Lower limb deep vein thrombosis in patients with suspected pulmonary embolism detected with ^{99m}Tc-MAA simultaneously with lung perfusion scan

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Abstract

The aim of this study was to evaluate the incidence of deep vein thrombosis (DVT) in patients with suspected pulmonary embolism (PE) and the relation between PE and the site of DVT by using technetium-99m-macroaggregated human serum albumin (^{99m}Tc-MAA) radionuclide venography (RNV). *Technetium-99m-MAA radionuclide venography was performed* simultaneously with lung perfusion scintigraphy in 123 patients with suspected PE. *The incidence of DVT* in patients with suspected PE was 58.54%. The incidence of DVT in patients with PE was 77.46%, while in patients without PE was 32.69%. The rate of proximal DVT in patients with PE was 74.55%, while in patients without PE was 47.06%. The average embolic lung segments in patients with proximal DVT and patients with distal DVT were 6.2±2.3 and 3.1±1.2, respectively. *In conclusion*, lower limb ^{99m}Tc-MAA RNV demonstrated a high incidence (58.54%) of DVT in patients with suspected PE. The prevalence of DVT was higher in patients with PE than in patients without PE. Pulmonary embolism was more likely to occur in patients with proximal DVT, and more embolic lung segments were detected in patients with proximal DVT.

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Introduction

Pulmonary embolism (PE) is a common disease in Western countries. It has been estimated that the incidence of PE is 1 case per 1000 persons per year in the United States [1]. In China where PE has been perceived as less common for a long time, the incidence of PE in hospitalized patients increased from 0.27% in the 1970s to 0.94% in this century [2].

Over the last several decades, physicians have realized that PE is not a local disease but rather a complication of venous thromboembolism (VTE), sometimes due to an intra-atrial thrombus [3] but most commonly due to deep vein thrombosis (DVT). More than 90% of acute PE is caused by DVT from veins in the lower limb or pelvis [4]. Searching for DVT of the lower limb plays an important role in the treatment plan of PE, especially for inferior vena cava filter placement [5]. However, DVT is not easily diagnosed. Clinical examinations are unreliable for the diagnosis of DVT [6]. A more accurate method is the use of medical imaging to detect DVT of the lower limb [7-11].

Contrast X-ray venography is regarded as the gold standard diagnostic test for DVT, but it is invasive and thus cannot be used as a routine application. Ultrasonography is the most commonly used test. However, it has limited sensitivity for detecting DVT below the knee, especially in obese patients (important because obesity is a VTE risk factor) [12]. Computed tomographic venography can accurately detect DVT, and recently it is recommended in combination with CT pulmonary angiography (CTPA) to evaluate both PE and DVT in a one-step diagnostic study [13]. However, the high radiation exposure of both studies leads many radiologists to argue its use as a routine application [14].

Technetium-99m-macroaggregated human serum albumin (^{99m}Tc-MAA) radionuclide venography (RNV) is a method with lower radiation dose than X-ray imaging. It is also usually performed simultaneously with lung perfusion scintigraphy to evaluate both DVT and PE in a same setting, but this combination does not add an extra radiation exposure to patients. In this study, we will analyze the use of ^{99m}Tc-MAA RNV performed simultaneously with lung perfusion scan to detect DVT in patients with suspected PE.

Materials and methods

This was a retrospective study and was approved by the Institutional Review Board. Informed consent was waived. A review of patients' data with suspected PE who were referred to perform ^{99m}Tc-MAA RNV and lung perfusion scintigraphy in the department of

nuclear medicine was undertaken. One hundred and twenty three patients (72 male, 51 female, 24-85 years, mean 56 years) were included between January, 2003 and December, 2010. Detailed review of the patient files and records was performed. All available images were reviewed by two experienced radiologists with more than 20 years experience in nuclear medicine. Possible doubts or disagreements were resolved by a third radiologist.

