Original Article

Clinical relevance of chronic respiratory disease in Korean patients with pulmonary thromboembolism

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Background: Data regarding clinical and radiological features of patients with pulmonary thromboembolism (PTE) and concomitant chronic respiratory disease (CRD) are limited. Accordingly, the aim of the present study was to investigate clinico-radiological features of this patient population.

Methods: Patients with PTE were retrospectively classified into one of two groups: those with and without CRD. Clinical characteristics, blood biomarkers, and computed tomographic (CT) findings were compared between the groups.

Results: Of 1,207 PTE patients included, CRD was detected in 128 (11%). The most common CRD was chronic obstructive pulmonary disease [41 (32%)], followed by bronchial anthracofibrosis [32 (25%)]. In multivariate analysis, unprovoked PTE [odds ratio (OR) 1.99, 95% confidence interval (CI): 1.29–3.05, P=0.002], dyspnea (OR 1.54, 95% CI: 1.11–2.34, P=0.041), lower respiratory tract infection (LRTI) (OR 3.90, 95% CI: 2.13–7.14, P<0.001), Pulmonary Embolism Severity Index (PESI) class IV–V (OR 5.24, 95% CI: 3.43–8.00, P<0.001), in-situ pulmonary artery thrombosis (OR 10.62, 95% CI: 3.71–30.45, P<0.001), and pulmonary artery enlargement (OR 1.65, 95% CI: 3.71–30.45, P<0.001) were found to be independent clinical factors related to CRD in patients with PTE. CRD was an independent predictor of PTE-related in-hospital mortality (OR 3.96, 95% CI: 1.32–11.88, P=0.014).

Conclusions: Patients with PTE and concomitant CRD were characterized by higher incidences of dyspnea, LRTI, PESI class IV–V, and *in-situ* pulmonary artery thrombosis, compared with non-CRD patients. In these patients, CRD was a predictor of PTE-related in-hospital mortality.

Keywords: Comorbidity; computed tomography; lung diseases; prognosis; pulmonary embolism

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Introduction

Venous thromboembolism (VTE), which encompasses deep vein thrombosis (DVT) and pulmonary thromboembolism (PTE), can be categorized into provoked or unprovoked according to the presence or absence of a disease or condition that predispose to VTE (1,2). Provoking risk factors vary, ranging from major transient risk factors, including recent major surgery, to persistent risk factors, such as active cancer (3). In addition, some PTE patients have various comorbid conditions, which may or may not contribute to the development of VTE (2). However, it is difficult to determine whether the mere presence of

comorbidities is sufficient to develop VTE or only coexisting conditions. Evidence suggests that chronic inflammatory conditions, such as inflammatory bowel disease (4,5), autoimmune disease (6), and chronic infections (7), can serve as persistent provoking factors (3).

There is accumulating evidence regarding the clinical relevance of chronic respiratory diseases (CRDs), including chronic obstructive pulmonary disease (COPD), asthma, and idiopathic pulmonary fibrosis (IPF), in patients with PTE. IPF patients have a two-fold higher risk for VTE than the general population (8) and can experience clinical deterioration due to PTE (9). PTE can also cause acute exacerbation of COPD (10). Moreover, the risk for developing PTE is significantly increased in patients with asthma compared with the general population (11). Along with cancer and heart failure, CRD constitutes components determining the Pulmonary Embolism Severity Index (PESI) (12) or Simplified PESI score (13), the most widely adopted clinical prediction rule of PTE to predict the short-term prognosis of PTE. Therefore, coexisting CRD in PTE is presumed to play a role in predicting short-term prognosis. However, data regarding clinical and radiological features of PTE patients with CRD are lacking. We hypothesized that patients with PTE and concomitant CRD exhibit distinctive clinico-radiologic features. Thus, we investigated the clinical characteristics and laboratory and computed tomographic (CT) findings in patients with PTE and coexisting CRD.

