miRNAs) are a class of non-coding RNAs with a length of about 22 nucleotides. They participate

in important cellular pathways related to proliferation and apoptosis. They are widely present in various body fluids and possess excellent stability through binding with carrier proteins. This makes miRNAs an ideal noninvasive biomarker (Morelli VM, Brækkan SK, Hansen JB, et al., 2020). Researches have indicated that miRNAs can regulate various hemostatic factors, influence platelet activation and aggregation, and play a crucial role in venous thrombosis (Nourse J, Braun J, Lackner K, et al., 2018). In 2011, Xiao et al. were the first to investigate the potential of miRNAs as biomarkers for diagnosing acute PE (Xiao J, Jing ZC, Ellinor PT, et al., 2011). Their study revealed that miRNA-134 was significantly elevated in patients with acute PE, demonstrating a sensitivity of 68.8% and a specificity of 68.2%. Through a systematic review and meta-analysis, Deng et al. identified that miRNAs may serve as potential novel biomarkers for the diagnosis of acute PE (Deng HY, Li G, Luo J, et al., 2016). However, large-scale and multi-center studies are necessary to further validate their diagnostic efficacy. In recent years, an increasing number of studies have demonstrated that miRNAs are up-regulated in acute PE, highlighting their potential as diagnostic markers (Liu T, Kang J & Liu F., 2018; Wang Q, Ma J, Jiang Z, et al., 2018; Wang Q, Ma J, Jiang Z, et al., 2018). Wang et al. attempted to enhance diagnostic efficiency by combining miRNA-27a/b with D-dimer, resulting in area under the curve (AUC) values of 0.909 and 0.867, respectively (Wang Q, Ma J, Jiang Z, et al., 2018). Although prior research has indicated the promising advantages of miRNAs for diagnosing acute PE, existing studies exhibit low reproducibility, necessitating further investigation.

3.3 C-Reactive Protein

C-reactive protein (CRP) is an acute-phase reactant and a non-specific biomarker of systemic inflammation that is widely utilized in clinical practice. Research has demonstrated that CRP can serve as a diagnostic indicator for PE. This association may be linked to the presence of activated macrophages within thrombotic plaques associated with PE, which are capable of secreting tumor necrosis factor α and other cytokines that promote the synthesis of CRP (Granholm F, Bylund D, Shevchenko G, et al., 2022). Previous studies have demonstrated that CRP exhibits a sensitivity of 95.7% and a negative predictive value of 98.4% in the diagnosis of PE, indicating relatively strong predictive performance (Steeghs N, Goekoop RJ, Niessen RW, et al., 2005). This suggests that CRP may serve as a potential biomarker for PE screening. Consequently, some researchers have proposed utilizing CRP either independently or in conjunction with clinical probability assessments for the purpose of PE screening (Stoeva N, Kirova G, Staneva M, et al., 2018). While current researches indicate the potential of CRP in predicting acute PE, further comprehensive and in-depth studies are necessary to validate its clinical significance.

4. Imaging Evaluation Method

Imaging examination is the preferred method for evaluating LEDVT. The use of ultrasound, computed tomography venography (CTV), and magnetic resonance imaging (MRI) to assess LEDVT forms the foundation of thrombosis research and analysis. Currently, most studies concentrate on the diagnosis and quantitative assessment of LEDVT; however, there still remains lacking in utilizing imaging techniques to evaluate the risk of acute PE in patients with LEDVT.

4.1 Evaluate LEDVT by Ultrasound

Ultrasonography plays a crucial role in assessing the stage and age of LEDVT. Previous studies have demonstrated that the clinical stage of LEDVT is closely associated with the risk of acute PE. Based on the onset timing, LEDVT can be categorized into three stages: acute, subacute, and chronic (Kahn, S.R., et al., 2008). The acute stage is characterized by an onset time of $\leqslant$14 days, primarily presenting with sudden swelling and pain in the affected limb, accompanied by depressed edema and a significant increase in skin temperature. The subacute phase is defined as the duration of the disease lasting from 15 to 30 days, while the chronic phase is identified when the disease persists for more than 30 days. The existing ultrasound diagnostic criteria can approximately differentiate the stage of thrombus based on the extent of venous occlusion and thrombus echogenicity. However, there is insufficient evidence to support the reliability of these criteria as tools for assessing thrombus age and predicting the risk of acute PE.

