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Detection of Deep Vein Thrombosis by Follow-up Indirect Computed Tomography Venography after Pulmonary Embolism

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Background: Information regarding the incidence and risk factors for deep vein thrombosis (DVT) detected by follow-up computed tomographic (CT) venography after pulmonary embolism (PE) is sparse. The aim of the present study was to identify the predictors of DVT in follow-up CT images, and to elucidate their clinical significance.
Methods: Patients with PE were classified into the following three cohorts based on the time of indirect CT venography follow-up: within 1 month, 1 to 3 months, and 3 to 9 months after the initial CT scan. Each cohort was subdivided into patients with or without DVT detected by follow-up CT. Clinical variables were compared between the two groups.
Results: Follow-up CT revealed DVT in 61% of patients with PE within 1 month, in 15% of patients with PE at 1 to 3 months, and in 9% of patients with PE at 3 to 9 months after the initial CT scan. Right ventricular (RV) dilation on the initial CT (odds ratio [OR], 8.30; 95% confidence interval [CI], 1.89–36.40; p=0.005) and proximal DVT at the initial presentation (OR, 6.93; 95% CI, 1.90–25.20; p=0.003) were found to independently predict DVT in follow-up CT images within 1 month, proximal DVT at the initial presentation was found to independently predict DVT in follow-up CT images at 1 to 3 months (OR, 6.69; 95% CI, 1.53–29.23; p=0.012), and central PE was found to independently predict DVT in follow-up CT images at 3 to 9 months (OR, 4.25; 95% CI, 1.22–4.83; p=0.023) after the initial CT scan. Furthermore, the detection of DVT by follow-up CT independently predicted the recurrence of venous thromboembolism (VTE) (OR, 4.67; 95% CI, 2.24–9.74; p<0.001).
Conclusion: Three months after PE, DVT was not detected by follow-up CT in most patients with PE. RV dilation on the initial CT, central PE, and proximal DVT at the initial presentation were found to predict DVT on follow-up CT, which might predict VTE recurrence.

Keywords: Deep-Vein Thrombosis; Multidetector Computed Tomography; Pulmonary Embolism; Recurrence; Venous Thromboembolism

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Introduction

Venous thromboembolism (VTE) is a disease that encompasses both deep vein thrombosis (DVT) and pulmonary embolism (PE). The majority of pulmonary emboli originate from blood clots in the deep veins of the lower extremities. After the development of DVT, blood clots in deep veins generally resolve. Residual vein obstruction (RVO) is defined as the presence of blood clots at the site of initial DVT after a period of time, as assessed by compression Doppler ultrasonography[1]. The incidence of RVO after an initial episode of DVT has been reported to be 61%–65% at 6 months and 42%–55% at 12 months[2-4]. Detection of RVO using ultrasonography is associated with a modestly increased risk of VTE recurrence[5].

However, RVO does not play a major role in the identification of patients at higher risk of VTE recurrence after discontinuation of anticoagulation following the first unprovoked event[6].

If computed tomographic (CT) venography is added to CT pulmonary angiography, the sensitivity of CT for the diagnosis of VTE improves from 83% to 90%[7]. Indirect CT venography is as accurate as ultrasonography for the diagnosis of DVT[8,9]. However, the inclusion of CT venography as well as repeated CT scanning increases radiation exposure risk[10]. Furthermore, when DVT is detected by follow-up CT, it is difficult to differentiate residual vein thrombosis from new or recurrent vein thrombosis. However, for PE patients that undergo repeat CT venography for DVT, the incidence of DVT and the factors responsible for its development have not yet been reported. The aim of the present study was to identify clinical predictors of DVT as assessed by follow-up CT venography at different times after initial CT, and thus, to elucidate the clinical significance of DVT.

Materials and Methods

1. Study design

Patients who had been diagnosed with PE by multidetector-row CT (MDCT) and hospitalized at Kyungpook National University Hospital (KNUH), a tertiary referral center, in Daegu, South Korea between March 2003 and August 2015 were enrolled. The exclusion criteria were as follows: no available medical record or CT scan and the non-availability of interpretable CT scans due to poor image quality. PE patients that had undergone follow-up CT pulmonary angiography and indirect CT venography within 270 days of their initial CT scan were classified into three cohorts according to time: within 30 days (1 month), day 31–90 (1–3 months), and day 91–270 (3–9 months). Each cohort was dichotomized into patients with DVT (DVT group) or without DVT (control group). Clinical parameters in these groups were compared in order to identify predictors of DVT on follow-up CT images. This study was approved by the Institutional Review Board of KNUH (No. 2015-12-029), which waived the requirement for written informed consent due to the retrospective nature of the study.

