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Original Article

Clinical Manifestations and Prognostic Factors of Pulmonary Embolism in Adult Patients Visiting the Emergency Department: A Single Institute Experience

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Background and Purpose: To investigate the clinical manifestations of a pulmonary embolism (PE) in patients visiting the emergency department (ED) and to identify possible prognostic factors among the patients.

Methods: Patients who suspected as PE and presented to the ED with chest tightness, chest pain, or syncope were enrolled. Wells score, revised Geneva score, and PE Severity Index (PESI) were all recorded for analysis. Twelve patients who were diagnosed with a PE after a serial work-up were further analyzed for possible prognostic factors. The demographic characteristics, serum lab data, clinical presentations, management strategies, computed tomography (CT) angiography findings, and final outcomes were analyzed retrospectively. Chi-squared tests with Fisher's exact tests, and t-test analyses were applied to evaluate the prognostic factors.

Results: Among the 763 patients enrolled, poor prediction effectiveness of Geneva score and Wells score were noticed, and PESI was also found with no significant predictive value in our study group. The initial vital signs, syncope, chest pain, leg edematous changes, dyspnea, D-dimer levels, CT angiography-measured thrombus diameter, the presence of a right atrium (RA) or right ventricular (RV) thrombus, and presence of lung consolidations all revealed no predictive values in this study ($p > 0.05$). Notably, the presence of a cardiac disease history showed possible prognostic factors for satisfactorily predicting patient outcomes ($p = 0.02$). The presence of left atrium (LA) thrombus showed a border significant differences in comparison ($p = 0.05$).

Conclusions: Although the number of patients analyzed was relatively low, our findings suggest that a history of cardiac disease is predictive of a relatively lethal or severe condition in patients with a PE. The diagnosis and prediction of outcomes for patients with a PE remains a challenge and further study is necessary in the future.

Key words: *pulmonary embolism, clinical manifestation, CT angiography, prognostic factor*

Introduction

Untreated pulmonary embolism (PE) is a potentially lethal condition and the emergent administration of anticoagulant treatment within an appropriate time frame is crucial. However, accurate diagnosis is a prerequisite for standard life-saving treatment protocol application, which remains a challenge in the emergen-

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cy department (ED). In the past few decades, several predictive clinical measurement tools (including Wells rule and revised Geneva score),[1,2] laboratory tests (D-dimer testing),[3] and imaging tools (including computed tomographic pulmonary angiography and lung scintigraphy)[4,5] have been developed and applied to clinical practice for years. Another challenging problem is the lack of efficient tools for the prediction of treatment outcomes in patients diagnosed with a PE. Various imaging modalities have been suggested to have predictive value including echocardiography for right ventricular (RV) dysfunction evaluation and computed tomography (CT) angiography for the measurement of the ratio of the size of the RV compared to the left ventricular (LV);[6] several laboratory serum markers for predicting possible progressive heart failure (including B-type natriuretic peptide [BNP], N-terminal pro B-type natriuretic peptide [NT-proBNP], troponin T, heart-type fatty acid-binding protein [H-FABP], and others) were also proposed.[7,8] The above studies were mainly based on reports from the western hemisphere. Due to the nature of differences of thrombogenicity between races, PE may present with different clinical manifestations with different outcomes under the current protocol for recommended therapy. The lack of studies using diagnostic tools and predictive tools conducted in Asia or Taiwan, may further contribute to the issue of PE management in Taiwan. In this study, we focused on patients visiting the ED with a possible PE and aim to evaluate possible predicting factors in patients with a PE in Taiwan.