In recent years, several scholars have investigated the risk of PE in patients with LEDVT utilizing ultrasound imaging. Kaya et al. developed a novel Lower Extremity Venous Doppler Ultrasound Scoring System (LEVDUS) that quantitatively assesses the length and staging characteristics of thrombi. This innovative approach has significantly enhanced the predictive efficiency for PE (Kaya AT & Akman B., 2024). The findings indicate that LEVDUS demonstrates superior performance in predicting subsegmental PE and above, compared to D-dimer levels. Furthermore, LEVDUS not only offers an objective imaging foundation for assessing the risk of PE but also establishes a standardized diagnostic language for both imaging specialists and clinicians. Jamin A et al. (2023) employed two distinct metric methods grounded in two-dimensional entropy (DispEn2D and FuzEn2D) to quantitatively analyze the texture features of LEDVT ultrasonic images. The findings indicated that FuzEn2D could effectively predict the risk of PE in patients with LEDVT, achieving an AUC of 0.72. This machine

learning approach, based on image texture features, offers a novel technical pathway for PE risk prediction and demonstrates promising application prospects.

4.2 Evaluate LEDVT by CTV

Jeong MJ et al. analyze the correlation between proximal thrombus density and acute PE. Their findings indicated that high-density thrombus serves as an independent predictor of acute PE, demonstrating a predictive efficiency superior to that of the Wells score, which is commonly utilized in clinical practice (Jeong M-J, Kwon H, Noh M, Ko G-Y, Gwon DI, Lee JS, Kim M-J, Choi JY, Han Y, Kwon T-W et al., 2019). This study underscores the significant clinical application potential of LEDVT density in assessing the risk for PE.

4.3 Evaluate LEDVT by MRI

MRI primarily encompasses Magnetic Resonance Direct Thrombus Imaging, MRDTI (MRDTI), contrast enhanced magnetic resonance venography (MRV), and black-blood thrombus imaging (BTI) in the assessment of LEDVT. These modalities demonstrate significant potential for effective staging evaluation of LEDVT. Moody et al. developed MRDTI based on the pathological characteristics of thrombi. This innovative technique is capable of detecting metabolites of hemoglobin within thrombi, such as Fe3+-rich methemoglobin. It not only sensitively identifies LEDVT, but also provides valuable insights into the staging of thrombi (Moody, A.R., et al., 1998). Contrast-enhanced MRV technology can also provide some clues for LEDVT staging. In the acute stage, the venous tube diameter was dilated, and the thin tube wall with annular reinforcement was seen. In subacute stage, mixed signal thrombus and thickened tube wall were seen. Chronic stage showed narrowing of venous lumen and low signal thrombus. As a relatively novel imaging technology, BTI effectively suppresses venous blood flow signals, allows for a more direct visualization of thrombus signal changes, thereby reflecting the dynamic evolution of thrombus components. Furthermore, it aids in the accurate determination of thrombus staging and age. Dam et al. conducted a prospective international multicenter study involving 305 patients with clinically suspected acute recurrent ipsilateral LEDVT. MRDTI was performed within 24 hours, and management strategies were stratified based on the imaging results: patients in the negative MRDTI group did not receive any treatment, while those in the positive group initiated anticoagulation therapy or adjusted their existing anticoagulation regimen. The incidence of VTE among patients with negative MRDTI was monitored over a follow-up period of three months. The findings revealed that the incidence of VTE in this cohort was only 1.1%, underscoring the significant role of MRDTI in both the diagnosis and management of acute recurrent ipsilateral LEDVT (van Dam LF, Dronkers CEA, Gautam G, …, Theia Study Group, 2020).

