Clinical Relevance of Pleural Effusion in Patients with Pulmonary Embolism

Sun Ha Choi^a Seung-Ick Cha^a Kyung-Min Shin^b Jae-Kwang Lim^b
Seung-Soo Yoo^a Shin-Yup Lee^a Jaehee Lee^a Chang-Ho Kim^a
Jae-Yong Park^a Deok Heon Lee^c

Departments of ^aInternal Medicine, ^bRadiology and ^cThoracic and Cardiovascular Surgery, School of Medicine, Kyungpook National University, Daegu, South Korea

Keywords

Computed tomography · Pleural effusion · Pulmonary embolism · Pulmonary infarction

Abstract

Background: Data regarding pleural effusion due to pulmonary embolism (PE) are limited. **Objectives:** The aim of this study was to investigate the clinical characteristics of PE patients with pleural effusion caused by PE. **Methods:** Patients with PE were retrospectively analyzed and divided into 2 groups based on computed tomography: a group with pleural effusion due to PE (effusion group) and a group without pleural effusion (control group). Clinical characteristics were compared between the 2 groups. **Results:** The study population consisted of the effusion group ($n = 127$) and the control group ($n = 651$). Serum C-reactive protein (CRP) level was significantly higher in the effusion group than in the control group. The percentages of high-risk Simplified PE Severity Index (57 vs. 47%, $p = 0.008$), central PE (84 vs. 73%, $p = 0.013$), right ventricular dilation (45 vs. 36%, $p = 0.053$), and pulmonary infarction (40 vs. 8%, $p < 0.001$) were higher in the effusion group than in the control group. Multivariate analysis demonstrated that pulmonary infarction (odds ratio [OR] 6.20, 95% confidence interval [CI] 3.49–

10.91, $p < 0.001$) and CRP level (OR 1.05, 95% CI 1.101–1.09, $p = 0.023$) were independent predictors of pleural effusion due to PE. The presence of pleural effusion was not a predictor of short-term outcomes or length of hospital stay. **Conclusions:** Patients with more severe PE are likely to have pleural effusion caused by PE. However, pleural effusion was not a proven predictor of short-term outcome or length of hospital stay. Pulmonary infarction and CRP levels were independent risk factors for the development of pleural effusion.

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Introduction

Pulmonary embolism (PE) is the fourth leading cause of pleural effusion in the United States, after congestive heart failure, parapneumonic effusion, and malignancy [1], and it is also considered one of the leading causes among patients with undiagnosed pleural effusion [2]. Among patients with PE, the percentage of those with pleural effusion varies with the assessment method and study population: 23–52% of those assessed by chest radiography have pleural effusion [3–6], as do 20–55% of those assessed by computed tomography (CT) [4, 7, 8].

As the amount of pleural effusion caused by PE is usually small, diagnostic thoracentesis is not routinely performed [9]. Several studies have been dedicated to analyze pleural fluid in PE patients with pleural effusion [4, 10, 11]. Many patients had bloody or blood-tinged pleural effusions [4, 9–11], and most pleural effusions due to PE are exudates [4, 9, 10]. A few studies have evaluated the clinical characteristics of PE patients with pleural effusion [5, 12]. However, data regarding clinical comparisons between PE patients who have pleural effusion and PE patients who do not have pleural effusion are limited [7]. In addition, there is no recent study of patients with pleural effusion caused by PE but no other comorbid condition [6].

The aim of this study was to investigate and compare the clinical characteristics of PE patients with pleural effusion caused by PE and with PE patients without pleural effusion, and to determine predictors of pleural effusion due to PE. Finally, we tried to elucidate the clinical relevance of pleural effusion in PE patients.