Methods

Participants

This study was approved by the Institutional Review Board and Ethics Committee of Cardinal Tien Hospital. From January 2016 through October 2017, patients who presented to the outpatient ED of the participating hospital were eligible if there was a clinical suspicion of PE, defined as the acute onset or worsening shortness of breath or chest pain without another obvious etiology. The study hospital is regional hospital in northern Taiwan with the annual ED patients around 45,000 to 46,000 (there were 45,837 ED patients visited the study hospital in 2016). A total 763 cases involving patients with a suspected PE presenting with chest pain, dyspnea, or syncope were retrospectively enrolled for further analysis. Information on clinical presentations (including symptoms, signs, and physical examinations) and underlying disease history; laboratory serum data (including D-dimer testing, cardiac enzyme levels, and arterial blood gas levels); and chest radiography and 12-lead electrocardiography (ECG) results were collected. We defined history of cardiac disease as those patients with coronary arterial disease, atrial fibrillation, atrial flutter, congestive heart failure, or all other cardiogenic diseases; we further defined prior thromboembolism history as those patients with a prior history of acute myocardial infarction, ischemic type cerebrovascular incidents, deep vein thrombosis, other inherited thrombotic disorders, or other thrombophilic disorders. We also included autoimmune disease history, defined as patients with systemic lupus erythematosus, antiphospholipid syndrome, multiple sclerosis, or other related autoimmune diseases. The Wells score system and revised Geneva score were applied for the patients with a possible PE. The PE Severity Index (PESI) was used in diagnosed PE cases to evaluate the possible prognostic predictive value. For Wells score system, revised Geneva score, and PESI, we re-calculated the scores after reviewing all the patients' medical records. D-dimer levels were assessed in all patients and an age-adjusted threshold (age × 10 ng/mL, rather than a blanket 500 ng/mL, as proposed by Righini et al.) was used to obtain the positive D-dimer test result.[3] Echocardiography and/or CT angiography were performed for further confirmation in patients with a positive D-dimer test. Echocardiography was performed by licensed cardiologist by consultation at our ED. CT angiography films were reviewed by radiologist for final report to confirm the presence of PE.

Patients with a final diagnosis of PE underwent follow-up evaluations for three months. Patients were instructed to return to the clinic or to the ED in case of recurrent respiratory symptoms or swelling of the legs. The overall condition of the patients was evaluated at the end of the follow-up period. We analyzed the above factors to determine 30-day mortality rates to evaluate the prognostic value of these factors.

Statistical Analysis

Statistical analyses were performed using the Statistical Package for the Social Sciences for Windows (SPSS version 22.0, IBM, Armonk, NY, USA) software. The chi-square test with Fisher's exact test

was used to compare categorical data. A t-test was applied for continuous values between the groups. A p value < 0.05 was considered statistically significant.

Results

Our study consisted of 763 cases of patients with a suspected PE. Baseline characteristics are shown in Table 1. The calculated probability of a PE is determined through Wells scores and revised Geneva scores for patients presenting with chest pain, dyspnea and syncope. As shown in Table 1, 61% of patients with suspicious presentations had high Wells scores (> 6), and 74% of patients with a suspected PE had high revised Geneva scores (> 11). However, only 12 patients (1.6%) were diagnosed with a PE after serial work-up. Based on the threshold for a high score using these systems (for Wells score: > 6, for revised Geneva score: > 11), the sensitivity of the test for the applied Well scores and revised Geneva scores is 83.3% and 75.0% (shown in Table 2), respectively, and the specificity of Well scores and revised Geneva scores is 39.3% and 26.1%, respectively. Therefore, we consider these tools to have poor positive predictive values (for Wells score: 2.14%, for revised Geneva score: 1.6%). These results indicated the unreliability of both Wells scores and revised Geneva scores in our study group.

