นิพนธ์ต้นฉบับ

ผลการตรวจทางรังสีวิทยากับปัจจัยทำนายความรุนแรงของผู้ป่วยโรคลิ่มเลือดอุดกั้นในปอดเฉียบพลัน โรงพยาบาลสมเด็จพระยุพราชสระแก้ว

นรินทร อู่ทรัพย์, พ.บ.
กลุ่มงานรังสีวิทยา โรงพยาบาลสมเด็จพระยุพราชสระแก้ว จังหวัดสระแก้ว

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บทคัดย่อ

ที่มาของปัญหา : โรคลิ่มเลือดอุดกั้นในปอดเฉียบพลันเป็นหนึ่งในภาวะที่พบบ่อยที่มีความน่าสนใจและท้าทายในเวชปฏิบัติ ซึ่งส่งผลให้เกิดอัตราการเสียชีวิตที่ค่อนข้างสูง

วัตถุประสงค์: ศึกษาลักษณะทางรังสีวิทยากับปัจจัยทำนายความรุนแรงของผู้ป่วยโรคลิ่มเลือดอุดกั้นในปอดเฉียบพลันโรงพยาบาลสมเด็จพระยุพราชสระแก้ว

วัสดุและวิธีการ: คัดเลือกผู้ป่วยที่ผ่านเกณฑ์การวินิจฉัยโรคลิ่มเลือดอุดกั้นในปอดเฉียบพลัน ศึกษาลักษณะทางคลินิกและลักษณะทางรังสีวิทยาโรงพยาบาลสมเด็จพระยุพราชสระแก้ว ข้อมูลต่างๆ ถูกรวบรวมและนำมาวิเคราะห์ โดยแบ่งประเภท เป็นประเภทรุนแรงและไม่รุนแรง

ผลการศึกษา: ผู้ป่วยที่ได้รับการวินิจฉัยโรคลิ่มเลือดอุดกั้นในปอดเฉียบพลันที่เข้าเกณฑ์การคัดเลือก 79 คน เป็น กลุ่มที่มีอาการรุนแรง 17 คน (ร้อยละ 21.5) อายุเฉลี่ย คือ 56.3±14.9 ปี อาการแสดงที่พบบ่อยที่สุด คือ อาการเหนื่อยหอบ (ร้อยละ 62.0) สาเหตุที่พบบ่อยที่สุดคือ โรคมะเร็ง ลักษณะปัจจัยทางรังสีวิทยาพบว่าภาพรังสีทรวงอกที่มีเส้นเลือดแดงส่วนกลางของปอดโต (prominent central PA), การลดลงของเลือดไปเลี้ยงบริเวณที่ปอดที่ขาดเลือด และเงาโป่งของหลอดเลือดดำส่วนกลางปอด มีความสัมพันธ์กับความรุนแรงของผู้ป่วยโรคลิ่มเลือดอุดกั้นในปอดอย่างมีนัยสำคัญทางสถิติ (p < 0.05) ลักษณะปัจจัยเอกซเรย์คอมพิวเตอร์ พบว่าดัชนีการอุดกั้นของหลอดเลือดแดงปอด, ขนาดหัวใจห้องล่างขวาเทียบกับห้องล่างซ้าย (RV/LV ratio), การเบ้ของผนังกั้นหัวใจห้องล่าง (VSB) grade 2, การท้นกลับของสารทึบรังสี (IVC reflux) grade 4-6, การลดลงของขนาดห้องหัวใจห้องบนซ้ายเทียบกับขนาดของเส้นเลือดดำที่ปอด, ขนาด SVC, ขนาดของห้องหัวใจด้านขวาบน และเส้นเลือดแดงส่วนกลางของปอดโต มีความสัมพันธ์กับความรุนแรงของผู้ป่วยโรคลิ่มเลือดอุดกั้นในปอดอย่างมีนัยสำคัญทางสถิติ (p < 0.05) และจากการใช้การวิเคราะห์พหุตัวแปร (multivariate analysis) พบว่าขนาดของห้องหัวใจด้านขวาบน, ภาพรังสีทรวงอกที่มีเส้นเลือดแดงส่วนกลางของปอดโต และ การท้นกลับของสารทึบรังสี (IVC reflux) Grade 4-6 สามารถใช้ทำนายความรุนแรงของผู้ป่วยโรคลิ่มเลือดอุดกั้นในปอดอย่างมีนัยสำคัญทางสถิติได้