Technetium-99m-MAA RNV was performed using a GE Hawkeye VG dual headed detector scanner with a low energy general purpose collimator. The patient was supine on the scanning table and tourniquets were applied above the ankles to avoid superficial vein flow and to promote radionuclide tracer flow/concentration in the deep vein. Intravenous access to bilateral dorsal veins was established with two three-way stopcocks connected with a syringe. A dose of 74~111MBq /3mL of ^{99m}Tc-MAA was simultaneously injected slowly into each dorsal vein for 1min. Ten mL of normal saline were injected into the bilateral dorsal vein immediately to flush the ^{99m}Tc-MAA. The acquisition began at the same time as the injection at a rate of 40cm/min in whole body scan mode. Patients were scanned from toes to lower neck then tourniquets were released. Each patient either left the scanning table to walk or exercised his/her legs on the table for 3min. Another whole body scan (delayed-phase image) was then performed at a rate of 20cm/min. After the delayed-phase scan, the patient being still in the supine position, the lung perfusion scans(Q) in 8 projections(posterior, anterior, left lateral, right lateral, right anterior oblique, right posterior oblique, left posterior oblique, and left anterior oblique) was performed with 256×256 matrix. Images were collected with a 20% energy window setting at 140keV, each acquired in a minimum of 400,000k-counts. Patients with perfusion defects were referred to perform ventilation scan (V). Ventilation scintigraphy was conducted after the patients had quiet tidal inhalation of ^{99m}Tc-technegas which was made at the department of nuclear medicine of our institution.

The interpretation criteria of DVT were based on the following: (a) flow defect in the lower limb; (b) interruption of flow; (c) irregular or asymmetric filling of the deep vein (low flow); (d) presence of collateral vessels; and (e) abnormal radionuclide retention on delayed-phase images [10, 15]. Scoring was based on a 5-point scale, and more than 2 points was considered DVT positive. According to DVT two groups were formed proximal DVT (located in or above the popliteal vein) and distal DVT (below popliteal vein) according to the site of most proximal DVT.

The ventilation/perfusion (V/Q) scan was evaluated according to the modified PIOPED criteria [16]. Scans were considered normal when perfusion was normal. Perfusion defects were classified as segmental if they involved more than 75% of a segment. All other perfusion defects were defined as small defects (ie, less than 25% of the segment). Very low probability scans were assessed if the abnormalities were limited to 3 or less than 3, small perfusion defects. High probability scans were assessed by the presence of at least 2 segmental defects associated with normal ventilation (V/Q mismatched). Intermediate probability scans were classified as those that could not be placed in the normal/very low probability or the high probability categories. The diagnosis of PE was based on the following: patients with normal lung perfusion scans or with very low probability were excluded from PE. Patients with high probability V/Q scan were diagnosed as PE; patients with indeterminate scintigraphy were referred to further tests such as pulmonary angiography or further clinic follow-up to make the final diagnosis.

Statistical methods

Mean values and SD were calculated using standard formulas. The comparisons between mean values were made using Student's t test. The χ^2 test was used for the comparison of observed percentages.

Results

The detection of DVT

Of 123 patients, 71 were diagnosed with PE, 52 patients were negative for PE. There were 72 patients with detected DVT (72/123, 58.54%), 55 cases were found in patients with PE, whereas 17 cases in patients without PE. The incidence of DVT in patients with PE and patients without PE was 77.46% (55/71) and 32.69% (17/52), respectively. The incidence of DVT in patients with PE was significantly higher than in patients without PE (χ^2 =24.791, P<0.05). Two representative images of a patient with DVT and PE are presented in Figures 1 and 2.

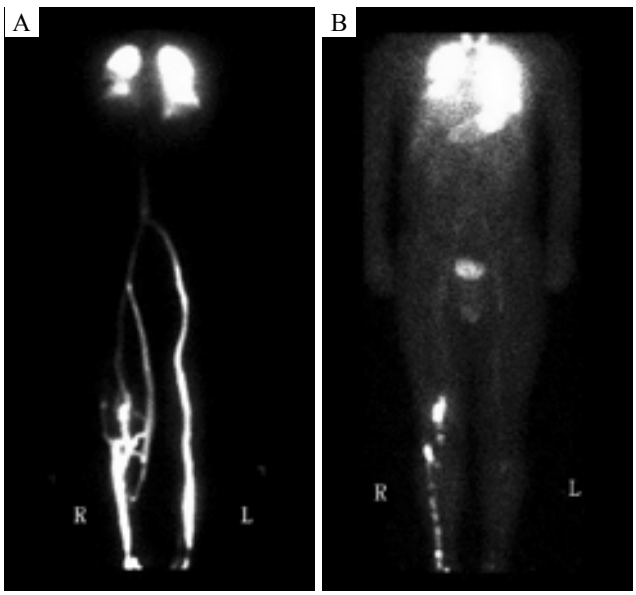
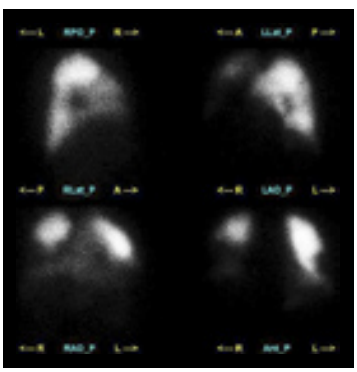


Figure 1. The ^{99m}Tc-MAA RNV image of a 39 years old man with PE. A. Flow defect and collateral vessels can be found in early-phase imaging. B. Irregular or asymmetric filling of the deep vein and abnormal radionuclide retention on delayed-phase imaging can also be noted in the right lower limb. The abnormal lung perfusion scan and more details of lung perfusion are shown in Figure 2.



