COMPARISON OF TC-99M APCITIDE SCINTIGRAPHY WITH CT ANGIOGRAPHY IN INTERMEDIATE PROBABILITY OF PULMONARY EMBOLI BY PIOPED CRITERIA USING PULMONARY ANGIOGRAPHY AS A GOLD STANDARD.

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ABSTRACT

Objectives: Ventilation-perfusion (V/Q) lung scintigraphy has been considered to be the first-line investigation for suspected pulmonary thromboembolism (PTE). An intermediate probability finding is problematic. Further investigation is needed to confirm or exclude clots. This study was aimed to evaluate the role of Tc-99m apcitide to diagnose PTE and to compare the diagnostic efficiency with CT angiography (CTA) and pulmonary angiography (PAgram).

Design: Prospective study comparing efficiency of Tc-99m apcitide scintigraphy and CTA to diagnose acute PTE by using PAgram as a gold standard.

Setting: Patients in tertiary care hospital (King Chulalongkorn Memorial Hospital)

Participants: Six out of eightteen patients with intermediate probability for PTE by V/Q lung scintigraphy.

Results: Six patients were studied by Tc-99m apcitide (planar and SPECT) scintigraphy and CTA. Four of these had PAgram. Only one positive planar Tc-99m apcitide study were observed. Three out of four patients had concordant results of SPECT Tc-99m apcitide with PAgram. In one patient with negative Tc-99m apcitide, CTA and PAgram were diagnosed to be pulmonary infarction. For 2 patients in whom PAgram were not performed, Tc-99m apcitide agreed with CTA. Tc-99m apcitide had more positive lesions than CTA and PAgram in 2 patients.

Conclusion: Tc-99m apcitide scintigraphy is a promising mean to detect active clots in PTE. It has a potential to detect more active clots than CTA.

Key Words: Pulmonary embolism, GPIIB/IIIA receptor, scintigraphy, helical CT, pulmonary angiography

V/Q = Ventilation and Perfusion, **PTE** = Pulmonary Thromboembolism, **CTA** = CT angiogram,
PAgram = Pulmonary Angiography, **PIOPED** = Prospective Investigation of Pulmonary Embolism Diagnosis

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INTRODUCTION

Untreated pulmonary thromboembolism (PTE) is a potentially fatal condition. Appropriate use of anticoagulant or thrombolytic agents improves survival.[1,2] However, effective therapy requires an accurate diagnosis. Lung scan is the principal imaging test for the diagnosis of this condition. The use of (ventilation and perfusion) V/Q lung scan is optimized when interpreted as very low, low or high probability of PTE according to the Prospective Investigation of Pulmonary Embolism Diagnosis (PIOPED) criteria with a concordant clinical likelihood of the disease.[3] In patients with lung scan interpretation of intermediate probability of PTE or patients with discordant clinical likelihood of PTE and lung scan interpretation will often require further investigations to diagnose deep venous thrombosis (DVT) using leg ultrasonography or venogram. If no DVT presents, an invasive method, pulmonary angiography (PAgram) should be performed. Many methods have been investigated to avoid performance of an invasiveness of PAgram. Recently, a new thrombus-avid, synthetic peptides labeled with gamma-emitting nuclide, Tc-99m apcitide (Acutect™; Diatide Inc.; Londonderry, NH), has shown its ability to detect acute DVT[4] and possibly pulmonary emboli.[5] CT angiography (CTA) is also a promising imaging method and has been recently used as a second-line procedure to clarify intermediate lung scintigraphic results.[6,7] This study is aimed to identify the use of Tc-99m apcitide scintigraphy to diagnose acute PTE and also to compare the efficacy of Tc-99m apcitide scintigraphy and CTA in detecting acute PTE using PAgram as a gold standard in patients with intermediate probability of PTE by V/Q lung scan.

MATERIALS AND METHODS

PATIENTS

Patients who had intermediate probability of PTE by PIOPED criteria were included in this study. Patients were excluded if they were pregnant or lactating, and if hepatic or renal function were impaired. All patients had clinical suspicion of having PTE or DVT not exceeding 30 days prior to the study. Pre-administered anticoagulant is not a contraindication for this study. Tc-99m apcitide scintigraphy and CTA were performed to diagnose PTE. Pulmonary angiography (PAgram) was used for gold standard. Each method was done within 7 days apart. The study was approved by Ethical Committee of the Faculty of Medicine of the institute. Informed consents were signed by each patient.