4.4 The Potential Value of Deep Learning in the Diagnosis and Management of Thromboembolic Diseases

As a pivotal technology in the realm of artificial intelligence, deep learning possesses the capability to autonomously extract intricate features from images. In recent years, significant advancements have been achieved within the medical domain, particularly in the diagnosis and treatment of thromboembolic diseases (Huang SC. et al., 2020; Liu W et al., 2020; Sun C et al., 2021; Christiansen SD et al., 2022; Yang X. et al., 2023; Zhu K et al., 2023). In the realm of thrombus detection, Huang et al. (2020) developed an end-to-end deep learning model utilizing the deep completion network PE-NET for the automatic detection of PE. When compared to existing 3D-Convolutional Neural network (CNN) models, this innovative approach demonstrated superior diagnostic efficiency and exhibited commendable performance in external validation sets, achieving an AUC of 0.85. Furthermore, it shows remarkable robustness. In terms of thrombus quantitative diagnosis, Liu et al. (2020) built a CNN based on the U-Net framework to automatically segment and calculate the volume of pulmonary artery thrombosis. The results show that the thrombus load automatically calculated by U-Net is significantly correlated with Qanadli score, Mastora score and right ventricular function parameters. Compared with the complicated semi-quantitative scoring method, the automatic quantitative analysis based on deep learning is more accurate and efficient. Sun et al. (2021) acquired MRI images from 110 subjects across three centers and developed a deep learning model utilizing a generative adversarial network for the automatic segmentation of LEDVT. In comparison to the thrombosis contours manually delineated by experienced radiologists and other existing segmentation models, their approach demonstrated superior segmentation performance and generalization capability. This work provides valuable technical support for the quantitative analysis of thrombus. In the realm of thrombus component analysis, Christiansen et al. (2022) employed a neural CNN to analyze in vitro MRI scan images of specimens from patients who underwent mechanical thrombectomy for acute stroke. Their findings indicated that this model effectively distinguished between thrombi rich in red blood cells and those deficient in red blood cells, achieving an AUC of 0.84 and an accuracy of 0.80. Thus, the analysis of thrombus components can be successfully realized. It is evident that deep learning technology significantly enhances the detection rate of thrombosis, improves the efficiency of imaging specialists, and increases both the sensitivity and specificity in diagnosing thromboembolic diseases. Furthermore, it plays a crucial role in the diagnosis and treatment of thrombotic conditions.

5. Conclusions

The incidence of LEDVT is rising annually and is increasingly affecting younger populations. Timely prediction of the risk of PE is crucial for improving patient prognosis. In current clinical practice, diagnostic systems that utilize clinical scales such as the Wells score, biomarkers like D-dimer, and imaging modalities such as ultrasound provide valuable insights into predicting the risk of acute PE. However, these methods often rely on a single dimension of information, and certain indicators may be influenced by subjective factors. Deep learning possesses robust capabilities for feature extraction and classification, enabling it to achieve high-precision detection. This technology holds significant research potential in the evaluation of thromboembolic diseases. Consequently, the development of an artificial intelligence prediction model based on multi-modal data is anticipated to facilitate more accurate risk stratification for PE by thoroughly exploring the underlying relationships among clinical parameters, biomarkers, and radiomics characteristics. Such advancements will provide an objective foundation for individualized treatment decisions and ultimately improve patient prognosis.

References

Calvo-Romero JM., (2004). Accuracy of D-dimer/fibrinogen ratio to predict pulmonary embolism: a prospective diagnostic study — a rebuttal. *J Thromb Haemost.*, *2*(10), 1862-3.

Christiansen SD, Liu J, Bullrich MB, Sharma M, Boulton M, Pandey SK, Sposato LA, Drangova M., (2022). Deep learning prediction of stroke thrombus red blood cell content from multiparametric MRI. *Interventional Neuroradiology*.