Among patients with a suspected PE, the most frequent symptoms are chest pain (75.0%), dyspnea (50.0%), and unilateral limb pain (58.3%), which were also commonly found in those diagnosed with PE. Syncope (16.7%) was relatively infrequent as shown in Table 2. All of the patients with a diagnosed PE had elevated D-dimers (100.0%) and only 33.3% of the diagnosed patients presented with an elevated troponin I level. Most of the diagnosed PE patients were found to have normal chest radiographs (91.7%) and sinus tachycardia on ECG (91.7%). The echocardiography revealed that 83.3% of the patients with a PE presented with RV dysfunction. Most of the patients with a PE (91.7%) presented with a thrombus within the main and lobar artery as observed with CT angiography. Evidence of deep vein thrombosis was found on venous Doppler sonography over lower limbs in 91.7% of the patients with a diagnosed PE.

The overall survival rate was 75%. The hospital-

Table 1. Patient's baseline characteristics (n = 763)

Variables	Mean ± SD (range)/n (%)
Age (years)	64 ± 15 (21–97)
Gender	
Male	358 (46)
Female	405 (54)
Heart rate (beats/min)	99 ± 7 (87–121)
Oxygen saturation (%)	91 ± 2 (86–96)
Systolic blood pressure (mmHg)	129 ± 12 (102–145)
Diastolic blood pressure (mmHg)	79 ± 9 (67–94)
Symptoms	
Chest pain	452 (59)
Dyspnea	523 (68)
Syncope	82 (10)
Probability of PE (by Wells score)	
≤ 4 (low)	59 (8)
> 6 (high)	466 (61)
Probability of PE (by revised Geneva score)	
≤ 3 (low)	61 (8)
> 11 (high)	564 (74)

PE: pulmonary embolism; SD: standard deviation.

Table 2. Clinical features and diagnostic methods in patients with pulmonary embolism

Clinical features and diagnostic methods	n (%)
Dyspnea	6 (50.0)
Chest pain	9 (75.0)
Syncope	2 (16.7)
Unilateral limb pain	4 (58.3)
Wells score > 6 (high probability of disease)	10 (83.3)
Revised Geneva score > 11 (high probability of disease)	9 (75.0)
Chest radiograph	
Normal	11 (91.7)
Wedge shaped opacity	1 (8.3)
ECG	
Sinus tachycardia	11 (91.7)
RV strain pattern	3 (25.0)
S1Q3T3 pattern	2 (16.7)
Cardiac echocardiography	
RV dysfunction	10 (83.3)
Thrombus in pulmonary arteries or RV	2 (16.7)
Pulmonary hypertension	4 (33.3)
Chest CT with and without contrast	
Thrombus in main and lobar artery	11 (91.7)
Thrombus in distal pulmonary artery	1 (8.3)
Venous Doppler lower limbs	
Evidence of DVT	11 (91.7)
D-dimer (positive, > 500 μg/L)	12 (100.0)
Troponin I (positive, ≥ 1 ng/mL)	4 (33.3)

CT: computed tomography; DVT: deep vein thrombosis; ECG: electrocardiography; RV: right ventricle; S1Q3T3 pattern: a large S wave in lead I, a Q wave in lead III and an inverted T wave in lead III together.

ization duration was 10.1 ± 8.2 d without a significant difference between survivors and non-survivors (p = 0.32). With regards to the evaluation of prognostic factors (Table 3), a history of cardiac disease showed the most significant correlation with mortality (p = 0.02). There were no significant differences between the survivors and non-survivors with regard to age, prior thromboembolism history, malignancy history, and autoimmune disease history. Although elevated D-dimer levels were found in all patients diagnosed with a PE, the level was not found to correlate with mortality (p = 0.11). We also applied the PESI to evaluate the possible prognostic value of the predicting tools but there appeared to be no difference between the groups (p = 0.13). Imaging studies conducted for the patients with a PE revealed that the presence of a left atrium (LA) thrombus showed possible correlation with death but not reach significance (p = 0.05). The thrombus diameter measured using CT, presence of a RV thrombus, occurrence of dilated right atrium (RA) and RV, and related lung consolidation found on chest CT all revealed no correlation with mortality (p > 0.05). The comparison results for the prognostic factors considered in this study are shown in Table 3.