Tc-99m APCITIDE SCINTIGRAPHY

Tc-99m apcitide scintigraphic studies were done a day after lung scintigraphy in most patients (5 of 6) except one which was done 5 days apart. 740 MBq of Tc-99m apcitide (Acutect™, Diatech Inc) was injected intravenously with blood pressure monitoring every 15 minutes for 1 hour after injection. Whole body planar anterior and posterior views were obtained 1 and 3 hours post injection, using a single-headed GE Camstar gamma camera equipped with a medium-energy, general purpose, parallel hole collimator. Energy was centered at 140 keV with 20% window width. Single photon emission computed tomographic (SPECT) data at 3 hours post injection were collected 30 seconds/view in 360 degree for 64 views using 128x128 matrix size. Reconstruction was performed by a backprojection algorithm using Hanning filter with frequency cutoff 0.8 cm.[1]

CT ANGIOGRAPHY

Spiral CT of the pulmonary artery was done on Siemens Somatom plus 4 machine. Intravenous application of 100 mL of non-ionic, iodinated contrast medium at a flow rate of 3 mL/

DVT = Deep Venous Thrombosis

second was then performed. Scan was started 25 seconds after the start of injection covering the whole lung with spiral technique using 3 mm. collimation, pitch 1.5 and interval reconstruction 1.5 mm. Patients were instructed to hold breath in deep inspiration during the scan. In dyspneic patients the protocol was adapted accordingly.

PULMONARY ANGIOGRAPHY

PAgram was performed by a radiologist and a cardiologist by using Siemens Polystar machine. Iodinated contrast medium was injected into the main pulmonary trunk and subsequently into the right or left pulmonary artery according to V/Q lung scintigraphic defect. Digital subtraction technique was applied.

Tc-99m apcitide scintigraphy and CTA were done in all patients but PAgram were done in 4 out of 6 patients.

INTERPRETATION

All interpreters were blinded of each other studies results and lung scintigraphic result (except for the radiologist who performed PAgram who knew the side of abnormality in V/Q scintigraphy).

Tc-99m apcitide scintigraphy was interpreted as positive if there were either a persistent collection of this tracer in the area of lung with intensity more than the lung background from 1 hour to 3 hours post injection, or a focal collection in SPECT. All the studies were interpreted twice by a nuclear medicine physician with a lag time of at least 3 months. If the results interpreted were not within the same lobe, a second nuclear medicine physician was asked to confirm the finding.

CTA and PAgram were interpreted separately by 2 experienced radiologists.

CTA interpreter looked for acute and subacute embolism using criteria[8] as follows; intraluminal filling defect, wall adherent with a convex shape, and lack of opacification.

Acute PTE was diagnosed if the interpreter observed any filling defects, peripheral occlusions, and/or wedge-shaped perfusion defects on PAgram in at least 2 views.

All the results were then collected and identified the region of abnormality as upper, middle, or lower lung zone of right or left side. Concordance and discordance results of both Tc-99m apcitide scintigraphy and CTA were then compare with PAgram result.

RESULTS

Six of eighteen patients with intermediate probability V/Q lung scintigraphy according to PIOPED criteria who matched criterias mentioned above (5 women, 1 man; aged 39-74 yr; mean age 56.5 yr) were enrolled into this study. Four patients had PAgram. In the other two, PAgram was not performed due to unstability condition in one patient and the other refused to have this test. Data of each patient are shown in Table1. There were no symptoms suspecting PTE in 2 patients (WJ and AK) but the V/Q lung scintigraphy showed intermediate probability and were included in this study. Patient WJ had previous lung perfusion scintigraphy that showed abnormality. This is mentioned as "old" in Table 1 and also showed a new abnormality in the current V/Q study.

At the start of the study, anticoagulants were given in 4 of 6 patients but not exceeding 4 days prior to the study. Table 2 presents the results of Tc-99m apcitide scintigraphy, CTA, and PAgram.

PIOPED = Prospective Investigation of Pulmonary Embolism Diagnosis.