2. Data collection

Demographic and clinical data were reviewed. Unprovoked PE was defined as the absence of provoking risk factors, including surgery, trauma, active cancer, pregnancy (up to 6 weeks postpartum), hormonal therapy, or immobilization (bed rest within the previous month for most of the day for ≥3 consecutive days), as previously defined[11]. Hypotension (systolic blood pressure <90 mm Hg) and tachycardia (heart rate >110/min) were recorded. PE severity index (PESI) was retrospectively calculated for patients admitted prior to 2007 and prospectively recorded in their medical records. As was noted in a previous report[12], an adverse outcome was defined as a serious clinical condition requiring inotropic support, cardiopulmonary resuscitation, or secondary thrombolysis or refractory hypoxia (impending respiratory failure or mechanical ventilation). Laboratory data were also reviewed, including serum N-terminal-pro-B-type natriuretic peptide and plasma troponin I levels.

3. Radiological evaluation

The follow-up CT protocol used was as follows[13]. CT scans were performed using MDCT scanners with 16 (Light Speed 16; General Electric, Milwaukee, WI, USA) or with 64 (Optima CT 660; General Electric and Aquilion 64; Toshiba Medical System, Tokyo, Japan) detector rows. Scans were obtained in the craniocaudal direction during a single inspiratory breath-hold, ranging from the apex of the lung to the diaphragm. The CT parameters used were 120 kVp and a 16×0.75 mm collimation with a pitch of <1.5. Low osmolar non-ionic contrast material (2 mL/kg; up to 150 mL) was injected through an antecubital vein at 3–4 mL/sec. Individual contrast optimization was achieved using bolus tracking within the main pulmonary artery. Indirect CT venography was performed from diaphragm to ankles in order to detect DVT, 140 seconds after the thoracic scan.

As previously described[13], PE was identified on CT images as a sharply delineated pulmonary arterial filling defect in at least two consecutive image sections, located centrally within the vessel or with acute angles at the vessel wall interface. The largest pulmonary artery with pulmonary emboli was checked and cases with emboli located in the right or left pulmonary artery or pulmonary trunk were referred to as central PE. The diameters of the right ventricle (RV) and left ventricle (LV) were measured at the widest points between the inner surface of the free wall and the surface of the interventricular septum, typically at the levels of the tricuspid and mitral valves, respectively[14]. These measurements were then used to calculate RV/LV diameter ratios. DVT was defined as a complete or partial intraluminal filling defect in a deep vein, as modified from previous studies[7,15,16]. A sharply marginated, low attenuation intravascular filling defect or complete absence of opacification of lumen favors acute DVT[15]. Finding that favored chronic DVT or residual vein thrombosis included a smaller vein than the adjacent artery, central or eccentric calcification, venous wall thickening, and a heterogeneously enhanced venous wall[15,16].

4. Statistical analysis

Statistical analysis was performed using SPSS for Windows version 22.0 (IBM Corp., Armonk, NY, USA). Data are expressed as medians with interquartile ranges for continuous

Table 1. Baseline characteristics of patients with follow-up CT venography within 1 month (n=67)