Methods

Study Design

This study was retrospectively conducted in a tertiary referral center, Kyungpook National University Hospital (KNUH) in Daegu, South Korea. Patients with PE who had been diagnosed by using multidetector-row CT between March 2003 and December 2015 were enrolled. The presence and causes of pleural effusion were determined by the consensus of 2 chest physicians (S.H.C. and S.-I.C.) on the basis of CT scans and medical records. Pleural effusion ipsilateral to pulmonary emboli or adjacent to pulmonary infarcts that could not be explained by any other condition was defined as pleural effusion due to PE. Patients with other conditions that were likely to have caused pleural effusion were excluded. Clinical characteristics, laboratory findings, and CT-based parameters were compared between patients with pleural effusion due to PE and PE patients without pleural effusion, and potential predictors of pleural effusion caused by PE were examined. This study was approved by the Institutional Review Board of the KNUH, which waived the requirement for written informed consent because of the retrospective nature of the study.

Data Collection

Demographic data, symptoms, vital signs, and predisposing or comorbid conditions were examined. PE was defined as unprovoked if no reversible provoking risk factors had occurred; these factors included surgery, trauma, active cancer, pregnancy and puerperium within 3 months of the event, and immobilization (bed rest for most of the day for ≥ 3 consecutive days) within 1 month of the event [13]. Ratings based on the Simplified PE Severity Index (sPESI) [14] were retrospectively calculated for patients before 2011 and have been prospectively recorded in their medical records since 2011. Outcome parameters, including in-hospital mortality (PE-related or PE-unrelated), adverse outcomes, and recurrence of venous thromboembolism were reviewed. As in a previ-

ous study, an adverse outcome was defined as a PE-related in-hospital death or PE resulting in a serious clinical condition requiring intensive care treatment, such as inotropic support and mechanical ventilation, impending respiratory failure or refractory hypoxia, cardiopulmonary resuscitation, or secondary thrombolysis [15]. A PE-related in-hospital death was defined as an in-hospital death that met one of the following criteria: (1) objective evidence of death directly caused by PE, and (2) death that could not be attributed to other causes and in which PE could not be excluded [15].

Blood samples were obtained within 12 h of the initial visit. Blood laboratory data, including erythrocyte sedimentation rate (ESR) and levels of N-terminal-pro-B-type natriuretic peptide (NT-proBNP), troponin I, C-reactive protein (CRP), and procalcitonin, were reviewed. Arterial blood gas analysis data consisted of the partial pressure of oxygen in arterial blood (PaO_2), the partial pressure of carbon dioxide in arterial blood (PaCO_2), the inspired oxygen fraction (FiO_2), and the $\text{PaO}_2/\text{FiO}_2$ ratio.

Radiological Evaluation

As in an earlier study [16], in this study, a PE was diagnosed on CT images as a sharply delineated filling defect that was seen in a pulmonary artery in at least 2 consecutive image sections and that either was located centrally within the vessel or formed acute angles with the arterial wall. PE-involved largest pulmonary arteries were determined as follows: pulmonary trunk, pulmonary (right or left pulmonary artery), interlobar or lobar, segmental, and subsegmental. Central PE was diagnosed when thrombi were visualized in the lobar or more proximal pulmonary arteries. The diameters of the right ventricle (RV) and left ventricle (LV) were measured at their widest points between the inner surface of the free wall and the surface of the interventricular septum; the RV diameter was typically measured at the level of the tricuspid valve, and the LV diameter was measured at the level of the mitral valve [17]. Subsequently, the RV/LV diameter ratios were calculated. An RV was considered dilated if the RV/LV diameter ratio measured on a CT scan equaled or exceeded 1 [15]. The extent of pleural effusion was assessed as follows: small, < 3 cm at maximal depth; moderate, 3–5 cm; and large, > 5 cm [18]. On the basis of modified criteria of a prior study [19, 20], a pulmonary infarction was defined as the presence of a peripheral consolidation in the region of a segmental or subsegmental PE.