All planar Tc-99m apcitide studies were negative except for patient WJ (Figure 1). The results present in Table 2 were from SPECT studies. When compared with PAgram results, Tc-99m apcitide can correctly detect PTE in 2 out of 3 sites (one site in PAgram is pulmonary infarction). CTA detects correctly in 1 out of 3 sites. Tc-99m apcitide scintigraphy was not positive in one patient who had pulmonary infarction detected by CTA and PAgram. In 1 patient (patient AK) that had negative PA gram, Tc-99m apcitide scintigraphy and CTA were both negative. In one patient (patient SLE), Tc-99m apcitide scintigraphy was positive in 2 more sites than CTA and PAgram (Figure 2). In 2 patients that PAgram were not performed, Tc-99m apcitide scintigraphy and CTA both showed negative result in one patient (patient SF) and showed some discordant result in the other (patient KM). For the latter patient, both methods concordantly detected the abnormality at RLL but Tc-99m apcitide scintigraphy detected one more lesion at RUL which was concordant with the lesion in V/Q lung scintigraphy.
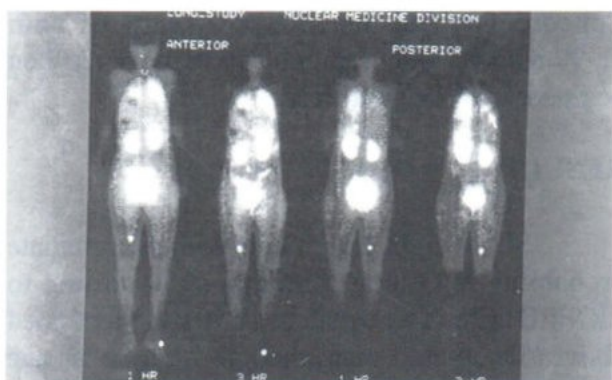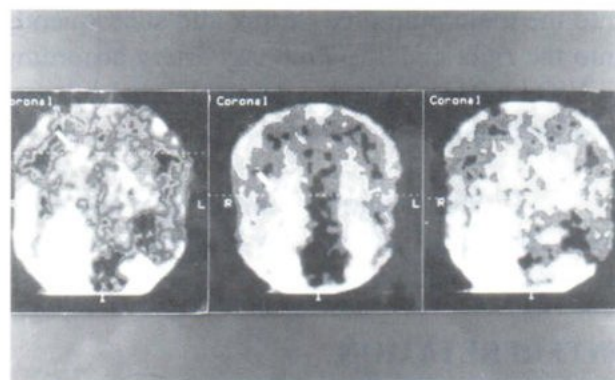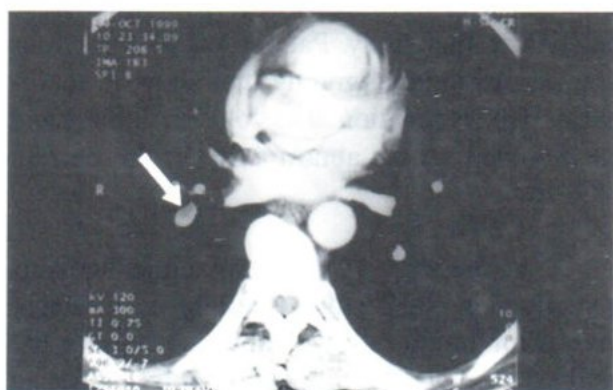

Fig. 1. Tc-99m apcitide whole-body planar scintigraphy at 1 and 3 hours post injection. A focus of abnormal uptake at the right lower lung field clearly seen at 3 hours (arrow). Also the other focus at right thigh.
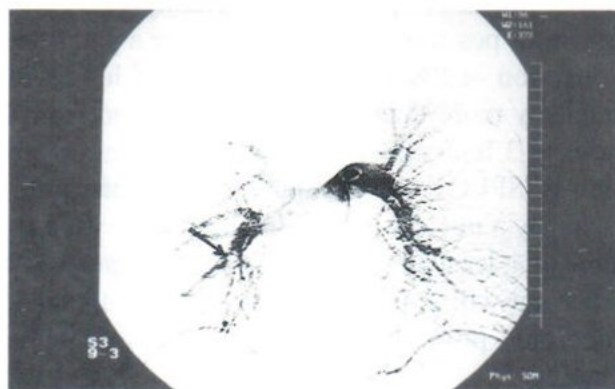

2A

Fig. 2A SPECT coronal views of Tc-99m apcitide revealed 3 foci of abnormal uptake at RUL, RLL, LLL (arrows)

2B

Fig. 2B Filling defect in right segmental pulmonary artery supplying RLL in CTA (arrow)

2C

Fig. 2C Pulmonary angiography (arrow).

