Original Article

Access this article online

Quick Response Code:

Website: www.eurasianjpulmonol.com

DOI: 10.4103/ejop.ejop_5_19

Factors associated with residual pulmonary thromboembolism detected by computed tomography pulmonary angiography

Özer Özdemir, Sinem Ermin[1], Pelin Özdemir[2], Özgür Batum[1], Bengi Sari Islam[3], Bahri Gümüs[4], Ufuk Yilmaz[1]

ORCID:
Özer Özdemir: https://orcid.org/0000-0002-8884-0682
Sinem Ermin: https://orcid.org/0000-0002-0400-9403
Pelin Özdemir: https://orcid.org/0000-0001-6534-4451
Özgür Batum: https://orcid.org/0000-0002-8353-3421
Bengi Sarı İslam: https://orcid.org/0000-0001-6958-9237
Bahri Gümüş: https://orcid.org/0000-0002-2044-4704
Ufuk Yılmaz: https://orcid.org/0000-0003-3676-4355

Abstract:

BACKGROUND: Complete resolution of pulmonary vascular obstruction is not totally achieved in patients with acute pulmonary thromboembolism (PE). In this study, we tried to identify the factors associated with residual PE.

MATERIALS AND METHODS: Patients with a diagnosis of acute PE from two centers were retrospectively analyzed. Residual PE was detected by computed tomography (CT) pulmonary angiography. Investigated parameters were unprovoked PE, clinical severity index (pulmonary embolism severity index score), D-dimer, troponin I, central pulmonary embolism, clot burden (Qanadli score), CT indexes of right ventricle (RV) overload (RV/left ventricle and pulmonary artery/aorta), massive PE, coexisting deep venous thrombosis signs and symptoms, and follow-up CT time.

RESULTS: On univariate analysis, follow-up CT time and clot burden at the time of diagnosis were significantly associated with residual PE ($P = 0.02$ and $P = 0.002$, respectively). Initial D-dimer levels were higher in patients with residual PE although statistical significance was not reached ($P = 0.08$). On multivariate analysis, clot burden and follow-up CT time remained significant (hazard ratio [95% confidence interval] of 4.31 [1.31–14.12] and 2.47 [0.92–6.62], respectively).

CONCLUSION: Our results suggest that higher clot burden may be an independent predictor for residual PE along with the timing of follow-up CT.

Keywords:

Incomplete resolution, pulmonary embolism, residual pulmonary embolism

Department of Pulmonology, Kemalpaşa State Hospital, Departments of [1]Pulmonology and [4]Radiology, Dr. Suat Seren Chest Diseases and Surgery Training and Education Hospital, Departments of [2]Pulmonology and [3]Radiology, Su Hospital, İzmir, Turkey

Address for correspondence:
Dr. Özer Özdemir, Department of Pulmonology, Kemalpaşa State Hospital, Sekiz Eylül Mh., Kırovası Küme, Bulvarı 8/1 Str., 35730 Kemalpaşa, İzmir, Turkey.
E-mail: ozer_ozdemir@yahoo.com

Received: 19-01-2019
Revised: 03-02-2019
Accepted: 18-04-2019
Published: 30-04-2020

Introduction

Acute pulmonary thromboembolism (PE) is a potentially life-threatening, relatively common condition that is usually a result of deep vein thrombosis (DVT) of the lower extremities. It has a heterogeneous and wide range of presentations with variable risks of morbidity, mortality, and recurrence. Anticoagulant therapy is the mainstay of the management of PE that decreases the mortality to a level as low as 1.8%.[1]

How to cite this article: Ozdemir O, Ermin S, Özdemir P, Batum Ö, Islam BS, Gümüs B, *et al*. Factors associated with residual pulmonary thromboembolism detected by computed tomography pulmonary angiography. Eurasian J Pulmonol 2020;22:29-35.

However, despite effective therapy with anticoagulants, it is known that complete resolution of thrombus is not routinely achieved in all patients. Depending on the follow-up test used, time of evaluation, and baseline characteristics of the patients, the ratio of the incomplete resolution of the clot may differ, but overall, over 50% of patients with PE have persistent defects at their follow-up scan 6 months after diagnosis.[2] This was also shown in patients with DVT that normalization of the ultrasonography findings was evident in 39% of patients at 6 months, 58% after 12 months, and 74% at 36 months.[3]

The presence of incomplete resolution of the clot may complicate the objective and accurate diagnosis of recurrent PE. Although clinical significance and future impact of residual PE are not clearly elucidated, the factors relating with the incomplete resolution of thrombus are an area of investigation.