Discussion

PE is a serious and potentially lethal disease. It is more common in men than in women owing to its relationship with smoking and comorbid diseases.[9] For patients younger than 55 years of age, the incidence rate of PE is higher in women owing to the use

Table 3. Prognostic factors of pulmonary embolism patients

Variables	All (n = 12)	Survivor (n = 9)	Non-survivor (n = 3)	*p*
Age (year)	57.6 ± 19.0	54.9 ± 20.9	65.7 ± 10.8	0.29
Gender				
Male	4	3	1	1.00
Female	8	6	2	
Prior thromboembolism history	7	5	2	1.00
Cardiac disease history	4	2	3	0.02
Malignancy history	4	4	0	0.49
Immune disease history	2	0	2	0.46
PESI	91.4 ± 21.6	86.7 ± 22.3	105.7 ± 13.7	0.13
D-dimer testing (μg/L)	6,038 ± 2,705	5,356 ± 2,656	8,083 ± 1,910	0.11
CT measured thrombus diameter (cm)	1.27 ± 0.82	0.90 ± 0.52	2.37 ± 0.47	0.17
Dilated RA and RV	8	5	3	0.49
RV thrombus	2	2	0	0.37
LA thrombus	3	1	2	0.05
Related lung consolidation under chest CT	4	3	1	1.00
Hospitalization duration (d)	10.1 ± 8.2	8.7 ± 4.7	14.3 ± 15.7	0.32

CT: computed tomography; LA: left atrium; PESI: Pulmonary Embolism Severity Index; RA: right atrium; RV: right ventricle.

of oral contraceptives and pregnancy. Further, a higher mortality rate due to PE has been reported in the female population.[10,11] The higher mortality rate was described in older female patients diagnosed with a PE and may be associated with a higher percentage of comorbid congestive heart failure and the immobilization status of the patients. However, gender seemed have no impact on mortality in our study as male and female mortality rates were both 25% in our study. The different results noted in our study may be due to the relative younger age of the patients in our study group.

The incidence of patients diagnosed for the first-time with a PE varies in previous studies depending on whether they included patients diagnosed with a PE by autopsy and if they included different races. The annual incidence of cases of diagnosed PE has increased gradually over recent years. Anderson et al. reported, for the first time, an incidence of 23 per 100,000 in patients diagnosed with PE;[12] however another study conducted by Hanson et al., which included men over the age of 50 with venous thromboembolism (VTE) diagnosed by autopsy, reported that the yearly incidence of PE was 182 per 100,000.[13] It is probable that autopsy data overestimate the incidence of PE owing to the detection of asymptomatic cases, where reliance on clinical diagnosis probably underestimates the incidence. The autopsied patients may present false positive results due to no blood flow in dead patients or declined blood flow in nearly death patients, emboli may be easily generated in major vessels. As previously shown in a reported study, about 28–41% of the PE cases resulted from VTE. A lower adjusted risk of VTE was observed among Hispanics (risk ratio [RR] = 0.7, 95% confidence interval [CI] = 0.3–1.5) and Asians (RR = 0.2, 95% CI = 0.1–0.5) than in Caucasians in a large cohort who were followed prospectively in the Kaiser Health System in Northern California.[11] The incidence of symptomatic first-time idiopathic and secondary VTE in Asians was approximately 3- to 5-fold lower than that in Caucasians.[14] The relatively low incidence of VTE in Asians has not been explained but may be associated with a lower prevalence of genetic factors predisposing them to VTE, such as factor V Leiden in Asian populations (0–0.5%) compared with Caucasians (5%).[15-17] In our study, the prevalence of patients visiting the ED with symptoms suspicious for PE was 1.57%.