	DVT (n=41)	Control (n=26)	p-value
Age, yr	66 (56–75)	63 (44–71)	0.229
Male sex	18 (43.9)	12 (46.2)	0.857
Ever-smokers	14/40 (35.0)	6/25 (24.0)	0.350
Body mass index, kg/m^2	24 (21-26)	24 (21-27)	0.741
Unprovoked PE	11 (26.8)	4 (15.4)	0.372
Risk factor for VTE			
Surgery or trauma	16 (39.0)	18 (69.2)	0.016
Cancer	3 (7.3)	2 (7.7)	>0.999
Immobilization	22 (53.7)	20 (76.9)	0.055
Previous VTE	5 (12.2)	1 (3.8)	0.392
Comorbid condition			
Diabetes mellitus	3 (7.3)	3 (11.5)	0.670
Chronic lung disease*	5 (12.2)	3 (11.5)	0.936
Stroke	10 (24.4)	2 (7.7)	0.108
Heart disease†	7 (17.1)	1 (3.8)	0.138
Chronic kidney disease	0 (0)	0 (0)	
Arthritis	3 (7.3)	1 (3.8)	>0.999
Varicose vein	1 (2.4)	0 (0)	>0.999
Hormonal therapy	0 (0)	0 (0)	
Systolic BP, mm Hg	125 (110–139)	126 (110–136)	
<90	2 (4.9)	0 (0)	0.518
Heart rate, /min	88 (81–101)	87 (78–97)	
Tachycardia, heart rate >110/min	5 (12.2)	3 (11.5)	>0.999
PESI	75 (64–98)	71 (59–96)	0.361
PESI class IV–V	7 (17.1)	1 (3.8)	0.138
Thrombolytic therapy	8 (19.5)	0 (0)	0.019
Vena cava filter insertion	14 (34.1)	5 (19.2)	0.187
VTE recurrence	13 (31.7)	1 (3.8)	0.006
Adverse outcome	6 (14.6)	0 (0)	0.074
NT-proBNP, pg/mL	804 (107–2,863)‡	249 (102–2,236)§	0.423
Troponin I, ng/mL	0.040 (0.026–0.250)∥	0.040 (0.025–0.079)¶	0.499
Time interval of CT scans, day	13 (10–20)	18 (11–23)	0.137
Central PE**	25 (61.0)	10 (38.5)	0.072
RV/LV diameter ratio	0.94 (0.80–1.41)	0.88 (0.81–0.97)	0.319
RV dilation on initial CT	18 (43.9)	5 (19.2)	0.038
DVT at initial presentation	34/41 (82.9)	14/25 (56.0)	0.017
Proximal DVT at initial presentation	29/41 (70.7)	10/25 (40.0)	0.014

Values are presented as median (interquartile range) or number (%).
CT: computed tomography; DVT: deep vein thrombosis; PE: pulmonary embolism; VTE: venous thromboembolism; BP: blood pressure; PESI: pulmonary embolism severity index; NT-proBNP: N-terminal-pro-B-type natriuretic peptide; RV: right ventricle; LV: left ventricle.
*Chronic lung disease includes chronic obstructive pulmonary disease, asthma, bronchiectasis, idiopathic pulmonary fibrosis, pneumoconiosis, and tuberculosis-destroyed lung. †Heart disease includes ischemic heart disease, congestive heart failure, and atrial fibrillation. ‡n=22. §n=12. ∥n=31. ¶n=17. **Central pulmonary arteries mean right or left pulmonary artery or more proximal location.

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variables and numbers with percentages for categorical variables. Continuous variables were compared using the Mann-Whitney U test and categorical variables using the chi-square or Fisher exact test. Unconditional multiple logistic regression analysis was used to identify factors that predict DVT on follow-up CT images and the recurrence of VTE. The Hosmer-Lemeshow test was used as a goodness-of-fit test to assess the fit of logistic regression models. p-values of <0.05 were considered statistically significant.

Results

1. DVT within 1 month after PE

Eight hundred and eighty patients were diagnosed with PE by MDCT during the study period. Of the 67 PE patients with available data for follow-up CT venography performed within 1 month of initial CT, 41 patients (61%) were found to have DVT by follow-up CT (Table 1). Of these patients, 15 probably had new or recurrent DVT; 13 had CT findings in favor of acute DVT and two with CT findings favoring residual vein thrombosis without DVT at initial evaluation. The most common reason for conducting a follow-up CT scan was assessment of response to therapy (38 [57%] patients), followed by insertion or removal of a vena cava filter (19 [29%] patients) (Figure 1). Median times between CT scans were not significantly different in the DVT and control groups. Patients of the DVT group experienced significantly less frequent surgery or trauma (16 [39%] vs. 18 [69%] patients, p=0.016) and showed a tendency toward less frequent immobilization (22 [54%] vs. 20 [77%] patients, p=0.055) than the control group. In the DVT group, central PE showed a trend toward a higher frequency (25 [61%] vs. 10 [39%] patients, p=0.072) and RV dilation on initial CT images was significantly more common (18 [44%] vs. 5 [19%] patients, p=0.038). The incidence of proximal DVT at initial CT was significantly higher in the DVT group (29/41 [71%] vs. 10/25 [40%] patients, p=0.014). Furthermore, systemic thrombolysis was more frequently used (8 [20%] vs. 0 [0%] patients, p=0.019), adverse outcomes tended to be more frequent (6 [15%] vs. 0 [0%] patients, p=0.074), and the recurrence rate of VTE was significantly higher in the DVT group (13 [32%] vs. 1 [3.8%] patients, p=0.006).