Statistical Analysis

Statistical analysis was performed by using IBM SPSS Statistics for Windows, version 23.0 (IBM Corp., Armonk, NY, USA). Data were expressed as means $\pm$ standard deviations or medians with interquartile ranges for continuous variables and as numbers with percentages for categorical variables. Between groups, continuous variables were compared by using the Student *t* test and Mann-Whitney U test for nonnormally distributed data. Categorical variables were compared by using the χ^2 test. Multiple logistic regression analysis was used to identify predictors of pleural effusion. The Hosmer-Lemeshow test was used as a goodness-of-fit test to assess the fit of logistic regression models. Length of hospital stay (LOS) was analyzed by using the Kaplan-Meier method; patients who died were censored from this analysis. Independent prognostic factors for LOS were identified by using a Cox regression model. *p* values < 0.05 were considered statistically significant.

Fig. 1. Patient inclusion flowchart. Of 881 patients with pulmonary embolism on computed tomography, 103 patients with other causes than pleural effusion were excluded.

Results

Clinical Characteristics

On the basis of CT scans, a total of 881 patients were identified as having PE. Pleural effusion was identified in 230 patients (26%), and 103 patients had pleural effusion caused by conditions other than PE: malignancies (32 [14%]), congestive heart failure (20 [9%]), and pneumonia (17 [7%]) (Fig. 1). After excluding the patients with causes of pleural effusion other than PE, the remaining patients were divided into the effusion group ($n = 127$; patients who had pleural effusion due to PE) and the control group ($n = 651$; patients who did not have pleural effusion). The extent of pleural effusion was small in most patients (112 [88%]), moderate in 13 (10%), and large in 2 (2%). Except for body mass index values, demographic data did not significantly differ between the 2 groups (Table 1). Pleuritic chest pain (31 [24%] vs. 29 [5%], $p < 0.001$) and hemoptysis (14 [11%] vs. 16 [3%], $p < 0.001$) were significantly more common in the effusion group than in the control group, whereas unsuspected PE was significantly less common in the effusion group than in the control group (26 [21%] vs. 201 [31%], $p = 0.017$). No significant differences in risk factors for venous thromboembolism existed between the 2 groups. The frequencies of hypotension (7 [6%] vs. 13 [2%], $p = 0.022$) and tachycardia (24 [19%] vs. 67 [10%], $p = 0.004$) were significant-

ly higher in the effusion group than in the control group. According to the sPESI, high-risk patients comprised a significantly greater percentage of the effusion group than of the control group (72 [57%] vs. 305 [47%], $p = 0.008$). The patients of the effusion group significantly more often underwent systemic thrombolysis than those of the control group (14 [11.0%] vs. 36 [5.5%], $p = 0.028$), whereas most patients of both groups received anticoagulation. PE-related in-hospital deaths (4 [3%] vs. 5 [1%], $p < 0.001$) were significantly more common and adverse outcomes (18 [14%] vs. 59 [9%], $p = 0.078$) tended to be more common in the effusion group than in the control group.

Laboratory and Computed Tomographic Findings

Laboratory findings are presented in Table 2. Levels of CRP (6.28 mg/dL [1.56–11.62 mg/dL] vs. 1.26 mg/dL [0.44–4.43 mg/dL], $p < 0.001$) and ESR (26 mm/h [9–50 mm/h] vs. 18 mm/h [8–86 mm/h], $p = 0.026$) were significantly higher in the effusion group than in the control group. Serum NT-proBNP levels tended to be higher in the effusion group, although the difference was statistically insignificant.

