Clinical Characteristics of Patients with Peripheral Pulmonary Embolism

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Key Words

Computed tomography · Pulmonary arteries · Pulmonary embolism · Treatment

Abstract

Background: The clinical relevance of emboli limited to the segmental or sub-segmental pulmonary arteries and the role of anticoagulation in patients with these conditions remains to be clarified. **Objectives:** To determine the clinical characteristics and treatment outcomes of peripheral pulmonary embolism (PE), and in particular, isolated sub-segmental PE (ISSPE). **Methods:** We reviewed the data for 334 patients who were diagnosed with a PE by computed tomographic (CT) pulmonary angiography and indirect CT venography. **Results:** All patients were classified into one of three groups: central (245 patients, 73.4%); segmental (67 patients, 20.1%), and sub-segmental (22 patients, 6.6%). An incidental CT finding (63.6%) was the most common presentation in the segmental and sub-segmental groups. Compared with the central group, the sub-segmental group had less frequent proximal deep venous thrombosis (14 vs. 47%, Bonferroni's corrected $p = 0.002$), and greater preservation of oxygenation levels ($p < 0.05$) without hemodynamic instability. The recurrence of PE and deaths related to PE did not occur in the sub-segmental group, although approximately 30% of the patients did not receive anticoagulation therapy. **Con-**

clusions: Patients with ISSPE may have a more benign clinical presentation, as compared to the central type, and may follow a good clinical course without mortality or recurrence.

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Introduction

In the early 1990s when helical computed tomography (CT) was introduced for the diagnosis of a pulmonary embolism (PE) [1], it could reliably detect a central PE but was limited in excluding a small PE [2, 3]. Recently, the advent of multi-detector row CT (MDCT) improved visualization up to the levels of the segmental and sub-segmental pulmonary arteries [4], thereby enhancing more confidently the diagnosis of smaller PEs [5]. Currently, MDCT has replaced scintigraphy as the imaging study of choice in the diagnosis of PEs in many institutions [6]. In 2007, MDCT angiography fulfilled the conditions to replace pulmonary angiography as the reference standard for the diagnosis of an acute PE [7].

Clinicians' interest in small PEs, particularly PEs limited to the sub-segmental arteries (isolated sub-segmental PE, ISSPE) dates back to the data based on conventional pulmonary angiography [8]. Peripheral PEs, in which emboli do not extend proximally beyond the seg-

mental or sub-segmental pulmonary arteries, has not uncommonly been detected on MDCT scans regardless of whether it is incidentally detected or diagnosed in suspected patients. Recently, the clinical relevance of peripheral PEs and the role of anticoagulation in these patients have been questioned in several reports [5, 9, 10]. In a previous study [5], patients with ISSPE less frequently had dyspnea, a high clinical probability of PE, and proximal deep venous thrombosis (DVT), as compared with segmental or more proximal groups. Among the 30 patients with ISSPE, eight were left untreated and none of them experienced a thromboembolic event during the 3-month follow-up period. However, these studies have mostly been focused on the radiologic aspects and data regarding clinical features are sparse or have been indirectly obtained [5]. The aim of this study was to determine the clinical characteristics and treatment outcomes of peripheral PEs, especially ISSPEs.

Materials and Methods

Study Population

We searched the computer database of the Kyungpook National University Hospital (a tertiary referral center in Daegu, South Korea) for patients ≥ 18 years of age who underwent CT pulmonary angiography and indirect CT venography and were diagnosed with a PE at that institution between September 2003 and December 2008. A total of 334 patients with PEs were collected and classified into 3 groups by the largest PE-involved pulmonary arteries: central (main trunk, right or left pulmonary artery, intermediate arteries, or lobar arteries); segmental, and sub-segmental (fig. 1). To determine the locations of the most proximal pulmonary arteries in which emboli were detected, CT scans were reviewed separately by 2 experienced radiologists (K.M.S. and J.L.) who were blinded to the patients' clinical information. In case of discrepancies in their readings, a final decision was reached by consensus. This study was approved by the institutional review board of the KNUH, and written informed consent was waived because this study was retrospective.

Clinical Data

The following baseline data of the patients were recorded at presentation: age, gender, smoking history, body mass index (BMI), presenting manifestations, duration of symptoms, and presence or absence and location of DVT. To assess the clinical probability, we retrospectively scored the clinical prediction rules using the Wells [11] and Revised Geneva scores [12] from the medical records. The risk factors for PEs and comorbid conditions were reviewed. A patient who had smoked at least once a day for >1 year in his or her lifetime was regarded as an ever-smoker. The cumulative cigarette dose (pack years) was calculated using the following formula: pack years = packs per day $\times$ years smoked.