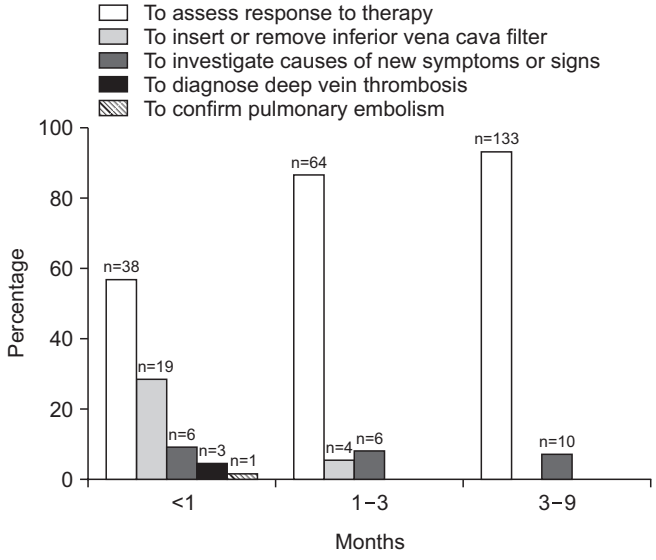

Figure 1. Reasons of follow-up computed tomographic venography. The most common reason why the patients undergo after pulmonary embolism is for assessment of response to treatment.

2. DVT at 1–3 months after PE

Follow-up CT venography was performed at 1–3 months in 71 PE patients, and 11 (15%) patients exhibited DVT (Table 2). Of these 11, three had CT findings favoring acute DVT. Most patients (n=64, 87%) underwent follow-up CT for the assessment of response to therapy (Figure 1). Median time between initial and follow-up CT was significantly shorter in the DVT group than in the control group (69 [49–78] vs. 80 [69–86] days, p=0.044). Cancer was significantly more common (4 [36%] vs. 6 [10%] patients, p=0.036) and the median PESI tended to be higher (76 [72–96] vs. 70 [62–82], p=0.089) in the DVT group. As was found in the "within 1 month" cohort, higher rates of VTE recurrence (3 [27%] vs. 0 [0%] patients, p=0.003) and proximal DVT occurrence (7/10 [70%] vs. 15/58 [26%] patients, p=0.010) were also observed in the DVT group at 1–3 months.

3. DVT at 3-9 months after PE

A total of 143 PE patients underwent indirect CT venography follow-up at 3–9 months, and 13 (9%) patients had DVT (Table 3). Of these 13 patients, two were considered likely to have new or recurrent DVT: one had a CT finding favoring acute DVT and the other, who had no DVT at initial evaluation, exhibited CT findings in favor of chronic or residual DVT. In most patients (n=133, 93%), follow-up CT scans were performed in order to assess response to therapy (Figure 1). Median time between initial and follow-up CT was not significantly different between the DVT and control groups. The DVT group was characterized by older age (75 [68–79] vs. 65 [55–72] years, p=0.009), female predominance (12 [92%] vs. 81 [62%] patients, p=0.034), and a trend toward a lower incidence of surgery or trauma (2 [15%] vs. 53 [41%] patients, p=0.082). PESI (81 [71–109] vs. 71 [60–83], p=0.036) and frequency of central PE (9 [69%] vs. 43 [33%] patients, p=0.015) were more common in the DVT group than in the control group. In contrast to the other two cohorts, incidences of proximal DVT at initial evaluation and VTE recurrence were not significantly different in these two groups.

Table 2. Baseline characteristics of patients with follow-up CT venography at 1–3 months (n=74)