Deng HY, Li G, Luo J, et al., (2016). MicroRNAs are novel non-invasive diagnostic biomarkers for pulmonary embolism: a meta-analysis. *J Thorac Dis.*, *8*(12), 3580-3587.

Esiene A, Tochie J N, Metogo J a M, et al., (2019). A comparative analysis of the diagnostic performances of four clinical probability models for acute pulmonary embolism in a sub-Saharan African population: a cross-sectional study. *BMC Pulm Med.*, *19*(1), 263.

Gkana A, Papadopoulou A, Mermiri M, et al., (2022). Contemporary Biomarkers in Pulmonary Embolism Diagnosis: Moving beyond D-Dimers. *J Pers Med.*, *12*(10), 1604.

Granholm F, Bylund D, Shevchenko G, et al., (2022). A Feasibility Study on the Identification of Potential Biomarkers in Pulmonary Embolism Using Proteomic Analysis. *Clin Appl Thromb Hemost.*, *28*, 10760296221074347.

Heit JA, (2015). Epidemiology of venous thromboembolism. *Nat Rev Cardiol*, *12*(8), 464-74.

Ho ATN, Bellamy N, Naydenov SK., (2021). Trends in mortality of acute pulmonary embolism. *Semin Respir Crit Care Med.*, *42*(2), 171-175.

Huang SC, Kothari T, Banerjee I, Chute C, Ball RL, Borus N, Huang A, Patel BN, Rajpurkar P, Irvin J et al., (2020). PENet-a scalable deep-learning model for automated diagnosis of pulmonary embolism using volumetric CT imaging. *NPJ digital medicine*, *3*, 61.

Jamin A, Hoffmann C, Mahe G, Bressollette L, Humeau-Heurtier A., (2023). Pulmonary embolism detection on venous thrombosis ultrasound images with bi-dimensional entropy measures: Preliminary results. *Medical Physics.*, *50*(12), 7840-7851.

Jeong M-J, Kwon H, Noh M, Ko G-Y, Gwon DI, Lee JS, Kim M-J, Choi JY, Han Y, Kwon T-W et al., (2019). Relationship of Lower-extremity Deep Venous Thrombosis Density at CT Venography to Acute Pulmonary Embolism and the Risk of Postthrombotic Syndrome. *Radiology*, *293*(3), 687-694.

Kahn, S.R., et al., (2008). Determinants and time course of the postthrombotic syndrome after acute deep venous thrombosis. *Ann Intern Med.*, *149*(10), 698-707.

Kara H, Bayir A, Degirmenci S, Kayis SA, et al., (2014). D-dimer and D-dimer/fibrinogen ratio in predicting pulmonary embolism in patients evaluated in a hospital emergency department. *Acta Clin Belg.*, *69*(4), 240-5.

Kaya AT, Akman B., (2024). Relationship of the Novel Scoring System for Lower Extremity Venous Thrombosis with Pulmonary Embolism. *Acad Radiol.*, *31*(9), 3811-3824.

Khan, F., et al., (2021). Venous thromboembolism. *Lancet*, *398*(10294), 64-77.

Krutman M, Wolosker N, Kuzniec S, et al., (2013). Risk of asymptomatic pulmonary embolism in patients with deep venous thrombosis. *J Vasc Surg Venous Lymphat Disord.*, *1*(4), 370-5.

Kucher N, Kohler HP, Dornhöfer T, et al., (2003). Accuracy of D-dimer/fibrinogen ratio to predict pulmonary embolism: a prospective diagnostic study. *J Thromb Haemost.*, *1*(4), 708-13.

Liu T, Kang J, Liu F., (2018). Plasma Levels of microRNA-221 (miR-221) are Increased in Patients with Acute Pulmonary Embolism. *Med Sci Monit.*, *24*, 8621-8626.