In this study, we explored the factors associated with the presence of residual PE in the follow-up computed tomography pulmonary angiography (CTPA) of patients with acute PE.

Materials and Methods

The hospital records of patients with a diagnosis of pulmonary thromboembolism from two centers (a tertiary reference hospital and a secondary hospital) between 2012 and 2017 were retrospectively analyzed. The study was approved by the local ethics committee. The study was conducted in accordance with the ethical principles stated in the Declaration of Helsinki.

Study population

All patients included in the study were over 18 years old. Patients with a confirmed diagnosis of PE by CTPA who received anticoagulant therapy and had a control CTPA after follow-up period were eligible for the study. Data of demographic characteristics, comorbidities, risk factors for venous thromboembolism (VTE), clinical probability score (Wells score), clinical severity index of pulmonary embolism (pulmonary embolism severity index [PESI] score), CTPA findings, D-dimer, troponin I and N-terminal prohormone of brain natriuretic peptide (NT-proBNP) levels, symptoms and signs of coexisting DVT, and treatment options were driven from hospital records.

Computed tomography

CT was performed by two different tomography devices in two different centers (16-section multidetector CT scanner [Somatom Emotion 16; Siemens Healthcare, Forchheim, Germany] and 128-section multidetector scanner [Somatom Perspective 128; Siemens Healthcare, Forchheim, Germany]).

The scanning parameters for 16-section multidetector CT scanner were as follows: tube voltage, 130 kVp; pitch, 1.5; collimation, 16 mm × 1 mm; reconstruction interval, 1 mm; and rotation time, 0.6 s. The scanning parameters for 128-section multidetector CT scanner were as follows: tube voltage, 130 kVp; collimation, 64 mm × 0.6 mm; pitch, 1.5; reconstruction interval, 0.75 mm; and rotation time, 0.6 s. For CTPA, a bolus of 60 mL of iodinated contrast material was injected through a catheter in the antecubital vein at a rate of 4 mL/s using an automatic injector.

Residual pulmonary thromboembolism was defined as any pulmonary arterial filling defects in at least two consecutive CT images that was seen in follow-up CTPA during the treatment period, and localization and size of residual thrombosis were in accordance with the diagnostic CTPA and not compatible with recurrence.

Anatomic severity of clot burden was identified by Qanadli score.[4] Briefly, each lung is considered to have ten arteries, three in the upper lobe, two in the middle lobe and lingula, and five in the lower lobe. A weight factor was assigned depending on the degree of vascular obstruction: 1 point for partial obstructions and 2 points for total obstructions. The presence of embolus in the most proximal pulmonary artery (PA) is given a value according to the number of branches from that proximal artery. In this way, the maximum CT obstruction index is 40 points.

Furthermore, other CTPA variables of the right ventricle (RV) and left ventricle (LV) diameters and aorta (AO) and main PA diameters were also measured, and their ratio was obtained. RV and LV diameters were measured at the widest points between the inner surface of free wall and the surface of the interventricular septum, at the levels of tricuspid and mitral valve, respectively.[5] The diameters of the pulmonary trunk and ascending AO were measured at the level of pulmonary trunk bifurcation.[6,7] Radiological distribution of pulmonary embolism, the presence of pleural effusion, and the proximity of affected arteries were also obtained.

Patients with a follow-up CTPA in the treatment period were included in the study. Complete resolution was determined if no pulmonary embolism was detected on follow-up pulmonary CTPA.

Statistical analysis

Statistical analysis was performed using IBM SPSS Statistics for Windows, version 20.0 (IBM Corp., Armonk, New York, USA). Data were presented as numbers with percentages for categorical variables and as means for continuous variables. Categorical variables were compared using Chi-square test. Continuous variables were compared using Mann–Whitney U-test, if variables

were not normally distributed. If normal distribution was present, Student's *t*-test was used for comparison. Multiple logistic regression analysis with the backward stepwise method was used to identify factors affecting incomplete resolution of pulmonary embolism. Receiver operating characteristic (ROC) analysis was applied to identify cutoff points with best sensitivity and specificity. The Hosmer–Lemeshow test was used as a goodness-of-fit test to assess the fit of logistic regression analysis. $P < 0.05$ was considered statistically significant.