	DVT (n=11)	Control (n=63)	p-value
Age, yr	66 (47–73)	64 (54–70)	0.855
Male sex	7 (63.6)	21 (33.3)	0.090
Ever-smokers	3/10 (30.0)	17 /62 (27.4)	>0.999
Body mass index, kg/m^2	24 (22–26)	24 (21–27)	>0.999
Unprovoked PE	3 (27.3)	26 (41.3)	0.511
Risk factor for VTE			
Surgery or trauma	4 (36.4)	24 (38.1)	>0.999
Cancer	4 (36.4)	6 (9.5)	0.036
Immobilization	5 (45.5)	30 (47.6)	0.894
Previous VTE	0 (0)	3 (4.8)	0.460
Comorbid condition			
Diabetes mellitus	2 (18.2)	11 (17.5)	>0.999
Chronic lung disease*	0 (0)	3 (4.8)	>0.999
Stroke	1 (9.1)	6 (9.5)	>0.999
Heart disease†	1 (9.1)	3 (4.8)	0.482
Chronic kidney disease	0 (0)	0 (0)	
Arthritis	1 (9.1)	10 (15.9)	>0.999
Varicose vein	0 (0)	0 (0)	
Hormonal therapy	0 (0)	0 (0)	
Systolic BP, mm Hg	135 (124–151)	123 (111–147)	0.144
<90	0 (0)	1 (1.6)	>0.999
Heart rate, /min	101 (96–113)	89 (75–102)	0.009
Tachycardia, heart rate >110/min	4 (36.4)	5 (7.9)	0.024
PESI	76 (72–96)	70 (62–82)	0.089
PESI class IV–V	2 (18.2)	8 (12.7)	0.638
Thrombolytic therapy	0 (0)	4 (6.3)	0.620
Vena cava filter insertion	2 (18.2)	3 (4.8)	0.157
VTE recurrence	3 (27.3)	0 (0)	0.003
Adverse outcome	1 (9.1)	9 (14.3)	>0.999
NT-proBNP, pg/mL	338 (55–890)‡	318 (72–2,349)§	0.616
Troponin I, ng/mL	0.057 (0.030–0.336)‖	0.040 (0.040–0.160)¶	0.558
Time interval of CT scans, day	69 (49–78)	80 (69–86)	0.044
Central PE**	3 (27.3)	20 (31.7)	0.767
RV/LV diameter ratio	0.97 (0.78–1.19)	0.88 (0.76–1.05)	0.236
RV dilation on initial CT	5 (45.5)	19 (30.2)	0.317
DVT at initial presentation	9/10 (90.0)	27/58 (46.6)	0.015
Proximal DVT at initial presentation	7/10 (70.0)	15/58 (25.9)	0.010

Values are presented as median (interquartile range) or number (%).
CT: computed tomography; DVT: deep vein thrombosis; PE: pulmonary embolism; VTE: venous thromboembolism; BP: blood pressure; PESI: pulmonary embolism severity index; NT-proBNP: N-terminal-pro-B-type natriuretic peptide; RV: right ventricle; LV: left ventricle.
*Chronic lung disease includes chronic obstructive pulmonary disease, asthma, bronchiectasis, idiopathic pulmonary fibrosis, pneumoconiosis, and tuberculosis-destroyed lung. †Heart disease includes ischemic heart disease, congestive heart failure, and atrial fibrillation. ‡n=9. §n=44. ‖n=9. ¶n=51. **Central pulmonary arteries mean right or left pulmonary artery or more proximal location.

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Table 3. Baseline characteristics of patients with follow-up CT venography at 3–9 months (n=143)

	DVT (n=13)	Control (n=130)	p-value
Age, yr	75 (68–79)	65 (55–72)	0.009
Male sex	1 (7.7)	49 (37.7)	0.034
Ever-smokers	2/13 (15.4)	35/126 (27.8)	0.513
Body mass index, kg/m^2	23 (21–26)	25 (22–29)	0.405
Unprovoked PE	7 (53.8)	51 (39.2)	0.306
Risk factor for VTE			
Surgery or trauma	2 (15.4)	53 (40.8)	0.082
Cancer	2 (15.4)	8 (6.2)	0.226
Immobilization	4 (30.8)	65 (50.0)	0.248
Previous VTE	0 (0)	4 (3.1)	>0.999
Comorbid condition			
Diabetes mellitus	1 (7.7)	20 (15.4)	0.692
Chronic lung disease*	2 (15.4)	9 (6.9)	0.262
Stroke	2 (15.4)	10 (7.7)	0.299
Heart disease†	2 (15.4)	11 (8.5)	0.335
Chronic kidney disease	1 (7.7)	3 (2.3)	0.320
Arthritis	2 (15.4)	27 (20.8)	>0.999
Varicose vein	0 (0)	2 (1.5)	>0.999
Hormonal therapy	0 (0)	3 (2.3)	>0.999
Systolic BP, mmHg	120 (113–147)	125 (111–140)	0.746
<90	1 (7.7)	0 (0)	0.091
Heart rate, /min	87 (71–109)	84 (74–98)	0.938
Tachycardia, heart rate >110/min	3 (23.1)	9 (6.9)	0.080
PESI	81 (71–99)	71 (60–83)	0.036
PESI class IV–V	1 (7.7)	10 (7.7)	>0.999
Thrombolytic therapy	1 (7.7)	5 (3.8)	0.442
Vena cava filter insertion	0 (0)	1 (0.8)	>0.999
VTE recurrence	2 (15.4)	12 (9.2)	0.617
Adverse outcome	1 (7.7)	6 (4.6)	0.495
NT-proBNP, pg/mL	1,169 (245–2,246)‡	244 (66–1,508)§	0.190
Troponin I, ng/mL	0.040 (0.040–0.110)‖	0.040 (0.015–0.129)¶	0.410
Time interval of CT scans, day	123 (104–197)	146 (104–189)	0.950
Central PE**	9 (69.2)	43 (33.1)	0.015
RV/LV diameter ratio	1.06 (0.76–1.30)	0.92 (0.76–1.10)	0.461
RV dilation on initial CT	8 (61.5)	51 (39.2)	0.119
DVT at initial presentation	11/13 (84.6)	95/122 (77.9)	0.734
Proximal DVT at initial presentation	7/13 (53.8)	65/122 (53.3)	0.969