Data of arterial blood gas analysis, including partial pressure of oxygen in arterial blood (PaO_2), oxygen saturation in arterial blood (SaO_2), and alveolar-arterial oxygen difference P(A-a)O_2 , se-

rum biomarkers of PEs including the levels of N-terminal-pro-B-type natriuretic peptide (NT-proBNP), D-dimer, troponin-I, and creatine kinase-MB (CK-MB), and the presence of hypotension (systolic blood pressure <90 mm Hg), T-wave inversion on the precordial leads of the electrocardiogram (ECG), and right ventricular (RV) dysfunction on echocardiography were examined. Lastly, we compared anticoagulation, response to treatment, recurrence of PE, and causes of death among groups. By modifying the method of Musset et al. [13], we categorized the deaths on the basis of available information as related to PE (certainly or possibly), not related to PE or unknown.

Radiologic Data

On CT scan, a PE was diagnosed as a sharply delineated pulmonary arterial filling defect present in at least 2 consecutive image sections and located centrally within the vessel or with acute angles at the interface with the vessel wall [14]. A DVT was defined as a low-attenuating partial or complete intraluminal filling defect surrounded by a high-attenuating ring of enhanced blood that was seen on at least 2 consecutive transverse images [15]. A proximal DVT was defined as a thrombosis at the level of the popliteal vein or above and a distal DVT as a thrombosis affecting the axial calf veins. The changes in the PE upon follow-up CT scan were classified as follows [16]: (1) normalization, when no PE was identified; (2) improvement, if the PE was remarkably reduced in size and/or extent; (3) no change, if no remarkable change was noted; (4) aggravation, when the size and/or extent of the PE had progressed; and (5) undetermined, when objective assessment was difficult.

CT scans were performed using MDCT scanners with 16 detector rows (Light Speed 16; General Electric, Milwaukee, Wisc., USA) or with 64 detector rows (Aquilion 64; Toshiba Medical System, Tokyo, Japan). The scan was obtained in the craniocaudal direction during a single inspiratory breath hold, ranging from the apex to the diaphragm. The CT parameters used were 120 kVp and a 0.75-mm collimation with a pitch <1.5 . Low osmolar non-ionic contrast material (2 ml/kg; up to 150 ml) was injected through an arm vein at 3–4 ml/s. Individual contrast optimization was achieved using bolus tracking within the main pulmonary artery. Indirect CT venography was performed from the diaphragm to the ankles to detect DVT 140 s after a thoracic scan.

Statistical Analysis

Statistical analyses were performed using SPSS software, version 12.0 (SPSS Inc., Chicago, Ill., USA). The data are expressed as the mean $\pm$ standard deviation or the median with interquartile range for continuous variables and percentages for categorical variables. Among the groups, the continuous variables were compared by 1-way analysis of variance (ANOVA) and the Kruskal-Wallis test if non-normally distributed. In multiple comparisons, Scheffe's and Tukey's methods were used as a post-hoc test if equal variances were assumed and Dunnett's T3 method was adopted if equal variances were not assumed. Categorical variables were compared using a χ^2 test among groups and Bonferroni's correction was used as a post-hoc follow-up test. To summarize the survival of the patients, we used the Kaplan-Meier test to construct survival curves, which were then compared with the results of log-rank tests.

Fig. 1. Computed tomographic pulmonary angiography demonstrated emboli in the sub-segmental (**a**, arrow), segmental (**b**, arrow), and right and left pulmonary arteries (**c**, arrowheads) along with lobar pulmonary artery (**c**, arrow).

Results

Demographic Characteristics

The demographic data are summarized in table 1. The central group included 245 patients (73.4% of the total), the segmental group contained 67 patients (20.1%) and the sub-segmental group had 22 patients (6.6%). Gender and smoking history (prevalence of ever-smokers and pack-years) did not significantly differ among these groups. There was a significant difference in BMI among the 3 groups ($p = 0.038$) but in the post-hoc test, the central group just had a tendency for a higher BMI than the

sub-segmental group ($p = 0.073$ by Scheffe's method and $p = 0.058$ by Tukey's method).