Methods

Study design

The present retrospective study was performed at the Kyungpook National University Hospital (KNUH), a tertiary referral center located in Daegu, South Korea. Data from consecutive hospitalized patients with PTE diagnosed via CT angiography between March 2003 and December 2017 were collected. Patients with suspected chronic thromboembolic pulmonary hypertension were not included. CRD included COPD, asthma, bronchiectasis, interstitial lung disease, bronchial anthracofibrosis, and tuberculosis-destroyed lung. The presence or absence of coexisting CRDs was determined by consensus of two chest physicians (H Park and SI Cha) based on medical records. The diagnosis of COPD and asthma was adopted from a review of patient medical records. Bronchial anthracofibrosis was diagnosed based on CT findings that fulfilled the following criteria: bronchostenosis that caused smooth narrowing of multiple lobar or segmental bronchi; calcified or non-calcified lymph node enlargement adjacent to narrowed bronchi; and these two criteria which could not be attributed to other causes (14). The diagnosis of tuberculosis-destroyed lung was based on CT finding of lung parenchymal destruction with lung volume loss and/or bronchiectatic changes in more than one lobe in patients with previous pulmonary tuberculosis and with no evidence of active tuberculosis, such as culture for respiratory specimens (15). All PTE patients were divided into those with CRD (CRD group) and without CRD (control group); clinical characteristics, blood biomarkers, and CT findings were compared between the two groups. This study was approved by the Institutional Review Board of the KNUH. Given the retrospective nature of the present study and the use of anonymized patient data, requirements for informed written consent were waived.

Data collection

Demographic information and data regarding presenting manifestations, vital signs, risk factors for VTE, and comorbid conditions, were reviewed. Unprovoked PTE was defined as the absence of provoking risk factors, including trauma, surgery, 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 (10). The PESI score was calculated retrospectively (13). Outcome variables, including PTE-related in-hospital mortality, adverse outcomes, and VTE recurrence, were examined. PTE-related in-hospital death was defined as an in-hospital death that met one of the following criteria: objective evidence of death directly caused by PTE; and death that could not be attributed to other causes and in which PTE could not be excluded (16). An adverse outcome was defined as a PTE-related in-hospital death or PTE 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 (16). According to the 2014 European Society of Cardiology (ESC) guidelines (2), the severity of PTE in each patient was classified into four tiers: high, intermediate-high, intermediate-low, and low risk. Blood laboratory data included biomarkers, such as N-terminal-pro-B-type natriuretic peptide (NT-proBNP) and troponin I, and inflammatory markers, including

erythrocyte sedimentation rate, C-reactive protein, and procalcitonin.

Radiological evaluation

PTE was diagnosed on CT images as a sharply delineated filling defect in a pulmonary artery in at least two consecutive image sections and that was located either centrally within the vessel or formed acute angles with the arterial wall (17). The largest pulmonary artery involved by pulmonary thromboemboli was classified as follows: pulmonary trunk or right atrium, pulmonary (right or left pulmonary artery), interlobar or lobar, segmental, and subsegmental. Central PTE denoted thromboemboli located in the right or left pulmonary artery or more proximal sites. Similar to a previous study (16), 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; RV/LV diameter ratios were calculated; and RV dilation was defined as an RV/LV diameter ratio ≥1. The diameters of the pulmonary trunk and ascending aorta were measured at the level of pulmonary trunk bifurcation to obtain the pulmonary trunk-to-ascending aorta ratio (PA/AA ratio) (18,19); pulmonary artery enlargement was defined as having PA/AA ratio >1. Pulmonary infarction was defined as the presence of a peripheral consolidation in the region of segmental or subsegmental pulmonary emboli (20). Similar to a previous study (21), when a soft tissue density was visualized in distinctly narrowed, totally obstructed, or dilated pulmonary arteries or their branches from axial images, in-situ pulmonary artery thrombosis was diagnosed, from which patients with coexisting DVT on CT venography or ultrasonography were excluded.

Statistical analysis

Data are expressed as mean with standard deviation for continuous variables and as numbers with percentages for categorical variables. Continuous variables between groups were compared using Student's *t*-test, and categorical variables were compared using chi-squared test or Fisher's exact test. Multiple logistic regression analysis was used to identify clinical factors associated with CRD in PTE patients and predictors of PTE-related in-hospital mortality. The Hosmer-Lemeshow test was used as a goodness-of-fit test to assess the fit of logistic regression models. P value <0.05 were considered to be statistically significant. Statistical analysis was performed using SPSS version 23.0 (IBM Corporation, Armonk, NY, USA) for Windows (Microsoft Corporation, Redmond, WA, USA).