Values are presented as median (interquartile range) or number (%).
CT: computed tomography; DVT: deep vein thrombosis; PE: pulmonary embolism; VTE: venous thromboembolism; BP: blood pressure; PESI: pulmonary embolism severity index; NT-proBNP: N-terminal-pro-B-type natriuretic peptide; RV: right ventricle; LV: left ventricle.
*Chronic lung disease includes chronic obstructive pulmonary disease, asthma, bronchiectasis, idiopathic pulmonary fibrosis, pneumoconiosis, and tuberculosis-destroyed lung. †Heart disease includes ischemic heart disease, congestive heart failure, and atrial fibrillation. ‡n=10. §n=85. ‖n=11. ¶n=103. **Central pulmonary arteries mean right or left pulmonary artery or more proximal location.

Table 4. Multivariate analysis for predictors of deep vein thrombosis on follow-up CT

	Odds ratio	95% Confidence interval	p-value
Within 1 month			
RV dilation on initial CT	8.299	1.892–36.401	0.005
Proximal DVT at initial presentation	6.927	1.904–25.197	0.003
1–3 Months			
Proximal DVT at initial presentation	6.689	1.531–29.228	0.012
3–9 Months			
Central PE	4.254	1.221–4.831	0.023
PESI	0.976	0.951–1.003	0.080

CT: computed tomography; RV: right ventricle; DVT: deep vein thrombosis; PE: pulmonary embolism; PESI: pulmonary embolism severity index.

4. Predictors of DVT by CT venography during each time period

In each cohort, candidate variables for multivariate analysis were chosen from those with p-values of <0.10. In the "within 1 month" cohort, surgery or trauma, immobilization, central PE, RV dilation on initial CT, and proximal DVT at initial CT were selected as candidate variables (Hosmer-Lemeshow test, p=0.648). RV dilation (odds ratio [OR], 8.30; 95% confidence interval [CI], 1.89–36.40; p=0.005) and proximal DVT at initial CT (OR, 6.93; 95% CI, 1.90–25.20; p=0.003) were identified as independent predictors of the presence of DVT by follow-up CT within 1 month (Table 4). In the 1–3-month cohort, cancer, PESI, and the CT interval were chosen as candidates for multivariate analysis, while heart rate was excluded as it was included in the PESI score (Hosmer-Lemeshow test, p=0.684). The presence of proximal DVT by initial CT was a significant predictor for DVT on follow-up CT at 1–3 months (OR, 6.69; 95% CI, 1.53–29.23; p=0.012). In the 3–9-month cohort, surgery or trauma, PESI and central PE were included as candidate variables for multivariate analysis; age, male sex, hypotension, and tachycardia were excluded because they are components of PESI (Hosmer-Lemeshow test, p=0.722). In this cohort, central PE was found to be independently predict DVT at follow-up CT (OR, 4.25; 95% CI, 1.22–4.83; p=0.023).

5. Factors related to the recurrence of VTE

Patients were allocated into either VTE recurrence or non-recurrence group (Table 5). The presence of cancer (7 [19%] vs. 18 [7%] patients, p=0.016), PESI class IV–V (7 [19%] vs. 22 [9%] patients, p=0.050), RV dilation on initial CT (19 [53%] vs. 87 [35%] patients, p=0.040), and DVT on follow-up CT (19 [53%] vs. 46 [19%] patients, p<0.001) were significantly more frequent in the recurrence group. Multivariate analysis using these variables (Hosmer-Lemeshow test, p=0.806) revealed only DVT on follow-up CT significantly predicted VTE recurrence (OR, 4.67; 95% CI, 2.24–9.74; p<0.001) (Table 6).