Results

Two hundred and fifty-four patients were found to be eligible for the study. Patients with suspected pulmonary embolism without definitive diagnosis with CTPA (n = 45), patients without a control CTPA during the treatment period (n = 54), and patients whose diagnostic CT images were not eligible (n = 19) were excluded from the study. A total of 136 patients were included in the study. Among these 136 patients, 128-section multidetector CT was applied in 30 patients, and the remaining patients were diagnosed and evaluated by 16-section CT.

The mean age of the study population was 62.7 (21–95) years. 52.9% (n = 72) of the study population were male and 47.1% (n = 64) were female. Unprovoked pulmonary embolism was detected in 20.6% (n = 28) of patients.

Follow-up CTPA revealed residual pulmonary embolism in 25.7% (n = 35) of patients. The median time from the time of diagnosis to follow-up CTPA was 93.7 days (13–271 days). Residual PE positivity according to the follow-up CT time period is shown in Table 1.

Previous VTE diagnosis was present in 8.1% (n = 11) of patients. Forty-one (30.1%) patients also had DVT signs and symptoms at the time of the diagnosis. Twenty-eight patients were admitted to the intensive care unit and 14 patients had massive pulmonary embolism and 15 patients were initially treated with thrombolytic therapy. In 48 (32.4%) patients, thrombus was centrally located, either in the pulmonary trunk or in the main pulmonary arteries.

Clinical severity index, i.e., PESI Class IV–V patients, formed the 27.9% (n = 38) of the study population. Clot burden at presentation was calculated by Qanadli score, and the median Qanadli score of the study population was 10. Clinical characteristics of patients are presented in Table 2.

The results of the univariate analysis according to the presence of residual pulmonary embolism are presented in Table 3. For comparison of groups, ROC analysis

Table 1: Residual thrombus according to the control computed tomography time period (n=136)

	Residual PE (%)	Complete resolution (%)
0-3 months	22 (36.1)	39 (63.9)
3-6 months	12 (20.7)	46 (79.3)
6-9 months	1 (5.9)	16 (94.1)

PE: Pulmonary embolism

Table 2: Demographic characteristics of the study population

	n=136
Age, mean±SD (range)	62.7±15.6 (21-95)
Sex, males (%)	72 (52.9)
Unprovoked PE (%)	28 (20.6)
History of VTE (%)	11 (8.1)
Coexisting DVT signs and symptoms (%)	41 (30.1)
Central PE (%)	48 (32.4)
Pleural effusion (%)	30 (22)
Massive PE (%)	14 (10.3)
Primary fibrinolytic treatment (%)	15 (11)
Residual thrombus (%)	35 (25.7)
PESI class	
Very low (%)	24 (17.6)
Low (%)	30 (22.1)
Intermediate (%)	20 (14.7)
High (%)	12 (8.8)
Very high (%)	26 (19.1)
D-dimer, mean (range)	5221 (358-18700)
NT-proBNP, mean (range)	1964.6 (12-21300)
Troponin I, mean (range)	0.30 (0.001-6.48)
Qanadli score, median (range)	10 (1-40)
CT RV/LV (range)	1.05 (0.58-2.51)
CT PA/AO (range)	0.86 (0.64-1.44)
Follow up CT time, days (range)	93.7 (13-271)

PE: Pulmonary embolism, SD: Standard deviation, DVT: Deep venous thrombosis, PESI: Pulmonary embolism severity index, RV: Right ventricle, LV: Left ventricle, PA: Pulmonary artery, AO: Aorta, CT: Computed tomography, VTE: Venous thromboembolism, NT-proBNP: N-terminal prohormone of brain natriuretic peptide

was used to detect cutoff points for Qanadli score and D-dimer, and the cutoff point for Qanadli score was 7 and for D-dimer was 1984 ng/dl. The results of the ROC analysis are presented in Figure 1. For follow-up CT time, regarding that patients were treated at least 3 months, 90 days was taken as the cutoff point. For troponin I, the upper limit of laboratory normal values was taken as the cutoff point. In univariate analysis, only clot burden at presentation and follow-up CT time were found to be significantly associated with residual PE. Furthermore, D-dimer levels were higher in patients with residual PE with a significance level of 0.08. Clinical severity index, massive PE, the presence of DVT signs, RV/LV, PA/AO, central PE, or unprovoked PE were not associated with the presence of residual PE.