Liu W, Liu M, Guo X, Zhang P, Zhang L, Zhang R, Kang H, Zhai Z, Tao X, Wan J et al., (2020). Evaluation of acute pulmonary embolism and clot burden on CTPA with deep learning. *European radiology*, *30*(6), 3567-3575.

Moody, A.R., et al., (1998). Lower-limb deep venous thrombosis: direct MR imaging of the Thrombus. *Radiology*, *209*(2), 349-355.

Morelli VM, Brækkan SK, Hansen JB, et al., (2020). Role of microRNAs in Venous Thromboembolism. *Int J Mol Sci.*, *21*(7), 2602.

Nourse J, Braun J, Lackner K, et al., (2018). Large-scale identification of functional microRNA targeting reveals cooperative regulation of the hemostatic system. *J Thromb Haemost.*, *16*(11), 2233-2245.

Schaefer JK, Jacobs B, Wakefield TW, et al., (2017). New biomarkers and imaging approaches for the diagnosis of deep venous thrombosis. *Curr Opin Hematol*, *24*(3), 274-281.

Steeghs N, Goekoop RJ, Niessen RW, et al., (2005). C-reactive protein and D-dimer with clinical probability score in the exclusion of pulmonary embolism. *Br J Haematol.*, *130*(4), 614-9.

Stevens, S.M., et al., (2021). Antithrombotic Therapy for VTE Disease: Second Update of the CHEST Guideline and Expert Panel Report. *Chest.*, *160*(6), 545-560.

Stoeva N, Kirova G, Staneva M, et al., (2018). Recognition of unprovoked (idiopathic) pulmonary embolism-Prospective observational study. *Respir Med.*, *135*, 57-61.

Subramaniam RM, Mandrekar J, Blair D, et al., (2009). The Geneva prognostic score and mortality in patients diagnosed with pulmonary embolism by CT pulmonary angiogram. *J Med Imaging Radiat Oncol*, *53*(4), 361-365.

Sun C, Xiong X, Zhang T, Guan X, Mao H, Yang J, Zhang X, Sun Y, Chen H, Xie G., (2021). Deep Learning for Accurate Segmentation of Venous Thrombus from Black-Blood Magnetic Resonance Images: A Multicenter Study. *Biomed Research International*, *2021*, 4989297.

van Dam LF, Dronkers CEA, Gautam G, …, Theia Study Group, (2020). Magnetic resonance imaging for diagnosis of recurrent ipsilateral deep vein thrombosis. *Blood*, *135*(16), 1377-1385.

Wang Q, Ma J, Jiang Z, et al., (2018). Diagnostic value of circulating microRNA-27a/b in patients with acute pulmonary embolism. *Int Angiol.*, *37*(1), 19-25.

Wells PS, Anderson DR, Rodger M, et al., (2000). Derivation of a simple clinical model to categorize patients probability of pulmonary embolism: increasing the models utility with the SimpliRED Ddimer. *Thromb Haemost*, *83*, 416-20.

Xiao J, Jing ZC, Ellinor PT, et al., (2011). MicroRNA-134 as a potential plasma biomarker for the diagnosis of acute pulmonary embolism. *J Transl Med.*, *9*, 159.

Yang X, Yu P, Zhang H, Zhang R, Liu Y, Li H, Sun P, Liu X, Wu Y, Jia X et al., (2023). Deep Learning Algorithm Enables Cerebral Venous Thrombosis Detection with Routine Brain Magnetic Resonance Imaging. *Stroke*, *54*(5), 1357-1366.

Zhu K, Bala F, Zhang J, Benali F, Cimflova P, Kim BJ, McDonough R, Singh N, Hill MD, Goyal M et al., (2023). Automated Segmentation of Intracranial Thrombus on NCCT and CTA in Patients with Acute Ischemic Stroke Using a Coarse-to-Fine Deep Learning Model. *American Journal of Neuroradiology*, *44*(6), 641-648.