สรุป: คนไข้ที่มีการเพิ่มขนาดของห้องหัวใจด้านขวาบนเกิน 57.0 มม (52.0, 61.0), เส้นเลือดแดงส่วนกลางของปอดโต (Prominent central PA) (>3.3 ซม.) และพบการท้นกลับของสารทึบรังสี (IVC Reflux) Grade 4-6 สามารถทำนายความรุนแรงของโรคลิ่มเลือดอุดกั้นในปอดเฉียบพลันได้

คำสำคัญ: โรคลิ่มเลือดอุดกั้นในปอดเฉียบพลัน, ภาพถ่ายรังสีทรวงอก, ลักษณะเอกซเรย์คอมพิวเตอร์หลอดเลือดแดงของปอด

Original article

Radiographic findings with radiologic predictor of severity of acute pulmonary embolism in Sakaeo Crown Prince Hospital

Narinthon Ousap, M.D.

Department of Radiology , Sakaeo Crown Price Hospital, Sakaeo Province

Abstract

Background: Acute pulmonary embolism (APE) is a major public health problem that may present as a clinically challenging or life-threatening condition.

Objectives: To determine radiographic findings with a radiologic predictor of the severity of APE in Sakaeo Crown Prince Hospital.

Methods: Clinical and radiological data of 79 patients with APE were analyzed. All patients were classified by severity into massive and non-massive PE.

Result: 79 patients were recruited to participate in the study. Out of these 79 patients, 21.5% (17/79) were diagnosed with massive APE. The mean age was 56.30±14.90 years old (range 27 - 88). The most common chief complaint was dyspnea (62.0%). The most frequent risk factor was malignancy. Chest radiographic outcomes showing prominent central PA, a decrease in the vascularity of affected areas, and the presence of Knuckle sign were shown to be significantly related to massive PE (p<0.05). CTPE outcomes show that pulmonary obstructive index, RV/LV ratio, VSB grade 2, IVC reflux , decrease width LA/ pulmonary vein, SVC diameter, RA chamber diameter, intraluminal high attenuation and dilatation of central and segmental pulmonary arteries are significantly related to massive PE (p<0.05). Furthermore, dilatation of the RA chamber and prominent central PA and IVC reflux grade 4-6 were statistically significant factors in the prediction of the severity of APE in multivariate analysis.

Conclusions: An increase in the diameter of the RA chamber (ranging from 57.00 mm (52.00, 61.00)), Prominent central PA (cut off >3.32 cm) and IVC Reflux: Grade 4-6 can predict the severity of acute pulmonary embolism.

Keywords: Acute pulmonary embolism (APE), Chest Radiography, Computed tomography pulmonary angiogram (CTPA)

Introduction

Acute pulmonary embolism (APE) is a significant public health problem that may present as a clinically challenging and life - threatening condition.[1] APE is the third most common cardiovascular emergency condition after acute myocardial infarction and acute stroke.[2] Moreover, variation in age and sex of affected patients, the propensity to be masqueraded in affected patients in all disease departments, and the necessity of proper diagnosis and treatment to reduce mortality lead to challenges in the diagnosis of APE.

The true incidence of APE remains unclear, though it appears to be approximately 60-70 per 100,000 people of the general population.[3] The prevalence of PE in Asians is uncertain but undoubtedly underestimated.