Discussion

In the present study, rates of DVT as determined by follow-up CT venography were 61% in PE patients within 1 month, 15% at 1–3 months, and 9% at 3–9 months. Short-term prognostic markers of PE[11,12], such as RV dilation by CT and central PE, might be significant predictors of DVT by follow-up CT, but this finding was not consistent among the three cohorts (within 1 month, from 1 to 3 months, and from 3 to 9 months after initial CT). The presence of proximal DVT at initial evaluation also independently predicted DVT by follow-up CT conducted within 1 month or from 1 to 3 months, but not at 3 to 9 months. DVT on follow-up CT was found to be the only risk factor of VTE recurrence.

Information regarding the use of CT venography for identifying residual lesions after an initial episode of acute DVT is lacking. In previous studies based on compression ultrasonography, RVO following first DVT occurred in 70% of patients at 3 months[17] and in 61%–65% of patients at 6 months[2-4,18]. In the present study, DVT was observed in 15% of PE patients at 1–3 months and 9% of patients at 3–9 months by indirect CT venography during follow-up. Indirect CT venography is considered to be as accurate as ultrasonography for the diagnosis of DVT[8,9]. However, the present study was performed to identify the presence of DVT by follow-up CT after PE, while previous studies[2-4,17,18] were performed to detect RVO after DVT. In addition, in the present study, not all PE patients underwent an initial evaluation for DVT, and thus, the presence of DVT by follow-up CT did not indicate residual vein thrombosis. Furthermore, CT findings suggestive of recurrent or new DVT were observed in some patients. Consequently, direct comparisons could not be made between the present and previous studies with respect to the incidences of residual lesions.

Thrombus burden[19], age[4,20], cancer[4,21], immobilization[22], previous occurrence of recurrent episode[20], degree of occlusion of the initial clot[23], and symptom duration[23] have been reported to be negative predictors of complete resolution of blood clots in DVT patients as determined by compression ultrasonogra-

Table 5. Comparison of clinical parameters between VTE recurrence and non-recurrence groups (n=284)

	Recurrence (n=36)	Non-recurrence (n=248)	p-value
Age, yr	64 (55–73)	66 (54–73)	0.645
Male sex	14 (38.9)	94 (37.9)	0.909
Ever-smokers	11/36 (30.6)	66/240 (27.5)	0.703
Body mass index, kg/m^2	25 (21–26)	24 (22–27)	
Unprovoked PE	13 (36.1)	89 (35.9)	0.979
Risk factor for VTE			
Surgery or trauma	14 (38.9)	103 (41.5)	0.763
Cancer	7 (19.4)	18 (7.3)	0.016
Immobilization	13 (36.1)	133 (53.6)	0.049
Previous VTE	5 (13.9)	8 (3.2)	0.004
Comorbid condition			
Diabetes mellitus	7 (19.4)	33 (13.3)	0.323
Chronic lung disease*	4 (11.1)	18 (7.3)	0.499
Stroke	4 (11.1)	27 (10.9)	>0.999
Heart disease†	4 (11.1)	21 (8.5)	0.537
Chronic kidney disease	0 (0)	4 (1.6)	>0.999
Arthritis	6 (16.7)	38 (15.3)	0.835
Varicose vein	1 (2.8)	2 (0.8)	0.335
Hormonal therapy	0 (0)	3 (1.2)	>0.999
Systolic BP, mm Hg	116 (109–139)	125 (113–141)	0.176
<90	1 (2.8)	3 (1.2)	0.420
Heart rate, /min	89 (75–101)	87 (76–99)	0.764
Tachycardia, heart rate >110/min	3 (8.3)	26 (10.5)	>0.999
PESI	74 (62–102)	72 (62–86)	0.499
PESI class IV–V	7 (19.4)	22 (8.9)	0.050
Thrombolytic therapy	4 (11.1)	14 (5.6)	0.261
Vena cava filter insertion	4 (11.1)	21 (8.5)	0.537
Adverse outcome	4 (11.1)	19 (7.7)	0.510
NT-proBNP, pg/mL	352 (74–2,679)‡	318 (82–1,542)§	0.814
Troponin I, ng/mL	0.040 (0.033–0.170)‖	0.040 (0.020–0.143)¶	0.412
Time interval of CT scans, day	73 (21–175)	91 (47–137)	0.223
Central PE**	18 (50.0)	92 (37.1)	0.138
RV dilation on initial CT	19 (52.8)	87 (35.1)	0.040
Proximal DVT at initial presentation	16/35 (45.7)	117/234 (50.0)	0.636
DVT on follow-up CT	19 (52.8)	46 (18.5)	<0.001