Results

Clinical characteristics of PTE patients with CRD

A total of 1,216 hospitalized PTE patients were identified during the study period; however, nine without available enhanced CT scans were excluded. Ultimately, 1,207 PTE patients were included in this study and then divided into PTE patients with CRD [n=128 (11%)] and without CRD (n=1,079) (*Figure 1*). The most common CRD was COPD [41 (32%)], followed by bronchial anthracofibrosis [32 (25%)] and tuberculosis-destroyed lung [21 (16%)] (*Figure 2*).

The clinical characteristics of the CRD group are presented in *Table 1*. As expected, patients with CRD were significantly older (72.2±8.9 *vs.* 65.8±14.4 years, P<0.001) and had a significantly higher proportion of ever-smokers [59/128 (46%) *vs.* 360/1,057 (34%), P=0.008] than those without CRD. The CRD group more frequently presented with dyspnea [78 (61%) *vs.* 447 (41%), P<0.001]; however, pulmonary thromboemboli were less frequently incidentally detected on CT in the CRD group than in the control group [24 (19%) *vs.* 335 (31%), P=0.004]. The CRD group had a significantly higher percentage of unprovoked PTE [62 (48%) *vs.* 366 (34%), P=0.001] but significantly lower rates of immobilization [43 (34%) *vs.* 506 (47%), P=0.004] and trauma or surgery [14 (11%) *vs.* 251 (23%), P=0.001] than the control group. LRTI [22 (17%) *vs.* 53 (5%), P<0.001] and mycobacterial lung disease [11 (9%) *vs.* 42 (4%), P=0.021] more frequently occurred in the CRD group than in the control group. The CRD group had a significantly higher incidence of PESI class IV–V [65 (51%) *vs.* 191 (18%), P<0.001] than the control group. In contrast, the proportion of patients with high or intermediate-high risk according to the 2014 ESC guidelines and the frequency of adverse outcomes did not differ between the two groups. However, the CRD group experienced significantly higher PTE-related in-hospital mortality than the control group [5 (4%) *vs.* 12 (1%), P=0.027]. The rate of VTE recurrence was not significantly different between the two groups.

Laboratory and CT findings in PTE patients with CRD

The blood levels of NT-proBNP, troponin I, and

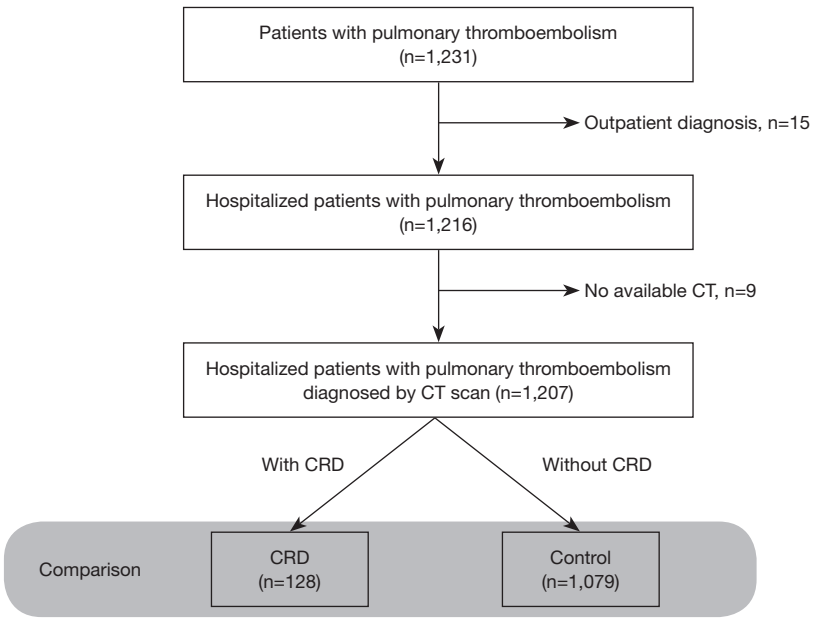

Figure 1 Flow chart of the study protocol. CT, computed tomography; CRD, chronic respiratory disease.