The CTPE is now considered to be the standard for diagnosis of APE given its safety, rapidity and accuracy.[4]

Several authors have studied to assess the severity of APE and to predict patients' outcomes, typically focusing on 30-day mortality; this has been relatively less studied in Asian populations. These studies have shown several conflicting outcomes[5] and are less appropriate for imaging outcomes focused on hemodynamics predictions in Thailand. For example, one of the previous studies, Philip A, et al[6] found that CT-predicted ventricular septal defect (VSD) is predictive of death due to PE, whereas RV/LV diameter ratio and embolic burden are not associated with short-term death due to PE. Furthermore, Berghaus, et al[7] found that central thrombus correlates with RV dysfunction and predicts clinical deterioration, whereas large thrombus burden does not correlate well with adverse outcomes. These studies are inconsistent with the study of Narumol Chaosuwannakit[8] which supported that RV/LV ratio and pulmonary obstruction index are potentially useful tools to predict mortality in patients with APE.

This research aimed to study these controversial factors and look for new interest factors under pathophysiology of disease to predict severity based on the hemodynamic status of patients.

Materials and Methods

This retrospective study enrolled one hundred twelve patients (112 patients). Patients who had incomplete data gained from medical records or a lack of complete imaging studies, had underlying heart disease or chronic lung disease, or received thrombolytic therapy were excluded from this study. Thereby, seventy-nine patients diagnosed with APE according to inclusion criteria from ICD -10 data in Sakaeo Crown Prince Hospital in the period from January 2011-July 2018 were studied. The present study has been approved by the ethical committee of Sakaeo Crown Prince Hospital.

Clinical parameters taken from the online hospital information system with blinded radiologic outcomes were analyzed, and the radiologic factors were studied.