On multiple logistic regression analysis, both clot burden and follow-up CT time remained significant in

Table 3: Clinical characteristics of patients according to the presence of residual pulmonary thromboembolism

Characteristics	Residual PE (*n*=35), *n* (%)	Complete resolution (*n*=101), *n* (%)	χ^2	*P*
Age (cut off ≥65 years)	14 (40)	47 (46.5)	0.45	0.56
Female sex	14 (40)	50 (49.5)	0.94	0.43
Presence of DVT signs and symptoms	7 (20)	34 (33.7)	2.30	0.14
Unprovoked PE	10 (28.6)	18 (17.8)	1.84	0.23
Qanadli score (cutoff >7)	26 (83.9)	42 (51.2)	10.00	0.002
D-dimer (cutoff >1984)	27 (90)	63 (74.1)	3.29	0.08
Troponin I (cutoff >0.3)	2 (7.7)	16 (20.5)	2.24	0.23
Central pulmonary embolism	14 (45.2)	31 (37.8)	0.51	0.52
Pleural effusion	7 (22.6)	23 (28)	3.72	0.6
Massive and submassive PE	7 (20)	17 (16.8)	0.18	0.80
Thrombolytic therapy	2 (5.7)	13 (12.9)	1.36	0.35
Follow-up CT time (cutoff ≤90 days)	22 (62.9)	39 (38.6)	6.18	0.02
PESI class IV-V	8 (27.6)	30 (36.1)	4.71	0.49
RV/LV (cutoff >1)	12 (38.7)	27 (33.3)	0.29	0.66
PA/AO (cutoff >1)	6 (19.4)	9 (11)	1.37	0.35

For statistical comparison, Chi-square test is used for all the above-mentioned variables. DVT: Deep vein thrombosis, PE: Pulmonary embolism, CT: Computed tomography, PESI: Pulmonary embolism severity index, RV: Right ventricle, LV: Left ventricle, PA: Pulmonary artery, AO: Aorta

Table 4: Multiple logistic regression analysis of factors associated with residual pulmonary embolism

Parameter	SE	Wald	HR (95% CI)	*P*
Follow-up CT time (cut off 90 days)	0.503	3.229	2.47 (0.92-6.62)	0.04
Qanadli score (cut off=7)	0.606	5.804	4.31 (1.31-14.12)	0.02

Backward Wald statistics; Hosmer-Lemeshow goodness-of-fit test *P*=0.237. CT: Computed tomography, HR: Hazard ratio, CI: Confidence interval, SE: Standard error

the model, with hazard ratio (95% confidence interval) of 4.31 (1.31–14.12) and 2.47 (0.92–6.62), respectively. Multiple logistic regression analysis results are shown in Table 4.

A secondary comparison of patients with residual PE and complete resolution was carried out according to the time period of follow-up CT, as 0–3 months, 3–6 months, and >6 months. Only one patient with residual PE was detected after 6 months of follow-up, so statistical comparison was not possible in this group. In patients with a follow-up CT in 0–3 months, Qanadli score and follow-up CT time were significantly different between the groups, as shown in Table 5, whereas in patients with follow-up CT between 3 and 6 months, there was no statistically different parameter between both the groups, as shown in Table 6.

Discussion

In our study, we explored the factors associated with residual PE detected by follow-up CTPA in patients with an initial diagnosis of acute pulmonary thromboembolism. We found that residual thromboembolism was associated with the time of the follow-up CT and clot burden at the time of diagnosis. Furthermore, initial D-dimer levels were also higher in patients with residual PE on the edge of significance. Both clot burden and follow-up CT

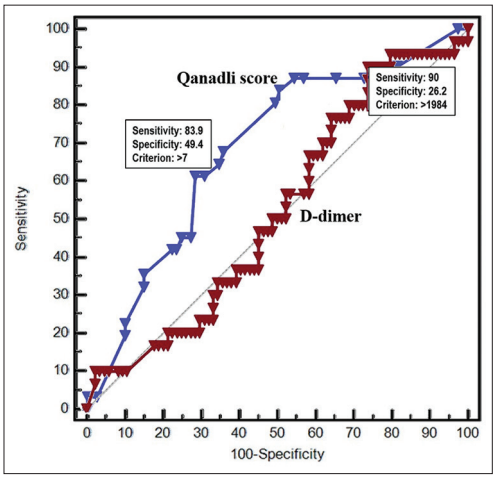

Figure 1: Receiver operating characteristic analysis curves for Qanadli score and D-dimer (area under curve for D-dimer is 0.52 and for Qanadli score is 0.68)

time remained significant in multiple logistic regression analysis.