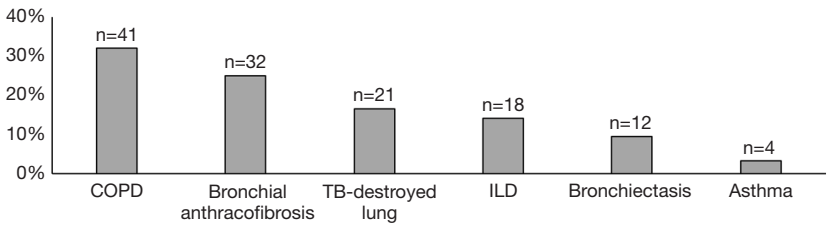

Figure 2 The distribution of coexisting chronic respiratory disease in patients with pulmonary thromboembolism. The most common chronic respiratory disease was chronic obstructive pulmonary disease (COPD), followed by bronchial anthracofibrosis and tuberculosis (TB)-destroyed lung. ILD, interstitial lung disease.

inflammatory markers were not significantly different between the CRD and control groups (*Table 2*). CT findings are summarized in *Table 3*. The distribution of the location of the largest pulmonary emboli was not different. The incidence of RV dilation on CT was similar between the two groups; however, pulmonary artery enlargement was significantly more common in the CRD group than in the control group [34 (27%) *vs.* 202 (19%), P=0.044]. *In-situ* pulmonary artery thrombosis, not pulmonary embolism, was also significantly more commonly found in the CRD group than in the control group [12 (9%) *vs.* 9 (1%), P<0.001]. The most common underlying condition of in-situ pulmonary artery thrombosis was tuberculosis-destroyed lung (n=10), followed by lung resection (n=4) and adhesive obliteration (n=4). The frequency of pulmonary infarction was not significantly different between the two groups.

Clinical parameters related to CRD in patients with PTE

Variables with P value <0.05 in univariate analysis, including unprovoked PTE, ever-smoker, dyspnea, incidental CT finding, immobilization, trauma or surgery, LRTI, mycobacterial lung disease, pulmonary artery enlargement, in-situ pulmonary artery thrombosis, and PESI class IV–V, were selected as candidate variables for multivariate analysis to investigate the clinical and radiological parameters associated with CRD in PTE patients. Multivariate analysis (Hosmer-Lemeshow test, P=0.820) demonstrated that unprovoked PTE [odds ratio (OR) 1.99, 95% confidence

Table 1 Clinical characteristics of patients with pulmonary thromboembolism (n=1,207)

Clinical parameter	CRD (n=128)	Control (n=1,079)	P value
Age, years	72.2±8.9	65.8±14.4	<0.001
Female sex	65 (50.8)	630 (58.4)	0.108
Ever smoker	59/128 (46.1)	360/1,057 (34.1)	0.008
BMI, kg/m^2	21.1±6.5	22.6±6.5	0.012
Obesity, BMI ≥30 kg/m^2	3 (2.3)	42 (3.9)	0.469
Duration of symptoms, day	6.7±9.1	8.0±21.6	0.538
Presenting manifestation			
Dyspnea	78 (60.9)	447 (41.4)	< 0.001
Incidental CT finding	24 (18.8)	335 (31.0)	0.004
Leg pain or swelling	10 (7.8)	128 (11.9)	0.189
Pleuritic chest pain	7 (5.5)	36 (3.3)	0.209
Hemoptysis	3 (2.3)	10 (0.9)	0.151
Syncope	1 (0.8)	15 (1.4)	>0.999
General weakness	1 (0.8)	13 (1.2)	>0.999
Hypoxemia	1 (0.8)	12 (1.1)	>0.999
Hypotension	1 (0.8)	4 (0.4)	0.430
Fever	0 (0)	4 (0.4)	>0.999
Unprovoked PTE	62 (48.4)	366 (33.9)	0.001
Predisposing or comorbid condition			
Immobilization	43 (33.6)	506 (46.9)	0.004
Cancer	27 (21.1)	206 (19.1)	0.587
Trauma or surgery	14 (10.9)	251 (23.3)	0.001
Lower respiratory tract infection	22 (17.2)	53 (4.9)	<0.001
Diabetes	19 (14.8)	159 (14.7)	>0.999
Cerebrovascular accident	12 (9.4)	125 (11.6)	0.470
Mycobacterial lung disease*	11 (8.6)	42 (3.9)	0.021
Ischemic heart disease	11 (8.6)	55 (5.1)	0.102
Atrial fibrillation	7 (5.5)	54 (5.0)	0.830
Neurodegenerative disorder	6 (4.7)	53 (4.9)	>0.999
Congestive heart failure	4 (3.1)	38 (3.5)	>0.999
Connective tissue disease	3 (2.3)	14 (1.3)	0.413
Chronic kidney disease	3 (2.3)	20 (1.9)	0.728
Psychiatric disease	2 (1.6)	43 (4.0)	0.220
Antiphospholipid syndrome	2 (1.6)	13 (1.2)	0.668
Chronic liver disease	2 (1.6)	17 (1.6)	>0.999