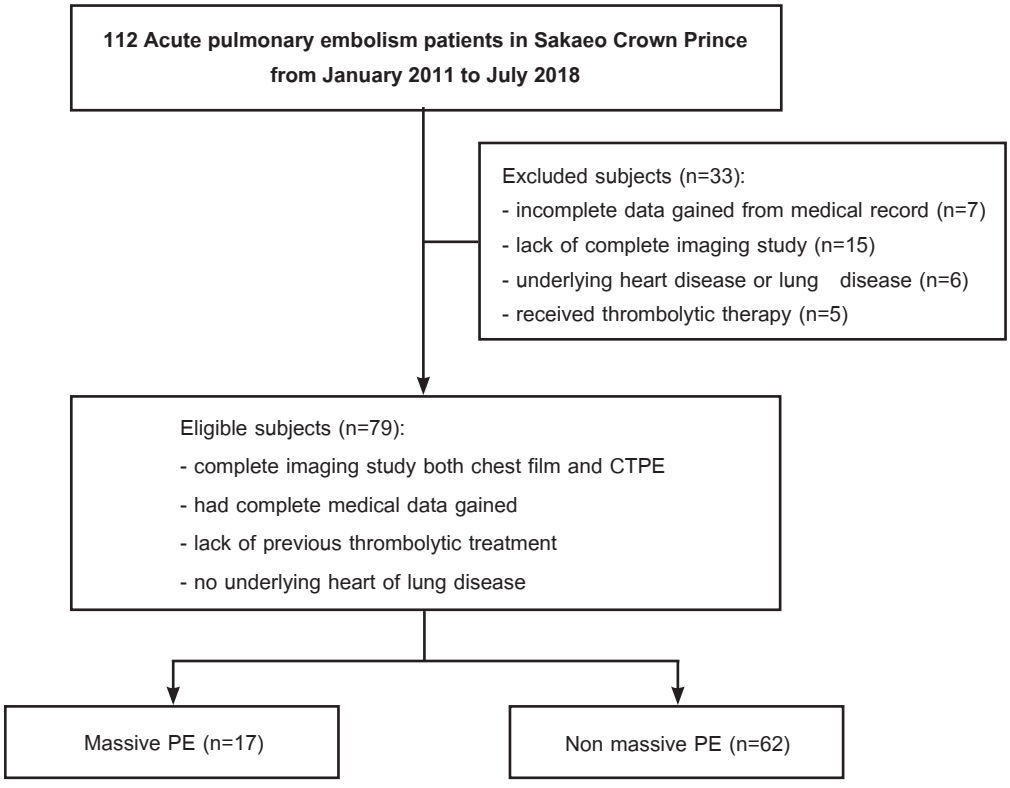

Figure 1 Study flow

Imaging protocol

CT technique

All scans were obtained using multidetector row computed tomography (MDCT) on a 128—MDCT scatter (Phillips, Eindhoven, the Netherlands). The standard protocol was followed, using standard dose rate and total dose of non -ionic contrast agents of CTPE.

Scans were performed on patients in the supine position, holding their breath at full inspiration. The scan areas included 2 -cm below the top of the diaphragm to a level slightly above the aortic arch during a single breath hold. The acquisition parameters are: 120 kVp, 250 mAs, pinch of 1.0 with width 0.5-second rotation time, with reconstruction at section widths of 1-mm (high-resolution CT and pulmonary embolism study). The images were obtained using mediastinal windows (window width 350 HU, window level 50 HU) and lung settings (window width 1500 HU, window level 500 HU), with multiplanar reconstructions.

All chest radiography and CT images were reviewed retrospectively at workstations by the author (with 12 years of experience in radiology), without awareness of any clinical settings. After that, a retrospective review of clinical settings from online OPD/IPD data was performed without awareness of imaging outcomes.

Terminology (according to the American Heart Association, 2011).

1. Massive Acute pulmonary embolism is defined as Acute PE with sustained hypotension. (< 90 mmHg systolic) > 15 minutes or requiring inotropic support.

2. Non-massive Acute pulmonary embolism is defined as Acute PE without evidence of sustained hypotension.(<90 mmHg systolic) > 15 minutes or requiring inotropic support.

Imaging analysis

1. Chest radiography The parameter factor setting following the 2011 Radiology Review Manual.

2. CT non measurement or qualitative data images The parameter factor setting following the 2011 Radiology Review Manual[9].

3. CT measurement data or quantitative data

- Clot burden or vascular obstruction index (percentage of vascular obstruction of pulmonary arterial tree caused by APE).

This was conducted using the scoring system of Qanadli et.al.[10] In the literature, in brief, this index is defined as the number of segmental artery branches that are blocked and corrected by a factor of one for partial blockage or a factor or two in cases of complete obstruction. The highest possible score is 40 (thrombus completely obstructing the pulmonary trunk), which corresponds to a 100% obstruction index.

- Ratio of right ventricular diameter to left ventricular diameter (RV/LV ratio)

This was measured using the axial image of the heart at its widest point, which is usually seen at the atrioventricular valve, by measuring between the inner surface of the free wall and the surface of the interventricular septum[11] After reviewing the literature, the author classified degree as (1) no right ventricular dysfunction (RVD) to mild degree RVD if the ratio was <1.2 (2) moderate RVD if the ratio was between 1.2-1.5 and (3) severe RVD if the ratio was>1.5

- Morphology of the interventricular septum

This was classified as (1) grade 0 or normal if normal septum (2) grade 1 if convex toward the right ventricle or flattened and (3) grade 2 if bowing convex toward the left ventricle.[12,13]

- IVC reflux

This was categorized using axial images divided into six categories according to the reviewed literature.[14] Classified as (1) no reflux into IVC) (2) trace of reflux into IVC (3) reflux into IVC but no hepatic veins (4) reflux into IVC with opacification of proximal hepatic veins (5) reflux into IVC with opacification of hepatic veins down to the mid-portion of the liver and (6) reflux into IVC with opacification of distal hepatic veins.