The incidence of residual PE differs among the studies according to the diagnostic test used, timing of test, and investigated study population. Our study group was mostly composed of hemodynamically stable PE patients, and massive PE patients treated with fibrinolytic therapy were only 11% of the study group. In this study population, we found residual PE in 25.7% (n = 35) of patients. In a systematic review evaluating the resolution of thromboembolism in patients with acute PE, it is stated that more than 50% of patients with PE still have defects 6 months after diagnosis and then after clot resolution enters a plateau phase.[2] In initial studies performing CT for the determination of residual PE, Remy-Jardin *et al*. found 52% residual defects in 62 patients survived from acute massive PE in a mean time of 11 months, and in Van Rossum *et al*.'s study, in 6 weeks, total resolution

Table 5: Comparison of patients with complete resolution and patients with residual pulmonary embolism in 0-3 months (*n*=61, 44.8% of total population)

	Residual PE (*n*=22; 36.1%)	Complete resolution (*n*=39; 63.9%)	*P*
Age	61.1±14.6	60.4±16.1	0.852
Sex - female	9 (40.9)	19 (48.7)	0.60
VTE history	3 (13.6)	4 (10.3)	0.69
Unprovoked PE	7 (31.8)	10 (25.6)	0.77
DVT signs and symptoms	5 (22.7)	10 (25.6)	1.00
Central PE	11 (57.9)	10 (33.3)	0.14
Pleural effusion	2 (10.5)	11 (36.7)	0.05
RV/LV	1.15 (0.68-2.51)	1.06 (0.61-2.2)	0.49
PA/AO	0.88 (0.65-1.29)	0.85 (0.64-1.3)	0.77
Qanadli (median)	20 (3-40)	7 (1-35)	0.003
D-dimer	5287.7 (358-10000)	5136.7 (550-14400)	0.62
Troponin I	0.15 (0.01-0.6)	0.58 (0.008-6.48)	0.80
NT-pro BNP	4594.7 (14-21300)	1111.7 (13-5197)	0.06
PESI IV-V	3 (16.7)	9 (25.7)	0.73
Time Interval of CT scans (days)	40.5 (13-87)	54.28 (15-88)	0.021

Data are presented as means for continuous variables (age, RV/LV, PA/AO, D-dimer, troponin I, NT-proBNP, and time interval of CT scans) or *n* (%) for categorical variables (sex, VTE history, unprovoked PE, DVT signs and symptoms, pleural effusion, and PESI IV-V). Student's *t*-test was used for comparison of age (*t*=0.187). Other continuous variables were not normally distributed, so Mann-Whitney U-test was used for comparison (*U* values are as follows; RV/LV, 243; PA/AO, 271; D-dimer, 261; NT-proBNP, 90; troponin I, 191; and time interval of CT scans, 276). Chi-square test was used for comparison of categorical variables (Chi-square values are as follows: sex, 0.35; VTE history, 0.16; unprovoked PE, 0.27; DVT signs and symptoms, 0.06; central PE, 2.87; pleural effusion, 4.08; and PESI IV-V, 0.56). DVT: Deep vein thrombosis, PE: Pulmonary embolism, CT: Computed tomography, PESI: Pulmonary embolism severity index, RV: Right ventricle, LV: Left ventricle, PA: Pulmonary artery, AO: Aorta, VTE: Venous thromboembolism, NT-proBNP: N-terminal prohormone of brain natriuretic peptide

of clot was seen in 32% of their patients.[8,9] In both of these studies, available CT technology was capable of imaging central pulmonary arteries. However, in general, different ratios of residual PE are pronounced in variable studies, changing from 15.6% to 36.1% in recent studies using CTPA for the analysis.[10-13]

One reason for heterogeneity is the difference of timing of follow-up test in studies. As our results also confirm, the earlier the follow-up CT is applied, the higher the residual PE ratios are detected. In their systematic review, Nijkeuter *et al*. also found that residual PE was present in 87% of patients 8 days after diagnosis, and this ratio decreased to 52% after 11 months.[2] Furthermore, Choi *et al*. found 24% complete resolution of PE in 3–7 days, increasing to 78% at 22–90 days.[12] In our study group, follow-up CT range was between 13 and 684 days, with a mean of 118 days. As our study is in retrospective design, it is hard to explain the reasons of early follow-up CT. Furthermore, it is not clear whether the PE seen on follow-up CTPA after treatment period is a residual PE or a recurrence. In our patient group, no residual PE was detected in CTPA tests performed after 183 days. No symptomatic deterioration and diagnosis of recurrence was present.