Central PE was significantly more common (106 [84%] vs. 475 [73%], $p = 0.013$) and RV dilation tended to be more common (57 [45%] vs. 233 [36%], $p = 0.053$) in the effusion group than in the control group (Table 3). In the

Table 1. Clinical characteristics of patients with pulmonary embolism (*n* = 778)

	Effusion (<i>n</i> = 127)	Controls (<i>n</i> = 651)	<i>p</i> value
Age, years	69 (51–76)	69 (60–75)	0.116
Female gender	72 (56.7)	368 (56.5)	0.973
Ever smoker	39 (31.5)	239 (37.4)	0.294
Body mass index	23.2±4.3	24.0±3.8	0.059
Duration of symptoms, days	6.2±11.0	9.2±25.5	0.245
Unprovoked pulmonary embolism	42 (33.1)	230 (35.3)	0.625
Presenting manifestation			
Dyspnea	56 (44.1)	275 (42.2)	0.699
Pleuritic chest pain	31 (24.4)	29 (4.5)	<0.001
Incidental finding on computed tomography scan	26 (20.5)	202 (31.0)	0.017
Hemoptysis	14 (11.0)	16 (2.5)	<0.001
Leg pain or swelling	8 (6.3)	98 (15.1)	0.009
Syncope	3 (2.4)	8 (1.2)	0.322
General weakness	2 (1.6)	5 (0.8)	0.378
Fever	1 (0.8)	1 (0.2)	0.197
Incidental finding of hypoxia	0 (0)	4 (0.6)	0.376
Hypotension	0 (0)	2 (0.3)	0.532
Predisposing or comorbid condition			
Immobilization	59 (46.5)	275 (42.2)	0.525
Trauma or surgery	35 (27.6)	170 (26.1)	0.735
Cancer	24 (18.9)	148 (22.7)	0.341
Stroke	14 (11.0)	73 (11.2)	0.950
Chronic pulmonary disease*	10 (7.9)	72 (11.0)	0.285
Respiratory tract infection	11 (8.7)	31 (4.8)	0.075
Pulmonary tuberculosis	2 (1.6)	14 (2.2)	0.757
Congestive heart failure	0 (0)	15 (2.3)	0.149
Hypotension, systolic blood pressure <90 mm Hg	7 (5.5)	13 (2.0)	0.022
Tachycardia, heart rate >110/min	24 (18.9)	67 (10.3)	0.004
Simplified pulmonary embolism severity index, high risk	72 (56.7)	305 (46.8)	0.008
Anticoagulation	121 (95.3)	596 (91.6)	0.201
Systemic thrombolysis	14 (11.0)	36 (5.5)	0.028
Length of hospital stay, days	12 (8–19)	11 (7–17)	0.460
In-hospital mortality	16 (12.6)	28 (4.3)	<0.001
Pulmonary embolism-related in-hospital mortality	4 (3.1)	5 (0.8)	<0.001
Adverse outcome	18 (14.2)	59 (9.1)	0.078
Venous thromboembolism recurrence	9 (7.1)	40 (6.1)	0.861

Data are presented as median (interquartile range), mean ± standard deviation, or *n* (%). * Chronic lung disease includes chronic obstructive pulmonary disease, asthma, bronchiectasis, idiopathic pulmonary fibrosis, pneumoconiosis, and tuberculosis-destroyed lung.

effusion group, most patients with central PE (98/106 [92.5%]) had peripheral as well as central pulmonary emboli. The percentage of patients with pulmonary infarction was significantly higher in the effusion group than in the control group (51 [40%] vs. 51 [8%], *p* < 0.001).

Predictors of Pleural Effusion in Patients with PE

Candidate variables with *p* values <0.10, including sPESI results, CRP levels, ESR levels, central PE, and pul-

monary infarction, were chosen for multivariate analysis for predictors of pleural effusion caused by PE (Hosmer-Lemeshow test, *p* = 0.387). The results of multivariate analysis indicated that pulmonary infarction (odds ratio [OR] 6.20, 95% confidence interval [CI] 3.49–10.91, *p* < 0.001) and CRP levels (OR 1.05, 95% CI 1.101–1.09, *p* = 0.023) were independent predictors of pleural effusion due to PE (Table 4).