In the sub-segmental and segmental groups, the patients presented most frequently with incidental CT findings (63.6 and 53.7%, respectively), dyspnea (18.2 and 23.9%, respectively) and leg pain or swelling (13.6 and 20.9%, respectively). The most common presenting manifestation of the central group was dyspnea (48.8%), followed by incidental CT findings (18.8%) and leg pain or swelling (18.3%). No significant differences in the clinical probability scores (Wells and Revised Geneva scores) were noted among the groups. However, according to the

Table 1. PE patient demographics (n = 334)

	Sub-segmental (n = 22)	Segmental (n = 67)	Central (n = 245)	p value
Age, years	70 (52–72)	65 (42–63)	66 (53–71)	0.677
Male gender	10 (45.5)	34 (50.7)	110 (44.9)	0.695
Smoking history				
Ever-smokers	7/20 (35.0)	24/64 (37.5)	86/243 (35.4)	0.949
Pack years	40 (25–40)	30 (18–50)	30 (13–40)	0.282
Body mass index	21 (19–24)	24 (22–25)	24 (22–26)	0.038 ^a
Presenting manifestations				<0.001
Dyspnea	4 (18.2)	16 (23.9)	117 (48.8)	
Chest pain	–	1 (1.5)	31 (12.9)	
Hemoptysis	1 (4.5)	–	3 (1.3)	
Leg pain or swelling	3 (13.6)	14 (20.9)	44 (18.3)	
Incidental CT finding	14 (63.6)	36 (53.7)	45 (18.8)	
Duration of symptoms, days	6 (3–20)	5 (2–21)	3 (1–8)	0.280
Wells score	2 (0–4)	2 (1–4)	2 (1–5)	0.115
Simplified clinical probability				0.056
PE likely	2 (9.1)	11 (16.4)	59 (24.1)	
PE unlikely	20 (90.9)	56 (83.6)	186 (75.9)	
Revised Geneva score	6 (2–12)	6 (4–8)	6 (4–8)	0.447
Deep vein thrombosis	9 (40.9)	41 (61.2)	177 (72.2)	0.004 ^b
Distal	6 (27)	20 (30)	61 (25)	0.709
Proximal	3 (14)	21 (31)	116 (47)	0.001 ^c

Data are presented as median (range), n (%) or n/N (%).

Multiple comparison: ^a sub-segmental vs. central, $p = 0.073$ (Scheffe's method) and $p = 0.058$ (Tukey's method); ^b sub-segmental vs. central, Bonferroni's corrected $p = 0.002$; ^c sub-segmental vs. central, Bonferroni's corrected $p = 0.003$.

simplified Wells rule, PE-likely frequency tended to be higher in the central group, as compared to the segmental and sub-segmental groups ($p = 0.056$).

Statistically significant differences in the prevalence of co-existing DVTs were noted among the 3 groups ($p = 0.004$). DVTs were less frequently observed in the sub-segmental group than in the central group (Bonferroni's corrected $p = 0.002$); in the remaining comparisons, significant differences were not found. Likewise, the frequency of proximal DVTs differed significantly among these groups ($p = 0.001$); in particular, the sub-segmental group had less frequent proximal DVTs compared with the central group (Bonferroni's corrected $p = 0.001$). However, there was no significant difference in the prevalence of distal DVTs among the groups.

Risk Factors and Comorbidities of Pulmonary Embolism

Distributions of risk factors and comorbid conditions of PEs are presented in table 2. The frequency of surgery or trauma was higher in the sub-segmental and segmen-

tal groups (Bonferroni's corrected $p < 0.001$, respectively) as compared with the central group. The prevalence of accompanying malignancy significantly differed among the 3 groups ($p = 0.021$), but the Bonferroni's corrected p value of any pair did not reach statistical significance. No significant differences in the remaining risk factors and comorbid illnesses among the groups were observed.

Laboratory Findings of Pulmonary Embolism

The segmental group had significantly lower NT-proBNP, CK-MB and troponin-I levels than the central group ($p < 0.001$, $p < 0.001$ and $p = 0.001$, respectively), unlike the sub-segmental group (table 3). However, the sub-segmental group had significantly higher PaO_2 and SaO_2 values and a lower P(A-a)O_2 , as compared with the central group ($p < 0.05$, respectively). T-wave inversion on the precordial leads of ECG differed significantly among the 3 groups ($p < 0.001$); this change on ECG was more common in the segmental group compared with the central group (Bonferroni's corrected $p < 0.001$). RV dysfunction on echocardiography was observed only in the central