- The diameter of the main pulmonary artery and the ascending aorta or the PA/AO ratio

This was measured on the transverse image at the point in which the right pulmonary artery is in contiguity with the main pulmonary artery.[15]

- The diameter of the superior vena cava (SVC diameter), and azygos vein (Azygos diameter)

This was measured on a transverse CT scan where the azygos vein reaches the superior vena cava (SVC).[16]

- The diameter of the left atrium and pulmonary vein ratio or the LA/pulmonary vein ratio

This was measured by selecting cuts of axial CT images at the left atrial level (LA), demonstrating the four pulmonary veins and measuring the widest point of the diameter. The LA/ pulmonary vein ratio was then calculated, which were found at various levels.[17-19,]

- The diameter of the right atrial chamber (RA chamber)

This was measured by selecting four view chambers cut, performed in the transverse diameter, perpendicular to the interatrial septum, measured from septal wall to lateral wall.

In accordance with the literature reviewed, a non-ECG-gated chest CT study of pulmonary hypertension patients proposed a right atrial (RA) enlargement cut-off of > 35 mm.[20]

Stat analysis The author divided the patients into two groups (non-massive and massive groups) according to underlying hemodynamic status. Categorial data were reported as count (%) and continuous data were expressed as the mean ± standard deviation (SD), median and interquartile range (IQR). Baseline characteristics and image parameters were analyzed using the Chi-square test, Fisher's exact test for categorical data and Independent t-test, and Mann-Whitney U for continuous data. Univariate and multivariate logistic regression models were applied to evaluate factor prediction of severity presented by odds ratio (95%CI) with *p*-value <0.05 considered to be statistically significant. Statistical analysis was performed by using statistical software programs.

Results

Patients' demographic data are shown Table 1. There was no significant difference between the two groups with regard to patients' demographic data, underlying disease and risk factor, or death within 1 month. The outcome of the chest radiograph (prominent central PA, Decrease vascularity and Knuckle sign) had a statistically significant relationship with massive APE, with a P-value < 0.001.

Table 1 Demographic characteristics data (n=79)

Factor	Total	Non-massive (n=62)	Massive (n=17)	*p* - value
Sex, n(%)				
Male	30 (38.0)	24 (38.7)	6 (35.3)	0.79
Female	49 (62.0)	38 (61.3)	11 (64.7)	
Age (years), mean±SD	56.30±14.90	56.21±14.23	56.65±17.62	0.91
Underlying disease, n(%)				
Yes	70 (88.6)	56 (90.3)	14 (82.4)	0.39
No	9 (11.4)	6 (9.7)	3 (17.6)	
Chief complaint				
Dyspnea	49 (62.0)	37 (59.7)	12 (70.6)	0.41
Dizziness	10 (12.7)	9 (14.5)	1 (5.9)	0.68
Fever	5 (6.3)	4 (6.5)	1 (5.9)	1.00
Chest pain	4 (5.1)	3 (4.8)	1 (5.9)	1.00
Dead within 1 month	25 (31.6)	18 (29.0)	7 (41.2)	0.34
X-ray finding				
Abnormal	65 (82.3)	56 (90.3)	9 (52.9)	0.001
Prominent central PA	38 (48.1)	23 (37.1)	15 (88.2)	< 0.001
Decrease vascularity	26 (32.9)	14 (22.6)	12 (70.6)	< 0.001
Knuckle sign	32 (40.5)	20 (32.3)	12 (70.6)	0.004
Pleural based opacity	14 (17.7)	8 (12.9)	6 (35.3)	0.06
Cardiomegaly	49 (62.0)	36 (58.1)	13 (76.5)	0.16

Table 2 shows that CTPE outcomes had a statistically significant relationship with massive APE, with a p-value of 0.05 ($p < 0.05$).