Table 2. Laboratory findings

	<i>n</i>	Effusion (<i>n</i> = 127)	<i>n</i>	Controls (<i>n</i> = 651)	<i>p</i> value
NT-proBNP, pg/mL	86	511 (104–2,874)	430	376 (107–1,611)	0.094
Troponin I, ng/mL	91	0.23±0.64	502	0.17±0.54	0.399
CRP, mg/dL	96	6.28 (1.56–11.62)	462	1.26 (0.44–4.43)	<0.001
ESR, mm/h	85	26 (9–50)	423	18 (8–36)	0.026
Procalcitonin, ng/mL	26	0.43±1.30	101	0.44±1.48	0.977
PaO ₂ /FiO ₂ , mm Hg	87	342±93	416	343±98	0.943
PaCO ₂ , mm Hg	88	30.0 (24.9–34.2)	408	29.5 (26.5–34.0)	0.871

Data are presented as median (interquartile range) or mean ± standard deviation. NT-proBNP, N-terminal-pro-B-type natriuretic peptide; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; PaO₂, pressure of oxygen in arterial blood; PaCO₂, partial pressure of carbon dioxide in arterial blood; FiO₂, inspired oxygen fraction.

Table 3. Radiologic findings

	Effusion (<i>n</i> = 127)	Controls (<i>n</i> = 651)	<i>p</i> value
Location of the largest pulmonary emboli			
Main or more proximal	57 (44.9)	224 (34.4)	0.025
Interlobar or lobar	49 (38.6)	251 (38.6)	0.996
Segmental	16 (12.6)	137 (21.0)	0.028
Subsegmental	4 (3.1)	39 (6.0)	0.200
Central pulmonary embolism*	106 (83.5)	475 (73.0)	0.013
Deep vein thrombosis	81/115 (70.4)	380/549 (69.2)	0.187
Proximal deep vein thrombosis	51 (47.5)	240 (47.1)	0.483
Right ventricle dilation on computed tomography	57 (44.9)	233 (35.8)	0.053
Pulmonary infarction	51 (40.2)	51 (7.8)	<0.001

Data are presented as *n* (%). * Central pulmonary arteries mean lobar pulmonary artery or more proximal location.

Pleural Fluid Analysis

The results of the pleural fluid analysis are presented as online supplementary material (online suppl. Table S1; see www.karger.com/doi/10.1159/000457132 for all on-line suppl. material). Diagnostic thoracentesis was performed in only 13 PE patients (10%), and of these patients, 12 (92%) had exudative pleural effusion. Serosanguinous fluid was noted in 9 patients (69%), and 4 patients (31%) had pleural fluid hematocrits of >1%. Only 2 patients underwent percutaneous catheter drainage.

Predictors of Mortality, Adverse Outcomes, and LOS

The presence of pleural effusion in PE patients was not a predictor of PE-related in-hospital mortality in multi-

Table 4. Multivariate analysis for predictors of pleural effusion due to pulmonary embolism

	OR	95% CI	<i>p</i> value
Pulmonary infarction	6.20	3.49–10.91	<0.001
CRP	1.05	1.01–1.09	0.023
Central PE	1.65	0.82–3.33	0.159
sPESI	1.22	0.74–2.04	0.438
ESR	1.00	0.97–1.01	0.735

Hosmer-Lemeshow test, *p* = 0.387. OR, odds ratio; CI, confidence interval; CRP, C-reactive protein; PE, pulmonary embolism; sPESI, Simplified Pulmonary Embolism Severity Index; ESR, erythrocyte sedimentation rate.

Table 5. Predictors of pulmonary embolism-related in-hospital mortality

	Univariate analysis			Multivariate analysis*		
	OR	95% CI	<i>p</i> value	OR	95% CI	<i>p</i> value
Age	1.00	0.96–1.05	0.876			
Female gender	0.61	0.16–2.29	0.465	0.75	0.16–3.49	0.716
Hypotension	4.90	0.58–41.11	0.144			
Tachycardia	1.43	0.29–6.97	0.657			
sPESI, high risk	2.15	0.53–8.62	0.282	0.85	0.18–4.02	0.837
NT-proBNP	1.00	1.00–1.00	0.158	1.00	1.00–1.00	0.521
Troponin I	1.02	0.29–3.64	0.977			
PaO ₂ /FiO ₂	1.00	0.99–1.00	0.129			
RV dilation on CT	6.01	1.24–29.13	0.011	7.15	0.82–62.67	0.076
Central PE	1.19	0.24–5.74	0.835			
Pleural effusion	4.20	1.11–15.87	0.034	3.35	0.70–15.95	0.129