Table 1 *(continued)*

Table 1 *(continued)*

Clinical parameter	CRD (n=128)	Control (n=1,079)	P value
Hypotension, systolic BP <90 mmHg	6 (4.7)	39 (3.5)	0.454
Tachycardia, heart rate >110/min	20/101 (19.8)	140/799 (17.5)	0.581
PESI score	107.2±24.2	83.8±26.0	<0.001
PESI IV-V	65 (50.8)	191 (17.7)	<0.001
Anticoagulation	120/126 (95.2)	1,006/1,065 (94.5)	0.838
Systemic thrombolysis	3 (2.3)	56 (5.2)	0.195
Early mortality risk[†]			
High risk	6 (4.7)	36 (3.3)	0.440
Intermediate-high risk	13 (10.2)	76 (7.0)	0.210
High or intermediate-high risk	19 (14.8)	112 (10.4)	0.133
Adverse outcome	9 (7.0)	115 (10.7)	0.222
All cause in-hospital mortality	9 (7.0)	61 (5.7)	0.547
PTE-related in-hospital mortality	5 (3.9)	12 (1.1)	0.027
VTE recurrence	9 (7.0)	64 (5.9)	0.694

Data are presented as mean ± standard deviation or n (%). BMI, body mass index; PTE, pulmonary thromboembolism; CT, computed tomography; BP, blood pressure: PESI, pulmonary embolism severity index; VTE, venous thromboembolism. [*], Mycobacterial lung disease includes pulmonary tuberculosis and nontuberculous mycobacterial lung disease. [†], Patients are classified according to the 2014 European Society of Cardiology guidelines.

Table 2 Laboratory findings

Blood biomarker	CRD		Control		P value
	n	Mean ± standard deviation	n	Mean ± standard deviation	
NT-proBNP, pg/mL	99	2,087±3,505	715	2,100±6,679	0.985
Troponin I, ng/mL	107	0.10±0.20	841	0.27±1.93	0.364
CRP, mg/dL	111	4.72±6.67	799	5.03±12.52	0.799
ESR, mm/hr	105	26±23	720	26±23	0.875
Procalcitonin, ng/mL	43	0.48±1.15	231	0.39±1.39	0.700

CRD, chronic respiratory disease; NT-proBNP, N-terminal-pro-B-type natriuretic peptide; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate.

interval (CI): 1.29–3.05, P=0.002], dyspnea (OR 1.54, 95% CI: 1.11–2.34, P=0.041), LRTI (OR 3.90, 95% CI: 2.13–7.14, P<0.001), PESI class IV–V (OR 5.24, 95% CI: 3.43–8.00, P<0.001), *in-situ* pulmonary artery thrombosis (OR 10.62, 95% CI: 3.71–30.45, P<0.001), and pulmonary artery enlargement (OR 1.65, 95% CI: 3.71–30.45, P<0.001) were independent clinical factors associated with CRD in PTE patients (*Table 4*).

Predictors of PTE-related in-hospital death

As noted above, the CRD group experienced a higher PTE-related in-hospital mortality than the control group. Age, sex, and parameters with P value <0.05 in univariate analysis, including CRD, cerebrovascular accident, central PTE, and RV dilation on CT, were chosen as candidate variables to examine predictors of PTE-related in-hospital death (*Table 5*). The multivariate analysis (Hosmer-Lemeshow test, P=0.701)

Table 3 Radiologic finding (n=1,207)