We applied both Wells scores and revised Geneva scores for the cases with a clinical suspicion for PE when the patient first presented to the ED. None

of the previously published studies have mentioned the utility of these scoring systems in Taiwan. Our study found a low positive predictive value for these scoring systems (Wells score: 2.14% and revised Geneva score: 1.6%) and low specificity (Wells score: 39.3% and revised Geneva score: 26.1%). This may be associated with the relatively higher efficiency of fibrinolytic activity among Asians, which may also be related to genetic differences among the races.[17] Another reason for this difference may be the misuse of medical resources in Taiwan, which may increase the difficulty of diagnosing a PE based on clinical presentations.[18] A revised scoring system for Asian patients may be necessary to develop in future.

In our study, the overall survival rate of patients with diagnosed PE after presenting to the ED was 75%. For prognostic values, cardiac disease history and presence of a LA thrombus are the only two factors that showed significant difference between the survivors and non-survivors in our study. In the literature review, acute RV dysfunction is a critical determinant of outcome in acute PE. In the International Cooperative Pulmonary Embolism Registry (ICOPER), age > 70 years, systolic blood pressure < 90 mmHg, respiratory rate > 20 breaths/min, cancer, chronic heart failure, and chronic obstructive pulmonary disease were all identified as prognostic factors.[19] In the Registro Informatizado de la Enfermedad ThomboEmbolica venosa study, immobilization for neurological disease, age > 75 years, and cancer were independently associated with an increased risk of death within the first three months after acute VTE.[20] Various prediction rules based on clinical parameters have been shown to be helpful in the prognostic assessment of patients with acute PE. Of those, the PESI is the most extensively validated score to date.[21,22] However, we did not find a significant difference among our study groups. This may due to racial differences within the study groups and patients displaying different clinical presentations among the races. Chung et al. reported that systemic lupus erythematosus and diabetes increases the risk of PE in patients from Taiwan.[23,24] Troponin I is a laboratory serum marker used for predicting the prognosis of PE owing to its association with RV dysfunction.[7] Our study did not find a significant correlation between troponin I and mortality.

Echocardiography results indicating RV dysfunction have been reported in ≥ 25% of patients with PE.[25] These findings have been identified as independent prognostic factors that are associated with poor outcomes,[26] but are heterogeneous and have been proved difficult to standardize.[27] In our study, RA and RV dilatation did not correlate with a poor prognosis. Meta-analyses have shown that RV dysfunction identified by echocardiography is associated with an elevated risk of short-term mortality in patients without hemodynamic instability, but its overall positive predictive value is low.[28] We also further analyzed the CT angiography-measured emboli diameter but there was no correlation with mortality. The presence of an LA thrombus was noted to have a borderline significant difference ($p = 0.05$) between survivors and non-survivors. None of the previous recent studies have mentioned this finding as a potential prognostic factor. We assume that this finding indicates a chain reaction of declined RV contractility with decreased LV pre-load and may be an early sign of left heart failure. However, due to the fact that only three patients in our study presented with positive findings of a LA thrombus, further CT angiography or echocardiography studies are crucial for confirmation of this prognostic factor.

There are some limitations to our study. First, it was a retrospective and single-institute study. The small sample size may result in insignificance after statistical analysis and declined power for mathematical analysis, which possibly leads the results unable to explain causal relationship. Second, the study is limited to emergency medicine and does not incorporate other outpatient departments including pediatric medicine. This results in the loss of any diagnosed PE cases in patients under the age of 18, which may cause the lack of identification of exposure risks in younger populations. Lastly, the small patient sampling number may account for the lack of statistical significance seen in a variety of factors. A larger prospective cohort study is required to support our findings.

In conclusion, the clinical presentation of patients from Taiwan in this study may differ from that of Caucasians or other races. This difference may result in the unreliability of utilizing Wells scores and revised Geneva scores to predict PE. The PESI did not have a significant predictive prognostic value in our study. However, cardiac disease history and the presence of LA thrombus effectively predicted prognosis. Based on these results, it is essential to develop a modified clinical scoring system for predicting disease and prognostic assessment for patients from Taiwan in the future.