There is no consensus on performing a follow-up diagnostic test after treatment period of acute pulmonary embolism, unless abnormal symptoms or signs are present. Perhaps one benefit of performing follow-up tests is to detect residual PE and prevent wrong classification of persistent vascular obstructions as recurrence.

Table 6: Comparison of patients with complete resolution and patients with residual pulmonary embolism in 3-6 months (*n*=58, 42.6% of the total population)

	Residual PE (*n*=12; 0.7%)	Complete resolution (*n*=46; 79.3%)	*P*
Age, mean±SD	62.6±15.8	63.15±16.3	0.91
Sex - female, *n* (%)	5 (41.7)	22 (47.8)	0.76
VTE history, *n* (%)	0	4 (8.7)	0.57
Unprovoked PE, *n* (%)	3 (25)	8 (17.4)	0.68
DVT signs and symptoms, *n* (%)	2 (16.7)	17 (37)	0.30
Central PE, *n* (%)	3 (27.3)	15 (39.5)	0.72
Pleural effusion, *n* (%)	5 (45.5)	9 (23.7)	0.25
RV/LV, mean (range)	1.14 (0.63-2.00)	0.99 (0.64-1.47)	0.74
PA/AO, mean (range)	0.91 (0.69-1.44)	0.87 (0.65-1.15)	0.68
Qanadli, median (range)	15 (2-30)	6.5 (2-35)	0.26
D-dimer, mean (range)	4048.6 (902-10000)	5348.6 (578-18700)	0.76
Troponin I, mean (range)	0.13 (0.01-0.37)	0.26 (0.003-1.80)	0.69
NT-proBNP, mean (range)	2150.4 (20-8694)	1242.8 (12-6802)	0.69
PESI IV-V, *n* (%)	4 (40)	15 (39.5)	1.00
Time interval of CT scans (days), mean (range)	107 (93-152)	109.8 (90-168)	0.91

Data are presented as means for continuous variables (age, RV/LV, PA/AO, D-dimer, troponin I, NT-proBNP, and time interval of CT scans) or *n* (%) for categorical variables (sex, VTE history, unprovoked PE, DVT signs and symptoms, pleural effusion, and PESI IV-V). Student's *t*-test was used for comparison of age (*t*=0.108). Other continuous variables were not normally distributed, so Mann-Whitney *U*-test was used for comparison (U values are as follows: RV/LV, 195; PA/AO, 192; D-dimer, 206,5; NT-proBNP, 126; troponin I, 179.5; and time interval of CT scans, 270). Chi-square test was used for comparison of categorical variables (Chi-square values are as follows: sex, 0.15; VTE history, 1.12; unprovoked PE, 0.36; DVT signs and symptoms, 1.78; central PE, 0.55; pleural effusion, 1.98; and PESI IV-V, 0.001). DVT: Deep vein thrombosis, PE: Pulmonary embolism, CT: Computed tomography, PESI: Pulmonary embolism severity index, RV: Right ventricle, LV: Left ventricle, PA: Pulmonary artery, AO: Aorta, VTE: Venous thromboembolism, NT-proBNP: N-terminal prohormone of brain natriuretic peptide

We found that the most significant parameter associated with residual PE was clot burden at the time of diagnosis. However, we did not observe any difference between massive and hemodynamically stable patient groups. Furthermore, CT signs of RV overload and pulmonary hypertension, RV/LV, and PA/AO did not differ among the patients with and without residual PE. Choi *et al*., in their study with 764 PE patients grouped according to the time interval of CT scans, found that only independent predictor parameter of residual PE was involvement of large pulmonary vessels.[12] They also found no difference of RV/LV and PA/AO in residual PE patients. However, Alonso-Martínez *et al*. found thrombotic burden, alveolar–arterial oxygen difference, and previous venous thromboembolic disease as factors associated with residual PE.[10] We found no significant association between the previous history of VTE, central PE, or unprovoked PE with residual PE.