Table 2. Risk factors of pulmonary embolism and comorbidities

	Sub-segmental (n = 22)	Segmental (n = 67)	Central (n = 245)	p value
Past history of venous thromboembolism	2 (9.1)	2 (3.0)	12 (4.9)	0.474
Surgery or trauma	14 (63.6)	28 (41.8)	44 (18.0)	<0.001 ^a
Malignancy	2 (9.1)	23 (34.3)	51 (20.8)	0.021
Immobilization ¹	6 (27.3)	13 (19.4)	55 (22.4)	0.726
Obesity (BMI >30)	–	2 (3.0)	3 (1.2)	1.000
Pregnancy or postpartum	–	–	3 (1.2)	1.000
Varicose vein	–	1 (1.5)	1 (0.4)	0.463
Neurologic disorder ²	3 (13.6)	1 (1.5)	19 (7.8)	0.057
Atherosclerosis obliterans	–	1 (1.5)	1 (0.4)	0.463
Arthritis ³	1 (4.5)	1 (1.5)	10 (4.1)	0.567
Collagen vascular disorders	1 (4.5)	–	4 (1.6)	0.233
Myeloproliferative disorders ⁴	–	1 (1.5)	1 (0.4)	0.463
Chronic lung diseases ⁵	17 (6.9)	6 (9)	4 (18.2)	0.129
Pulmonary tuberculosis or NTM infection	2 (9.1)	3 (4.5)	13 (9.1)	0.576
Pneumonia or lung abscess	–	2 (3)	4 (1.6)	0.743
Cardiovascular disorders ⁶	1 (4.5)	5 (7.5)	24 (9.8)	0.747
Chronic liver diseases	1 (4.5)	2 (3)	3 (1.2)	0.213
Chronic renal diseases ⁷	1 (4.5)	–	6 (2.4)	0.204
Dyslipidemia	–	–	5 (2.0)	0.708
Hypertension	6 (27.3)	15 (22.4)	80 (32.7)	0.256
Diabetes	6 (27.3)	14 (20.9)	41 (16.7)	0.389
Other endocrine disorders ⁸	–	–	5 (2.0)	0.708
Tetanus, burn, or bullous pemphigoid	–	1 (4.5)	6 (2.4)	1.000

NTM = nontuberculous mycobacteria. Data are presented as n (%).

^a Sub-segmental vs. central, Bonferroni's corrected $p < 0.001$; segmental vs. central, Bonferroni's corrected $p < 0.001$.

¹ Bed rest within past month for most of the day for ≥ 3 consecutive days; ² cerebrovascular accident, dementia, Parkinson's disease, or hydrocephalus; ³ rheumatoid arthritis, osteoarthritis, or gout; ⁴ polycythemia vera or essential thrombocytosis; ⁵ chronic obstructive pulmonary disease, asthma, tuberculosis-destroyed lung, bronchiectasis, or idiopathic pulmonary fibrosis; ⁶ congestive heart failure, ischemic heart disease, atrial fibrillation, or aortic dissection; ⁷ chronic renal failure or nephrotic syndrome; ⁸ Graves' disease, hypothyroidism, Cushing syndrome, or pheochromocytoma.

group ($p = 0.039$), but no individual pairing achieved statistical significance in multiple comparisons.

Anticoagulation, Treatment Outcome and Clinical Course

The proportion of patients who received anticoagulation therapy was as follows: central, 93.5% ($n = 229$); segmental, 80.6% ($n = 54$), and sub-segmental, 68.2% ($n = 15$). The sub-segmental and segmental groups underwent anticoagulation less frequently, as compared with the central group (Bonferroni's corrected $p < 0.001$ and $p = 0.001$, respectively; fig. 2a). Statistically significant differences in the causes of non-anticoagulation were not noted among the groups ($p = 0.141$; fig. 2b). In the sub-segmental group, the most common cause of non-antico-

agulation was missed diagnosis, in contrast with a poor general condition or refusal of anticoagulation in the segmental group and contraindications of anticoagulation in the central group.

Of patients who underwent follow-up CT scans, the proportion of normalization or improvement did not differ significantly among the 3 groups (central, segmental and sub-segmental): 93.7% (104/111), 90.0% (27/30) and 100% (9/9), respectively. The median duration of follow-up was 8 months (IQR 3–19 months). PE recurred only in the central group (2.4%, $n = 6$). No significant differences in overall survival among the 3 groups were found ($p = 0.052$; fig. 3a). There was also no statistically significant difference in PE-related deaths among the groups ($p = 0.662$; fig. 3b). However, PE-related deaths were not

Fig. 2. a The frequency of anticoagulation in each group. The sub-segmental (68.2%) and segmental (80.6%) groups underwent anticoagulation less frequently, as compared with the central group (93.5%). **b** Causes of non-anticoagulation in each group. Missed diagnosis was the most common cause of non-anticoagulation in the sub-segmental group, as opposed to a poor general condition or refusal of anticoagulation in the segmental group and contraindications of anticoagulation in the central group.