Table 2 CT measurement and CT non-measurement factor (n=79)

Factor	Total	Non-massive (n=62)	Massive (n=17)	*p* - value
CT measurement				
OB index, n(%)				
< 40%	46 (58.2)	42 (67.7)	4 (23.5)	
40-60%	4 (17.7)	12 (19.4)	2 (11.8)	< 0.001
> 60%	19 (24.1)	8 (12.9)	11 (64.7)	
RV/LV ratio				
0-1.2	52 (65.8)	50 (80.6)	2 (11.8)	
1.2-1.5	10 (12.7)	6 (9.7)	4 (23.5)	< 0.001
>1.5	17 (21.5)	6 (9.7)	11 (64.7)	
VSB, n(%)				
Grade 0-1 (normal to minimal bowing)	68 (86.1)	57 (92.7)	11 (64.7)	0.008
Grade 2 (deviated to left)	11 (13.9)	5 (8.2)	6 (35.3)	
IVC Reflux, n(%)				
Grade 0-3 (mild)	75 (94.9)	64 (98.4)	11 (82.3)	0.03
Grade 4-6(high grade)	4 (5.1)	1 (1.6)	3 (17.7)	
Decrease width LA/ Pulmonary vein, mean±SD	2.89±0.82	3.06±0.77	2.25±0.18	< 0.001
SVC diameter (cm), median (IQR)	1.90 (1.80, 2.10)	1.80 (1.70, 2.0)	2.00 (1.85, 2.45)	0.01
Azygos vein (cm), median (IQR)	0.80 (0.70, 1.0)	0.80 (0.70, 1.0)	1.00 (0.70, 1.15)	0.09
Dimeter of RA chamber (cm), Median (IQR)	36.0 (32.0, 48.0)	35.0 (31.0, 40.0)	57.00 (52.00, 61.00)	< 0.001
CT-non measurement				
Pleural effusion	34 (43.0)	24 (38.7)	10 (58.8)	0.13
Pericardial effusion	14 (17.7)	9 (14.5)	5 (29.4)	0.16
Pulmonary infarction	22 (27.8)	14 (22.6)	8 (47.1)	0.06
Intraluminal high attenuation	15 (19.0)	6 (9.7)	9 (52.9)	< 0.001
Dilatation of central and Segmental pulmonary	29 (36.7)	16 (25.8)	13 (76.5)	< 0.001

Table 3 Univariate analysis

Factor	Crude OR	95%CI	*p* - value
X-ray finding			
Abnormal (ref. normal)	8.30	2.33, 29.58	0.001
Prominent central PA	12.72	2.67, 60.69	0.001
Decrease vascularity	8.23	2.48, 27.35	0.001
Knuckle sign	5.04	1.56, 16.26	0.007
Pleural based opacity	0.27	0.08, 0.94	0.04
Cardiomegaly	2.35	0.69, 8.02	0.17
OB index, n(%)			
40-60% (ref. <40%)	1.75	0.29, 10.74	0.54
> 60% (ref. <40%)	14.44	3.66, 56.91	< 0.001

Table 3 Univariate analysis

Factor	Crude OR	95%CI	*p* - value
RV/LV ratio			
1.2-1.5 (ref. 0-1.2)	16.67	2.50, 111.09	0.004
>1.5 (ref. 0-1.2)	45.83	8.14, 258.09	< 0.001
VSB			
Grade 2 (ref. Grade 0-1)	6.22	1.61, 24.01	0.008
IVC Reflux			
Grade 4-6 (ref. Grade 0-3)	13.07	1.26, 135.23	0.03
Decrease width LA/ Pulmonary vein	0.15	0.05, 0.44	0.001
SVC diameter (mm)	4.15	1.11, 15.51	0.03
Azygos vein (mm)	6.99	0.66, 74.28	0.10
Dimeter of RA chamber (mm)	1.26	1.14, 1.40	< 0.001
Pleural effusion	2.26	0.76, 6.75	0.14
Pericardial effusion	2.45	0.70, 8.65	0.16
Pulmonary infarction	3.05	1.01, 9.37	0.04
Intraluminal high attenuation	10.50	2.95, 37.43	< 0.001
Dilatation of central and segmental pulmonary	9.34	2.70, 32.83	< 0.001

Table 3: univariate analysis of the potential factors of massive APE, statistically significant at P<0.05, presented as Odds ratio as demonstrated

In multivariate logistic regression analysis, factors that had a P-value < 0.1 from univariate analysis were selected for analysis in order to minimize the confounding factors.