Unprovoked PE is a challenging group of PE patients, in which the determination of anticoagulation duration is hard to decide. Contrary to our results, Pesavento *et al*., in their study with 647 PE patients, found that unprovoked PE was significantly associated with residual pulmonary obstruction detected by perfusion scans.[14] Furthermore, Wan *et al*. in unprovoked PE study population found residual perfusion defect in V/Q scan after 5–7 months of treatment in 60% of patients.[15] Both studies also found residual PE as a predictor of recurrence.

Which technique should be used for the detection of residual PE? We used CTPA, as it can already demonstrate minor filling defects even in subsegmental pulmonary arteries. It gives us an anatomic knowledge about pulmonary vasculature. Alternatively, perfusion lung scintigraphy as being the diagnostic utility of choice in chronic thromboembolic pulmonary hypertension gives us a functional information about pulmonary vasculature. In the study of Ma *et al*., the long-term functional consequences of residual PE were investigated, and patients were evaluated with both CTPA and perfusion scintigraphy after 12 months of diagnosis.[16] There was a significant correlation of CT obstruction index and pulmonary vascular obstruction in perfusion scintigraphy at 1 year. Both techniques might be chosen, although V/P scintigraphy has higher sensitivity and specificity for chronic PE.

Our study has some limitations. First, it is a retrospective study. Because of this, missing data did not allow us to consider some variables in our statistical analysis, such as NT-proBNP levels or echocardiographic findings. It has limited number of patients. The results should be confirmed in larger prospective studies.

One may think that usage of two different CT scanners, one with 16-section and another with 128-section, may have an impact on the final outcome of the study. It is expected to detect more residual filling defects with 128-section CT, as it has greater resolution for small vessels. However, in our study population, residual PE was present in 2 out of 30 patients (6.7%) evaluated with 128-section CT. Whereas, in the remaining 106 patients, residual PE was present in 33 patients (31.1%) ($P = 0.008$). However, also follow-up CT timings were longer in the 128-section group as 83.3% were applied after 3 months (with a mean of 130.2 days vs. 83.4 days, $P < 0.001$). Actually, in a favorable CTPA, the main purpose is to provide high contrast material opacification of the pulmonary arteries, ideally with minimum contrast material in the superior vena cava.[17,18] Because of this, the main reason for the difference of residual PE detected may be due to the difference of CT timing rather than the device difference, and this may not have a major impact on the final results, although device difference still stands as another limitation of our study.

The long-term consequences and clinical significance of residual PE are not clear. It is stated that it may be a predictor of recurrent VTE although the study results are conflicting. Poli *et al*., in 236 PE patients, found no correlation of perfusion defects on perfusion scintigraphy with recurrent VTE, whereas high D-dimer levels and residual vascular obstruction on compression ultrasound were significantly associated with thromboembolic recurrence.[19] However, residual pulmonary vascular obstruction detected by perfusion scintigraphy was found to be a significant predictor of recurrence in more recent studies.[14,20,21]

Conclusion

Detection of residual PE has particular importance as it may guide us for the determination of duration of anticoagulant therapy or future risks of adverse outcomes following an acute episode of PE. Predictor factors for residual PE are not clear, but patients with higher clot burden may be in particular importance.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

References

1. Jiménez D, de Miguel-Díez J, Guijarro R, Trujillo-Santos J, Otero R, Barba R, *et al*. Trends in the management and outcomes of acute pulmonary embolism: Analysis from the RIETE registry. J Am Coll Cardiol 2016;67:162-70.
2. Nijkeuter M, Hovens MM, Davidson BL, Huisman MV. Resolution