Conflicts of Interest Statement

None.

Acknowledgments

None.

Author Contributions

(1) Concepts, design, literature search, data acquisition, and manuscript preparation: all authors. (2) Definition of intellectual content: Hung-Chun Chung. (3) Clinical studies and manuscript editing: Ching-Ching Lee and Yu-Hua Lin. Data analysis, statistical analysis, manuscript review, and guarantor: Yu-Hua Lin.

References

1. Le Gal G, Righini M, Roy PM, et al. Prediction of pulmonary embolism in the emergency department: the revised Geneva score. *Ann Intern Med* 2006;144:165-171. doi:10.7326/0003-4819-144-3-200602070-00004
2. Wells PS, Anderson DR, Rodger M, et al. Derivation of a simple clinical model to categorize patients probability of pulmonary embolism: increasing the models utility with the SimpliRED D-dimer. *Thromb Haemost* 2000;83:416-420. doi:10.1055/s-0037-1613830
3. Righini M, Van Es J, Den Exter PL, et al. Age-adjusted D-dimer cutoff levels to rule out pulmonary embolism: the ADJUST-PE study. *JAMA* 2014;311:1117-1124. doi:10.1001/jama.2014.2135
4. Stein PD, Fowler SE, Goodman LR, et al. Multidetector computed tomography for acute pulmonary embolism. *N Engl J Med* 2006;354:2317-2327. doi:10.1056/NEJMoa052367
5. PIOPED Investigators. Value of the ventilation/perfusion scan in acute pulmonary embolism. Results of the prospective investigation of pulmonary embolism diagnosis (PIOPED). *JAMA* 1990;263:2753-2759. doi:10.1001/jama.1990.03440200057023
6. Ghaye B, Ghuysen A, Bruyere PJ, D'Orio V, Dondelinger RF. Can CT pulmonary angiography allow assessment of severity and prognosis in patients presenting with pulmonary embolism? What the radiologist needs to know. *Radiographics* 2006;26:23-39. doi:10.1148/rg.261055062
7. 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.
8. Konstantinides SV, Torbicki A, Agnelli G, et al. 2014 ESC guidelines on the diagnosis and management of acute pulmonary embolism. *Eur Heart J* 2014;35:3033-3069, 3069a-3069k. doi:10.1093/eurheartj/ehu283
9. Schissler AJ, Rozenshtein A, Schluger NW, Einstein AJ. National trends in emergency room diagnosis of pulmonary embolism, 2001–2010: a cross-sectional study. *Respir Res* 2015;16:44. doi:10.1186/s12931-015-0203-9
10. Barrios D, Morillo R, Guerassimova I, et al. Sex differences in the characteristics and short-term prognosis of patients presenting with acute symptomatic pulmonary embolism. *PLoS One* 2017;12:e0187648. doi:10.1371/journal.pone.0187648
11. White RH. The epidemiology of venous thromboembolism. *Circulation* 2003;107(23 Suppl 1):I4-I8. doi:10.1161/01.CIR.0000078468.11849.66
12. Anderson FA Jr, Wheeler HB, Goldberg RJ, et al. A population-based perspective of the hospital incidence and case-fatality rates of deep vein thrombosis and pulmonary embolism. The Worcester DVT study. *Arch Intern Med* 1991;151:933-938. doi:10.1001/archinte.1991.00400050081016
13. Hansson PO, Welin L, Tibblin G, Eriksson H. Deep vein thrombosis and pulmonary embolism in the general population: the study of men born in 1913. *Arch Intern Med* 1997;157:1665-1670. doi:10.1001/archinte.1997.00440360079008
14. White RH, Keenan CR. Effects of race and ethnicity on the incidence of venous thromboembolism. *Thromb Res* 2009;123(Suppl 4):S11-S17. doi:10.1016/S0049-3848(09)70136-7
15. Angchaisuksiri P, Pingsuthiwong S, Aryuchai K, et al. Prevalence of the G1691A mutation in the factor V gene (factor V Leiden) and the G20210A prothrombin gene mutation in the Thai population. *Am J Hematol* 2000;65:119-122. doi:10.1002/1096-8652(200010)65:2<119::AID-AJH5>3.0.CO;2-8
16. Gregg JP, Yamane AJ, Grody WW. Prevalence of the factor V-Leiden mutation in four distinct American ethnic populations. *Am J Med Genet* 1997;73:334-336. doi:10.1002/(SICI)1096-8628(19971219)73:3<334::AID-AJMG20>3.0.CO;2-J
17. Ho CH, Chau WK, Hsu HC, Gau JP, Chih CM. Prevalence of factor V Leiden in the Chinese population. *Zhonghua Yi Xue Za Zhi (Taipei)* 1999;62:875-878.
18. Tsai JCH, Liang YW, Pearson WS. Utilization of emergency department in patients with non-urgent medical problems: patient preference and emergency department convenience. *J Formos Med Assoc* 2010;109:533-542. doi:10.1016/S0929-6646(10)60088-5
19. Goldhaber SZ, Visani L, De Rosa M. Acute pulmonary embolism: clinical outcomes in the International Cooperative Pulmonary Embolism Registry (ICOPER). *Lancet* 1999;353:1386-1389. doi:10.1016/S0140-6736(98)07534-5
20. Laporte S, Mismetti P, Décousus H, et al. Clinical predictors for fatal pulmonary embolism in 15 520 patients with