Values are presented as median (interquartile range) or number (%).
VTE: venous thromboembolism; PE: pulmonary embolism; BP: blood pressure; PESI: pulmonary embolism severity index; NT-proBNP: N-terminal-pro-B-type natriuretic peptide; CT: computed tomography; RV: right ventricle; DVT: deep vein thrombosis.
*Chronic lung disease includes chronic obstructive pulmonary disease, asthma, bronchiectasis, idiopathic pulmonary fibrosis, pneumoconiosis, and tuberculosis-destroyed lung. †Heart disease includes ischemic heart disease, congestive heart failure, and atrial fibrillation. ‡n=26. §n=156. ‖n=32. ¶n=190. **Central pulmonary arteries mean right or left pulmonary artery or more proximal location.

Table 6. Multivariate analysis for predictors of venous thromboembolism recurrence

	Odds ratio	95% Confidence interval	p-value
Cancer	0.381	0.139–1.046	0.061
DVT on follow-up CT	4.666	2.235–9.743	<0.001

DVT: deep vein thrombosis; CT: computed tomography.

phy. In the present study, proximal DVT at initial presentation independently predicted the detection of DVT by follow-up CT within 3 months of initial PE diagnosis, but this did not apply after 3 months. The presence of proximal or femoral DVT has been reported to be associated with an increased risk for RVO using compression ultrasonography[4,21]. However, in the present study, proximal DVT at initial presentation did not influence the presence of DVT in PE patients at more than 3 months after the initial event, suggesting the location of original DVT does not affect DVT after a certain period of time has passed. Furthermore, RV dilation and central PE on initial CT images independently predicted DVT on follow-up CT within 1 month and at 3–9 months, respectively. However, these short-term prognostic factors of PE were not significant predictor of DVT at 1–3 months, when median time between initial and follow-up CT scans in the DVT group was significantly shorter than in the control group. It could be speculated that different times between CT scans were responsible for these results. Similarly, a previous study showed that the extent of PE was positively associated with a higher probability of residual DVT[24], although in another study, the clot burden of PE was not found to necessarily indicate that of DVT[25].

Patients with RVO by ultrasonography have a higher risk of post-thrombotic syndrome than those without RVO[26], and post-thrombotic syndrome increases the risk of recurrent VTE[27,28]. Nevertheless, RVO is not a clinically relevant predictor for VTE recurrence[1,5]. This can be explained as follows. RVO is unlikely to represent ongoing thrombus generation, and is more likely to reflect defective fibrinolysis[6], which alone has not been shown to enhance the risk of recurrent VTE[29,30]. In the present study, DVT on follow-up CT included recurrent or new DVT as well as residual vein thrombosis and thus, predicted VTE recurrence in patients with PE, although this finding was limited to the presence of DVT within 3 months of initial CT scan.

The present study has several limitations. First, its retrospective study design means that selection bias could not be avoided, and the number of patients included was not large enough to reach definitive conclusions. Second, as described above, not all patients underwent a diagnostic study for DVT and some patients with DVT by follow-up CT exhibited CT findings suggestive of new or recurrent DVT. Therefore, DVT detected by follow-up CT probably included new or recurrent DVT as well as residual vein thrombosis. Third, the timing of repeat CT scanning was not scheduled in advance, which is why intervening times were arbitrarily divided into three periods for the analysis. Fourth, the presence of permanent or persistent temporary risk factors of VTE is a known significant predictor for delayed thrombus regression[2], and unfortunately, due to the retrospective nature of the present study, we were unable to identify these risk factors.

In summary, the majority of PE patients may not exhibit DVT by follow-up CT after 3 months of initial diagnosis. Short-term prognostic markers of PE, such as RV dilation on initial CT and central PE, and proximal DVT at initial evaluation may predict the presence of DVT on follow-up CT, despite inconsistencies of CT results obtained at different follow-up times. The presence of DVT by follow-up CT was found to be a significant risk factor of VTE recurrence. Future prospective studies are required to confirm our findings.

Conflicts of Interest

No potential conflict of interest relevant to this article was reported.

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