of thromboemboli in patients with acute pulmonary embolism: A systematic review. Chest 2006;129:192-7.
3. Prandoni P, Lensing AW, Prins MH, Bernardi E, Marchiori A, Bagatella P, *et al.* Residual venous thrombosis as a predictive factor of recurrent venous thromboembolism. Ann Intern Med 2002;137:955-60.
4. Qanadli SD, El Hajjam M, Vieillard-Baron A, Joseph T, Mesurolle B, Oliva VL, *et al.* New CT index to quantify arterial obstruction in pulmonary embolism: Comparison with angiographic index and echocardiography. AJR Am J Roentgenol 2001;176:1415-20.
5. Araoz PA, Gotway MB, Harrington JR, Harmsen WS, Mandrekar JN. Pulmonary embolism: Prognostic CT findings. Radiology 2007;242:889-97.
6. Devaraj A, Wells AU, Meister MG, Corte TJ, Wort SJ, Hansell DM. Detection of pulmonary hypertension with multidetector CT and echocardiography alone and in combination. Radiology 2010;254:609-16.
7. Edwards PD, Bull RK, Coulden R. CT measurement of main pulmonary artery diameter. Br J Radiol 1998;71:1018-20.
8. Remy-Jardin M, Louvegny S, Remy J, Artaud D, Deschildre F, Bauchart JJ, *et al.* Acute central thromboembolic disease: Posttherapeutic follow-up with spiral CT angiography. Radiology 1997;203:173-80.
9. Van Rossum AB, Pattynama PM, Tjin A Ton E, Kieft GJ. Spiral CT appearance of resolving clots at 6 week follow-up after acute pulmonary embolism. J Comput Assist Tomogr 1998;22:413-7.
10. Alonso-Martínez JL, Anniccherico-Sánchez FJ, Urbieta-Echezarreta MA, García-Sanchotena JL, Herrero HG. Residual pulmonary thromboemboli after acute pulmonary embolism. Eur J Intern Med 2012;23:379-83.
11. den Exter PL, van Es J, Kroft LJ, Erkens PM, Douma RA, Mos IC, *et al.* Thromboembolic resolution assessed by CT pulmonary angiography after treatment for acute pulmonary embolism. Thromb Haemost 2015;114:26-34.
12. Choi KJ, Cha SI, Shin KM, Lim JK, Yoo SS, Lee J, *et al.* Factors determining clot resolution in patients with acute pulmonary embolism. Blood Coagul Fibrinolysis 2016;27:294-300.
13. Wang J, Xu M, Sun N, Cheng Z, Sui J. Factors associating with the presence of residual thrombosis after 3-month treatment of acute pulmonary embolism. J Thromb Thrombolysis 2018;45:27-35.
14. Pesavento R, Filippi L, Palla A, Visonà A, Bova C, Marzolo M, *et al.* Impact of residual pulmonary obstruction on the long-term outcome of patients with pulmonary embolism. Eur Respir J 2017;49. pii: 1601980.
15. Wan T, Rodger M, Zeng W, Robin P, Righini M, Kovacs MJ, *et al.* Residual pulmonary embolism as a predictor for recurrence after a first unprovoked episode: Results from the REVERSE cohort study. Thromb Res 2018;162:104-9.
16. Ma KA, Kahn SR, Akaberi A, Dennie C, Rush C, Granton JT, *et al.* Serial imaging after pulmonary embolism and correlation with functional limitation at 12 months: Results of the ELOPE study. Res Pract Thromb Haemost 2018;2:670-7.
17. Albrecht MH, Bickford MW, Nance JW Jr. Zhang L, De Cecco CN, Wichmann JL, *et al.* State-of-the-art pulmonary CT angiography for acute pulmonary embolism. AJR Am J Roentgenol 2017;208:495-504.
18. Moore AJE, Wachsmann J, Chamarthy MR, Panjikaran L, Tanabe Y, Rajiah P. Imaging of acute pulmonary embolism: An update. Cardiovasc Diagn Ther 2018;8:225-43.
19. Poli D, Cenci C, Antonucci E, Grifoni E, Arcangeli C, Prisco D, *et al.* Risk of recurrence in patients with pulmonary embolism: Predictive role of D-dimer and of residual perfusion defects on lung scintigraphy. Thromb Haemost 2013;109:181-6.
20. Planquette B, Ferré A, Peron J, Vial-Dupuy A, Pastre J, Mourin G, *et al.* Residual pulmonary vascular obstruction and recurrence after acute pulmonary embolism. A single center cohort study. Thromb Res 2016;148:70-5.
21. Villari L, Pancani R, Aquilini F, Marconi L, Carrozzi L, Palla A, *et al.* Role of perfusion defects at follow-up lung scan in predicting recurrences after a first episode of symptomatic pulmonary embolism: A retrospective analysis. Blood Coagul Fibrinolysis 2018;29:75-80.