Table 4 Multivariate analysis

Factor	adj.OR	95%CI	p-value
Dimeter of RA chamber (mm)	1.21	1.05, 1.39	0.007
Prominent central PA (ref. no)	20.54	1.45, 290.51	0.03
IVC Reflux: Grade 4-6 (ref. Grade 0-3)	2.37	1.02, 5.50	0.05

Discussion

This study concentrated on massive PE because it is the most severe form of PE and may ultimately result in sudden death following a massive obstruction of the pulmonary bed, a significant prognostic that remains controversial. Moreover, the recent radiologic official report of APE mainly focuses on the RV/ LV ratio, but avoids terms such as massive or sub-massive PE without knowledge of the patients' hemodynamics.

From the current study, the most common chief complaint was dyspnea (62.0%), which is correspondent with previous global studies in Thailand and other countries.[21] However, there were some of non-specific chief complaints (such as dizziness 12.7%, fever 6.3%, abdominal pain 5.1%, seizure 1.3% and asymptomatic symptom 1.3%) in this study as well, which supports the challenging and difficult nature of APE diagnosis.

Certain parameters have not yet been reported in the literature (decrease width LA/ pulmonary vein, RA chamber diameter, intraluminal high attenuation) that demonstrated that the dilatation of the RA chamber, and prominent central PA and

IVC reflux grade 4-6 were statistically significant factors for the prediction of the severity of APE in multivariate analysis.

The prominent central PA parameter. (cut off at >3.32 cm)[22] Explanation made by proximal dilatation of affected PA from clot occlusion pulmonary hypertension.

An important parameter for predicting severity in this study was reflux of the dye in the IVC, an indirect sign of tricuspid valve insufficiency that was frequently observed in right-sided heart failure.[23] This sign has not been yet been reported in a study from Thailand. The author found that IVC reflux grade 4-6 was a significant contributor to massive APE with an odds ratio of OR 2.37 (95%CI 1.02,5.50). In other words, it is said that high-grade IVC reflux patients contributed to massive APE 2.37 folds of low grade IVC reflux patients; and so on.

Another new prognostic parameter reviewed in this study is the investigation of the RA chamber's diameter. A correlation between the cut-off value and the severity of an APE has not yet been reported of in Thailand, nor in the worldwide community. According to pathophysiology, an increase in pulmonary vascular resistance may result in RV dilatation, impending RV failure, tricuspid regurgitation and acute Cor pulmonale, which might affect the RA chamber. A non-ECG-gated chest CT study of pulmonary hypertension patients proposed a right atrial (RA) enlargement cut-off of > 35 mm[24] Some of the previous literature found that RA dilatation on transthoracic echocardiography independently predicted fatal PE within 30 days.[25] A recent study found that the diameter of the RA chamber (mm) in the massive group had an average of 57.00 mm (52.00, 61.00), and it significantly contributed to massive APE with an odds ratio of OR 1.21(95%CI 1.05, 1.39).

A limitation of the present study is its small sample size. CTPE was not performed for every patient that was diagnosed with APE and some cases were examined with only non-enhanced study, while several cases were excluded from this study. Furthermore, all of the imaging and medical record data review were done solely by the author which may have affected the interpretation or accuracy of the measurement. Further studies with a larger sample size, meta-analysis, and prospective study design could be needed to reduce these variabilities and confounding effects.

An increase in the diameter of patients' RA chamber and prominent central PA and IVC Reflux: Grade 4-6 can predict the severity of acute pulmonary embolism. From the outcome of this study, this data shows that to improve, the innovation and adaptation of radiologic official reports to predict massive APE conditions absent of known hemodynamic status of patient is necessary.

Conflict of interest The author has no potential conflict of interest to disclose.

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