venous thromboembolism: findings from the Registro Informatizado de la Enfermedad TromboEmbolica venosa (RIETE) Registry. *Circulation* 2008;117:1711-1716. doi:10.1161/CIRCULATIONAHA.107.726232

21. Donźe J, Le Gal G, Fine MJ, et al. Prospective validation of the Pulmonary Embolism Severity Index. A clinical prognostic model for pulmonary embolism. *Thromb Haemost* 2008;100:943-948. doi:10.1160/TH08-05-0285
22. Chan CM, Woods C, Shorr AF. The validation and reproducibility of the Pulmonary Embolism Severity Index. *J Thromb Haemost* 2010;8:1509-1514. doi:10.1111/j.1538-7836.2010.03888.x
23. Chung WS, Lin CL, Chang SN, Lu CC, Kao CH. Systemic lupus erythematosus increases the risks of deep vein thrombosis and pulmonary embolism: a nationwide cohort study. *J Thromb Haemost* 2014;12:452-458. doi:10.1111/jth.12518
24. Chung WS, Lin CL, Kao CH. Diabetes increases the risk of deep-vein thrombosis and pulmonary embolism. A population-based cohort study. *J Thromb Haemost* 2015;114:812-818. doi:10.1160/TH14-10-0868
25. Kreit JW. The impact of right ventricular dysfunction on the prognosis and therapy of normotensive patients with pulmonary embolism. *Chest* 2004;125:1539-1545. doi:10.1378/chest.125.4.1539
26. Kucher N, Rossi E, De Rosa M, Goldhaber SZ. Prognostic role of echocardiography among patients with acute pulmonary embolism and a systolic arterial pressure of 90 mm Hg or higher. *Arch Intern Med* 2005;165:1777-1781. doi:10.1001/archinte.165.15.1777
27. ten Wolde M, Söhne M, Quak E, Mac Gillavry MR, Büller HR. Prognostic value of echocardiographically assessed right ventricular dysfunction in patients with pulmonary embolism. *Arch Intern Med* 2004;164:1685-1689. doi:10.1001/archinte.164.15.1685
28. Coutance G, Cauderlier E, Ehtisham J, Hamon M, Hamon M. The prognostic value of markers of right ventricular dysfunction in pulmonary embolism: a meta-analysis. *Crit Care* 2011;15:R103. doi:10.1186/cc10119