Table 3. Laboratory findings of pulmonary embolism

	Sub-segmental	Segmental	Central	p value
Hypotension	0/21 (0.0)	1/65 (1.5)	9/242 (3.7)	0.844
D-dimer, ug/l	748 (410–759; n = 13)	771 (212–1,234; n = 38)	719 (331–1,162; n = 174)	0.780
NT-proBNP, pg/ml	140 (89–4,956; n = 12)	81 (25–966; n = 22)	693 (210–3,425; n = 134)	<0.001 ^a
CK-MB, ng/ml	0.3 (0.4–6.2; n = 14)	0.5 (0.3–1.2; n = 40)	1.0 (0.6–2.7; n = 175)	<0.001 ^a
Troponin-I, ng/ml	0.04 (0.04–0.90; n = 14)	0.04 (0.03–0.05; n = 39)	0.06 (0.03–0.22; n = 178)	0.002 ^b
PaO ₂ , mm Hg	85.3 ± 12.2 (n = 13)	77.0 ± 16.8 (n = 31)	72.4 ± 15.5 (n = 159)	0.009 ^c
SaO ₂ , %	97 (96–99; n = 13)	96 (92–97; n = 31)	96 (93–97; n = 159)	0.024 ^c
P(A-a)O ₂ , mm Hg	26 (38–61; n = 13)	34.5 (27–72; n = 31)	47 (24–62; n = 159)	0.046 ^c
T-wave inversion on precordial leads	1/16 (6.3)	2/48 (4.2)	65/211 (30.8)	<0.001 ^d
RV dysfunction on echocardiography	0/4 (0.0)	0/9 (0.0)	34/103 (33)	0.039

NT-proBNP = N-terminal-pro-B-type natriuretic peptide; CK-MB = creatine kinase-MB; PaO₂ = partial pressure of oxygen in arterial blood; SaO₂ = oxygen saturation in arterial blood; P(A-a)O₂ = alveolar-arterial oxygen difference; RV = right ventricle. Data are presented as mean ± SD, median (range) or n/N (%).

^a Segmental vs. central, $p < 0.001$; ^b segmental vs. central, $p = 0.001$; ^c sub-segmental vs. central, $p < 0.05$; ^d segmental vs. central, Bonferroni's corrected $p < 0.001$.

noted in the sub-segmental group in contrast to 7 (2.9%) and 3 (4.5%) deaths in the central and segmental groups, respectively. All 3 patients from the segmental groups had aggravation of dyspnea and hypoxia during in-hospital stay and had serious comorbid conditions, including advanced gall bladder cancer with peritoneal carcinomatosis, extensive stage small cell lung cancer and bedridden status due to cerebral infarction.

Discussion

The present study was primarily focused on the clinical characteristics of peripheral PEs, particularly ISSPEs. Like the segmental group, the patients of the sub-segmental group presented most commonly with incidental CT findings, and proximal DVTs were less commonly found in this group as compared to the central group.

Fig. 3. a No significant differences in overall survival among the 3 groups were found ($p = 0.052$). **b** No patient died of PE-related causes in the sub-segmental group.

There were no significant differences in the risk factors of PEs and comorbid illnesses among the groups except for surgery or trauma, which accompanied the sub-segmental group more frequently as compared with the central type. The patients with PE limited to segmental or sub-segmental arteries had lower serum levels of biomarkers and less frequent ECG change of RV strain or more preserved oxygenation levels [higher PaO_2 and SaO_2 and lower P(A-a)O_2], when compared to those with the central type. Moreover, hypotension and RV dysfunction on echocardiography were not observed in the sub-segmental group, suggesting that ISSPE patients may be hemodynamically stable. Although approximately 30% of the sub-segmental group did not undergo anticoagulation, there was no case of death related to or recurrence of PE.