OR, odds ratio; CI, confidence interval; sPESI, Simplified Pulmonary Embolism Severity Index; NT-proBNP, N-terminal-pro-B-type natriuretic peptide; PaO₂, pressure of oxygen in arterial blood; FiO₂, inspired oxygen fraction; RV, right ventricle; CT, computed tomography; PE, pulmonary embolism. * Hosmer-Lemeshow test, *p* = 0.871.

Table 6. Multivariate analysis for predictors of adverse outcome due to pulmonary embolism

	Univariate analysis			Multivariate analysis*		
	OR	95% CI	<i>p</i> value	OR	95% CI	<i>p</i> value
Age	1.02	1.00–1.04	0.079			
Female gender	2.05	1.22–3.44	0.006	1.77	0.91–3.43	0.092
Hypotension	19.96	7.69–51.82	<0.001			
Tachycardia	2.04	1.19–3.50	0.009			
sPESI, high risk	2.94	1.76–4.93	<0.001	2.01	1.08–3.77	0.029
NT-proBNP	1.00	1.00–1.00	<0.001	1.00	1.00–1.00	0.005
Troponin I	1.33	0.96–1.84	0.084	1.16	0.81–1.66	0.424
PaO ₂ /FiO ₂	0.99	0.99–0.99	<0.001			
RV dilation on CT	3.34	2.05–5.45	<0.001	2.44	1.27–4.71	0.008
Central PE	3.70	1.67–8.19	<0.001	1.38	0.51–3.78	0.527
Pleural effusion	1.66	0.94–2.92	0.078	1.44	0.71–2.95	0.314

OR, odds ratio; CI, confidence interval; sPESI, Simplified Pulmonary Embolism Severity Index; NT-proBNP, N-terminal-pro-B-type natriuretic peptide; PaO₂, pressure of oxygen in arterial blood; FiO₂, inspired oxygen fraction; RV, right ventricle; CT, computed tomography; PE, pulmonary embolism. * Hosmer-Lemeshow test, *p* = 0.308.

ivariate analysis, despite statistical significance in univariate analysis (Table 1, 5). In addition, pleural effusion was not a predictor of adverse outcomes of PE (Table 6) or LOS (online suppl. Table S2).

Discussion

The main findings from the present study were summarized as follows. Compared to the control group, the effusion group had higher rates of hypotension, tachycardia, high-risk sPESI, central PE, and RV dilation. The

presence of pleural effusion due to PE was not a predictor of PE-related in-hospital mortality, adverse outcomes, and LOS in PE patients. In a multivariate analysis, only 2 independent risk factors for pleural effusion due to PE were found: pulmonary infarction and serum CRP levels.

Of the clinical characteristics, hypotension, tachycardia, and high-risk sPESI occurred more commonly among PE patients with pleural effusion. In univariate analysis, PE-related in-hospital mortality was significantly more frequent and adverse outcomes tended to be more frequent in the effusion group, although the differences did not reach statistical insignificance in multivariate analysis. These findings suggest that pleural effusion caused by PE is associated with more severe PE. In addition, NT-proBNP levels also tended to be higher in the effusion group. Moreover, central PE and RV dilation were found more often in the effusion group. Nonetheless, a previous study reported that the location of the clots and the number of arteries involved were not predictors of pleural effusion [12]. However, that study was conducted on PE patients with all-cause pleural effusion, not on patients with pleural effusion caused by PE. Despite its association with more severe PE, the development of pleural effusion was not an independent predictor of short-term outcome of PE, such as PE-related in-hospital mortality or adverse outcomes, in the present study.