Radiologic finding	CRD (n=128)	Control (n=1,079)	P value
Location of the largest pulmonary emboli			
Main or more proximal (central PTE)	40 (31.3)	384 (35.6)	0.378
Interlobar or lobar	49 (38.3)	426 (39.5)	0.849
Segmental	27 (21.1)	222 (20.6)	0.908
Subsegmental	12 (9.4)	47 (4.4)	0.018
RV dilation on CT	57 (44.5)	460 (42.6)	0.706
Pulmonary artery enlargement*	34 (26.6)	202 (18.7)	0.044
Pulmonary infarction	12 (9.4)	132 (12.2)	0.346
Pleural effusion	26 (20.3)	280 (25.9)	0.197
Deep vein thrombosis	69/100 (69.0)	598/888 (67.3)	0.737
In-situ pulmonary artery thrombosis	11 (8.6)	7 (0.6)	<0.001

Data are presented as n (%). PTE, pulmonary thromboembolism; RV, right ventricle; CT, computed tomography. *, Pulmonary arterial enlargement is defined by a pulmonary trunk to ascending aorta diameter ratio >1 on CT scan.

Table 4 Multivariate analysis for clinical parameter related to chronic respiratory disease in patients with pulmonary embolism

Variable	Odds ratio	95% confidence interval	P value
Unprovoked PTE	1.985	1.293–3.045	0.002
Dyspnea	1.544	1.109–2.341	0.041
Lower respiratory tract infection	3.903	2.133–7.142	<0.001
PESI IV-V	5.240	3.434–7.996	<0.001
In-situ pulmonary artery thrombosis	10.623	3.706–30.451	<0.001
Pulmonary artery enlargement*	1.651	1.038–2.627	0.034

Hosmer-Lemeshow test, P=0.820. PTE, pulmonary thromboembolism; PESI, pulmonary embolism severity index. *, Pulmonary arterial enlargement is defined by a pulmonary trunk to ascending aorta diameter ratio >1 on computed tomography scan.

Table 5 Multivariate analysis for predictors of pulmonary thromboembolism-related in-hospital mortality

Variable	Odds ratio	95% confidence interval	P value
Chronic respiratory disease	3.963	1.322–11.876	0.014
Cerebrovascular accident	4.986	1.752–14.195	0.003
Hypotension	5.486	1.623–18.543	0.006
RV dilation on CT	3.684	1.152–11.785	0.028

Hosmer-Lemeshow test P=0.701. RV, right ventricle; CT, computed tomography.

confirmed that CRD (OR 3.96, 95% CI: 1.32–11.88, P=0.014) was an independent predictor of PTE-related in-hospital mortality along with cerebrovascular accident, hypotension, and RV dilation on CT.

Discussion

In the present study, 11% of the patients with PTE had concomitant CRD. Compared with non-CRD patients, PTE patients with CRD were more likely to be older

with a higher proportion of ever-smokers, present with dyspnea, and be associated with LRTI. PTE patients with CRD demonstrated a higher PESI score and a higher incidence of PESI class IV–V than those without CRD. In addition, the PTE patients with CRD had a higher PTE-related in-hospital mortality rate than those without CRD; this association was confirmed through multivariate analysis. Multivariate analysis revealed that unprovoked PTE, dyspnea, LRTI, PESI class IV–V, in-situ pulmonary artery thrombosis, and pulmonary artery enlargement were associated with PTE in CRD patients.

Mechanisms how CRD predisposes to the development of VTE have been proposed. First, several studies reported that CRD, such as COPD (22,23) or IPF itself (24), is associated with a procoagulant state. Second, immobility caused by CRD can contribute to VTE pathogenesis and increase mortality rates during hospitalization and 30 days after VTE diagnosis (25). Third, various comorbid conditions of CRD, such as heart failure, ischemic heart disease, and chronic kidney disease, increases the risk for VTE (25). Finally, as reported above, PTE patients with CRD were more often associated with LRTI than non-CRD patients. LRTIs, such as pneumonia, have been reported to be correlated with the development of VTE (26), thus further increasing the risk for PTE. Compared to the non-CRD patients, the CRD patients were less frequently associated with immobilization and trauma or surgery in the present study. This finding contradicts the concept that immobility caused by CRD contributes to VTE. We speculate that this discrepancy may be due to the difference in the definitions between immobilization and immobility: in this study, immobilization, a more severe form, was defined as bed rest for most of the day for ≥3 consecutive days.