TABLE 1. Patient demographics, symptoms&duration, lung scintigraphic result, anticoagulant therapy

Patient	Age	Sex	Symptom/sign	Dura-tion *	Criteris for ITMED[+] By V/Q scan	Defect site	Days of anticoagulant
WJ	39	F	Leg edema	-	1 lare MM	Sup.RLL(new) R apex, L lingula, both lat-basal(old)	1
SF	57	F	Leg edema	1 mo	1 moderate MM	L sup-lingula	13
AK	74	F	Leg edema	-	1 mod. match, neg.CXR	Ant-basal LLL	4
KM	58	F	Leg edema +dyspnea	3 d	1 mod.MM	Post RUL	0
SLE	47	M	Dyspnea	2 d	1 mod.MM	Ant LUL	0
SL	64	F	Dyspnea	7 d	1 mod.MM	Ant-basal LLL	3

* Duration of lung symptoms

[+]ITMED = intermediate lung scintigraphy probability, MM - V/Q mismatched, mod. = moderate size, CXR = chest x-ray

TABLE 2. Results of Tc-99m apcitide scintigraphy, CTA, and PAgram

Patient	Tc-99m apcitide		CTA		PAgram	
	No.*	Site	No.	Site	No.	Site
WJ	1	RLL	1	LLL	2	RUL, RLL
SF	0	None	0	None	ND[+]	-
AK	0	None	0	None	0	None
KM	2	RLL, RUL	1	RLL	ND[+]	-
SLE	3	RUL, RLL, LLL	1	RLL	1	RLL
SL	0	None	0	LUL (infarct)	1	LUL

* No. = number of sites abnormality suspecting of PTE according to criteria mentioned above.

[+]ND = not done

DISCUSSION

Tc-99m apcitide is a radiolabeled synthetic peptide containing an arg-gly-asp (RGD) sequence which enables the binding to the GP IIb/IIIa receptor expressed on the activated platelets.[9,10] It has been successfully used for the detection of acute deep venous thrombosis[4,5,11,12,13,14] for many years. However, for the use in acute pulmonary embolism diagnosis, there were only few cases that were reported in a series of deep venous thrombosis study.[5] From our result, although there were not a large number of cases, Tc-99m apcitide scintigraphy is able to detect more positive lesions than CTA. These are considered to be true in cases of a new thrombus. Old thrombus or infarcted lung should not be positive in Tc-99m apcitide scintigraphy. This was confirmed in 2 patients, one (patient SL) with pulmonary infarction, the other (patient WJ) with old persistent defect seen in V/Q lung scintigraphy and had positive PAgram. Compared with CTA, Tc-99m apcitide agreed with CTA in 4 out of 6. Two of which were negative and the other two were positive for PTE. From all the data presented in this study, we found that there was no false negative for active clot detection by Tc-99m apcitide scintigraphy. However, there were some false positives of this test when we use PA gram as a gold standard. Two patients had positive Tc-99m apcitide lesions with negative CTA and PAgram (patient KM and SLE). The results may be false positive from some other conditions mentioned elsewhere[5,15] or peripheral lesions that could not be detected by the other 2 modalities.[16,17] In one of these 2 patients (patient KM), the positivity in Tc-99m apcitide scintigraphy was concordant with lung perfusion scintigraphy reflecting a possibility of true positive lesion. For the other false positive, inhomogeneity and high background causing difficulty of identifying true lesions may explain it. In these kind of patients, further delayed study may improve the lesion to background ratio. Some pitfalls of using Tc-99m apcitide scintigraphy are 1) the high background in the lung, even in the delayed study, making it difficult to detect clots by planar method. Thus, time consuming because of the need of SPECT, 2) The cost that is still high. The promising advantages are the direct targeting to the active clots and can be examined throughout the body in one study, which may be more cost-effective than performing other modalities in separate studies for deep venous thrombosis and PTE. Further study of more patients for sensitivity and specificity study, survival, and cost-effectiveness analysis should be done to see whether this test can be incorporated into the pulmonary embolism management line.

This study is the one to present a new imaging modality and new clinical potential indication for Tc-99m apcitide to help in the diagnosis of acute pulmonary thromboembolism.

CTA = CT angiogram, **V/Q** = Ventilation and Perfusion **PAgram** = Pulmonary Angiography, **PTE** = Pulmonary Thromboembolism

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