As in a previous report [7], in the present study, pulmonary infarction was more commonly found in PE patients with pleural effusion than in PE patients without pleural effusion. Hemoptysis and pleuritic chest pain suggestive of pulmonary infarction were more frequent in the effusion group. In a previous study, the pulmonary infarction group had a higher prevalence of pleural effusion than did the isolated dyspnea group and the circulatory collapse group [21]. In another study [4], however, wedge-shaped opacities that suggest pulmonary infarction occurred in equal proportions of patients with pleural effusion and those without the condition. However, that study included all PE patients with pleural effusion regardless of the cause of effusions. Hemorrhagic necrosis of an infarct induces or worsens pleural effusion by aggravating inflammatory reactions and causing hemorrhage in the pleural space [11], a finding that is supported by the higher CRP and ESR levels seen in the effusion group in our study. Therefore, pulmonary infarction contributes to the formation of pleural effusion in PE patients, although it is not necessary for the development of pleural effusion. However, as some PE patients had infectious or inflammatory diseases, the possibility that these comorbid conditions might influence those findings could not be excluded.

The extent of pleural effusion caused by PE was small in most cases, as was seen in previous studies [9, 22, 23]. Two patients with large-extent pleural effusion underwent pleural drainage. Of the 13 patients who underwent diagnostic thoracentesis, 12 (92%) had exudative pleural effusion. This finding matched the classical concept that pleural effusion in PE is exudate [4, 9, 10]. The underlying mechanisms of pleural effusion in PE can be explained as follows. First, cytokines such as vascular endothelial growth factor or inflammatory mediators released from platelet-rich emboli increase the permeability of the pulmonary capillaries. The increased interstitial fluid of the lung passes through the visceral pleura and leads to an increase in pleural fluid [23]. Second, ischemia of pulmonary capillaries distal to emboli may also increase permeability, although this occurrence may play a minor role [9]. These mechanisms may also explain why pulmonary infarction and CRP levels were independent predictors of pleural effusion due to PE. Of the 13 patients who underwent thoracentesis, 1 had transudative pleural effusion. The formation of transudates can be explained by an increase in the systemic venous pressure at the parietal pleural surface secondary to pulmonary hypertension and increase in the right ventricular pressure [9, 22]. Nevertheless, transudate in patients with PE is more likely to be due to other causes, such as congestive heart failure rather than pulmonary hypertension due to PE [9].

Given that pulmonary infarction was more frequently observed in the effusion, small peripheral pulmonary emboli are more likely to cause pleural effusion than central PE [20]. However, in the present study, central PE was more common in the effusion group than in the control group. This discrepancy can be explained by the finding that most patients with central PE had peripheral as well as central emboli, supporting that patients with pleural effusion exhibited higher clot burden and more severe PE.

This study has several limitations. First, as this is a retrospective study, selection bias was inevitable. Although 2 chest physicians examined and determined the causes of pleural effusion by consensus, the chance of misclassification due to retrospective design should be considered. Second, as PE patients who had been diagnosed only by CT were included in the present study, the exclusion of patients diagnosed by perfusion/ventilation scan or ultrasound for deep vein thrombosis and clinical prediction score might affect the results. Third, there have been no widely accepted diagnostic criteria for pulmonary infarction, although those used in a previous study [20] were adopted in this study. Fourth, missing laboratory data,

such as NT-proBNP levels, could have influenced our results. Lastly, the possibility that PE-specific therapy may have affected the clinical outcome could not be excluded.

In conclusion, patients with more severe PE are likely to have pleural effusion caused by PE. However, pleural effusion was not proven to predict short-term outcomes

or LOS in PE patients. Further studies with a larger patient population are required to explain why effusions may be a marker of severity but not outcome of PE. Additionally, pulmonary infarction and CRP levels were independent risk factors for the development of pleural effusion due to PE.

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