The prevalence of ISSPE was 6.6% in this study, which is similar to the 6% in an analysis of 383 pulmonary angiograms from the PIOPED study [17] and 4.2–27.9% reported in the literature using MDCT [7, 9, 17–21]. Extracted from the data of PIOPED II, typical presentations of PE (hemoptysis/pleuritic pain, uncomplicated dyspnea or circulatory collapse) were less common in patients with segmental PEs compared to patients with PEs in more proximal arteries [22]. As described above [5], the patients with ISSPE had less dyspnea, and less frequently had a high clinical probability of PE. Similarly, the most common presentation of peripheral PEs was an incidental CT finding unlike the central group. However, the

Wells and Revised Geneva scores were similar among the groups, although PE-likely patients tended to be more common in the central group, as compared to small PE groups. These may result from the fact that a considerable number of asymptomatic PE patients ($n = 95$, 28%) were included in the present study.

Of comorbid conditions and risk factors for PE, trauma or surgery and malignancy differed among the groups. The sub-segmental group was more frequently accompanied by trauma or surgery than the central group. This can be explained partly by the finding that PE was more often incidentally detected on CT scan after trauma or surgery as compared to the remaining cases (72.1 vs. 13.3%, $p < 0.001$). In contrast, the frequency of malignancy did not achieve statistical significance in the post-hoc tests.

Patients with PE limited to small peripheral arteries appear to have a more benign clinical presentation than patients with proximal PE [5, 23]. Similarly, the present study revealed that the segmental group exhibited lower levels of serologic biomarkers and a lower incidence of ECG changes of RV strain when compared with the central group. However, we do not know the reason why these statistical differences were not noted between the sub-segmental and central groups, considering that comorbid conditions, such as heart diseases, did not differ among the groups. It is noteworthy that hypotension and echocardiographic RV dysfunction did not develop in the sub-segmental group. Compared to the central group, the

sub-segmental group had co-existing proximal DVTs less commonly (14 vs. 47%) but not as rarely as that in a previous report (3.3 vs. 43.8%) [5]. The severity of PE should be understood as an individual estimate of PE-related fatality rather than the anatomical burden of pulmonary emboli [24]. In this context, combined DVT, in particular proximal DVT, is considered to be an independent risk factor of poor outcome of PE [25], although recurrence of venous thromboembolism and PE-related deaths did not differ among the 3 groups in the present study.

Recurrence of PEs did not occur in the segmental and sub-segmental groups, in contrast to 2.4% in the central group. Furthermore, none of the patients in the sub-segmental group died from PE-related causes. These results suggest that otherwise healthy individuals with ISSPEs may not be at a significantly increased risk for morbidity and mortality in accordance with a previous report [26]. As mentioned above, 7 of 22 patients did not receive anticoagulant in the sub-segmental group and none of this group experienced recurrence of PE and PE-related deaths irrespective of anticoagulation. This implies that missing of ISSPEs does not seem to adversely affect patient outcome. This can be explained by the fact that small emboli may be dissolved by intrinsic fibrinolytic activity from the lung vasculature [27]. The necessity to treat patients with ISSPEs cannot be answered in this study, similarly to previous studies [5].

In the segmental group, however, PE-related deaths ($n = 3$, 4.5%) occurred. Each of the 3 patients experienced sudden clinical deterioration, circulatory collapse and death during in-hospital stay, although emboli did not

extend beyond segmental pulmonary arteries on the initial CT scan. Considering this difference, the clinical course of the PE limited to segmental arteries may be different from ISSPE. Moreover, cardiopulmonary reserve is more likely to have influenced the prognosis of these patients, although pulmonary emboli were small.

Our study had several limitations. First, since our study was performed retrospectively, a selection bias could not be avoided. Second, as the patients were recruited from the database with a PE-positive CT scan, suspected PE and incidentally detected PE cases were included. Unsuspected PE patients with less severe clinical manifestations were likely to influence the differences of the clinical characteristics by the largest PE-involved pulmonary arteries. Third, there is a possibility of underestimation of small PE because we did not review negative CT images. Lastly, whether CT-based ISSPEs are true PEs remains questionable [28]. True positivity of PE on CT scan can be supported by the following criteria: (1) normalization or improvement of PE on follow-up CT scans ($n = 9$); (2) CT-matching defects on perfusion scan (1/7) [28]; (3) coexisting DVT on CT venography ($n = 9$) or ultrasound [26], and (4) multiplicity of pulmonary emboli on CT scan ($n = 12$) [29]. Overall, of 22 ISSPE patients, 17 (77%) had findings supportive of PE.

In conclusion, the most common presentation is the incidental CT finding in the peripheral PE. Patients with ISSPE may have a more benign clinical presentation, as compared to the central type, and may take a good clinical course without mortality and recurrence.

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