Short-term prognostic factors of PTE include clinical prediction rules, such as the PESI score, the levels of blood biomarkers, such as troponin I and NT-proBNP, and echocardiographic RV dysfunction or RV dilation on CT (2). The presence of CRD can directly increase the PESI score (12) by adding 10 points and indirectly by adding points, for example, due to age, with a mean difference of 6 in the present study. Thus, the CRD group had a significantly higher PESI score and a higher incidence of PESI class IV–V than the control group. On the other hand, the blood levels of biomarkers and the incidence of RV dilation on CT were not significantly different between the CRD and control groups. Consequently, the proportion of patients with high or intermediate-high risk according to 2014 ESC guidelines did not differ between the two groups in the present study.

The CT characteristics of PTE in patients with CRD are explored below. First, the frequency of in-situ pulmonary artery thrombosis was significantly higher in the CRD group. In the present study, the most common underlying condition of in-situ pulmonary artery thrombosis was tuberculosis-destroyed lung, which led to a higher incidence of in-situ pulmonary artery thrombosis in the CRD group than in the control group. This can be explained by the fact that South Korea has an intermediate prevalence of active tuberculosis, and chest physicians commonly encounter patients with tuberculosis-destroyed lung (21). Second, pulmonary infarction was less frequently observed in the CRD group than in the control group, despite the lack of statistical significance. The classical concept of pulmonary infarction is that pulmonary infarction occurs more commonly in patients with underlying conditions such as heart disease, chronic lung disease, and malignancy, compared with patients without these comorbidities (20). A previous study reported that the incidence of chronic lung disease did not differ between patients with and without pulmonary infarction (20). A more recent study demonstrated that younger PTE patients without cardiopulmonary comorbidities were at highest risk for pulmonary infarction (27). They proposed that older PTE patients have more developed bronchopulmonary collateral vessels due to chronic cardiopulmonary disease, which provides protection against pulmonary infarction after PTE. Finally, in the present study, the frequency of pulmonary artery enlargement was significantly higher in the CRD group than in the control group. This can be explained by reported findings of pulmonary artery enlargement in chronic lung diseases (28), including COPD (29), bronchial anthracofibrosis (14), tuberculosis-destroyed lung (30), and IPF (31,32).

Among the variables associated with treatment outcome, the CRD group demonstrated a significantly higher PTE-related in-hospital mortality rate than the control group. This finding was confirmed by multivariate analysis. A population-based study demonstrated that COPD patients were more likely to experience a complicated course and die in hospital and within 30 days of VTE diagnosis (25). Data from a registry suggested that COPD patients also have a worse three-month mortality rate than non-COPD patients (33). Based on these data, underlying CRD may unfavorably affect the short-term prognosis of PTE. PTE-related in-hospital mortality and adverse outcomes are endpoints that both signify the short-term prognosis of PTE. However, whereas PTE patients with CRD demonstrated a

higher PTE-related in-hospital mortality than those without CRD, the incidence of adverse outcomes did not differ between the two groups. This discrepancy can be explained, in part, by the fact that the severity of concomitant CRDs varied from a mild to severe form, which subsequently affected cardiopulmonary reserve to a very negligible extent in some PTE individuals or to a greater degree in others.

Several limitations of this investigation should be addressed. First, selection bias was inevitable, given that this was a retrospective study performed in a single center. Furthermore, because the study population was restricted to hospitalized PTE patients, CRD might less often complicate all-comers with PTE. Second, because the presence of concomitant CRD was identified through review of medical records, the possibility that the incidence of CRD was underestimated could not be excluded. Third, patients with various CRDs, such as COPD, were treated as a single group; however, diverse characteristics of each CRD may offset one another. Fourth, the all-cause in-hospital mortality reported in the present study was lower than that reported in previous studies. Thus, the possibility that PTE patients who died were excluded from this study should be considered. Finally, missing laboratory data, such as NT-proBNP levels, may have influenced the results.

In conclusion, patients with PTE and concomitant CRD were more likely to present with dyspnea in elderly individuals with a higher proportion of ever-smoker and less likely to be incidentally detected on CT, compared with PTE patients without CRD. LRTIs, such as pneumonia, more frequently accompanied the development of PTE in CRD patients. These patients were characterized by a high PESI score and in particular, in Koreans, a higher prevalence of in-situ pulmonary artery thrombosis. The presence of CRD may influence PTE-related in-hospital mortality in patients with PTE.

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None.

Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

Ethical Statement: This study was approved by the Institutional Review Board of the KNUH. Given the retrospective nature of the present study and the use of anonymized patient data, requirements for informed written consent were waived.

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