The site of DVT

Of the 55 cases of DVT in patients with PE, 25.45% (14/55) patients were found to have distal DVT, while 74.55% (41/55) were to have proximal DVT. Of the 17 cases of DVT without PE, 52.94% (9/17) were with distal DVT and 47.06% (8/17) were with proximal DVT. The rate of proximal DVT in patients with PE was significantly higher than in patients without PE (χ^2 =4.513, P<0.05).

The number of embolic lung segments in PE patients with different sites of DVT

There were 44 embolic lung segments found in 14 PE patients with distal DVT, the average was 3.1±1.2 embolic lung segments per patient. No patient with distal DVT suffered from a whole lung lobe embolism. There were 254 embolic lung segments found in 41 PE patients with proximal DVT, the average was 6.2±2.3 embolic lung segments per patient, and 18 patients suffered from a whole lung lobe embolism. There was a statistically significant difference in the number of embolic lung segments between patients with distal DVT and proximal DVT (t=4.873, P< 0.05).

Discussion

Technetium-99m-MAA RNV has been established for detecting DVT since the 1970s [17]. It has high overall concordance with the gold standard test of DVT [9, 16]. In our study, we used ^{99m}Tc-MAA RNV to detect DVT in patients with suspected PE, the result showed that the incidence of DVT in patients with suspected PE was 58.54% (72/123), and the incidence of DVT in patients with PE was 77.46% .This figure is higher than that of a meta analysis, which demonstrated that the prevalence of DVT was approximately 18% in patients with suspected PE and 36%-45% in those with proven PE [18]. We think that this difference may be explained by two aspects. One aspect is the higher threshold in our institution for referring patients with suspected PE for 99mTc-MAA RNV and lung perfusion scintigraphy, and the other is different medical imaging methods used in different studies. The meta analysis also demonstrated that there was a large heterogeneity of the prevalence of DVT, which ranged from 10% to 93% in proven PE, and the prevalence of DVT in our study using venography as detecting method, which was higher than in other studies using ultrosonography [18]. In our study, the incidence of DVT in patients with PE was similiar with Girard's report (the incidence was 81.7%), who used venography and pulmonary angiography to diagnose DVT and PE respectively [7]. This concordance with the gold standard test implies that ^{99m}Tc-MAA RNV is a reliable method for detecting DVT in patients with PE.

Our study demonstrated that the incidence of DVT in patients with PE was significantly higher than in patients without PE (77.46% *Vs* 32.69%). This implies that DVT of the lower limb is common in patients with PE. However, it should be noted that even in patients without PE, the incidence of DVT in our study was still high as 32.69%, and the incidence of DVT in patients with suspected PE was high as 58.54%. Since half of patients with suspected PE can be detected with DVT, it is necessary for patients with suspected PE to perform ^{99m}Tc-MAA RNV simultaneously when lung perfusion scintigraphy is performed. These patients detected by DVT and without PE should be in surveillance for PE for some time. After all, PE is considered as a complication of DVT and patients with DVT should be regarded as high-risk population for PE.

The other result of our study showed that the rate of proximal DVT in patients with PE was higher than in patients without PE. This result was concordant with another study using venography to detect DVT [19]. This implies that PE is more likely to occur in patients with proximal DVT than in those with distal DVT. Furthermore, it seems that the involved area of embolic lung is related to the site of DVT. In our study, 18 patients among patients with proximal DVT suffered from a whole lung lobe embolism, while no patients with distal DVT suffered from a whole lung lobe embolism, and more lung segments were embolic in patients with proximal DVT than in those with distal DVT. We conclude that this is because proximal DVT is bigger in size than distal DVT. Once the proximal DVT dislodges, it may obstruct the pulmonary lobe artery as a whole clot, or if broken into smaller pieces, obstruct more segmental arteries than distal DVT. Other researchers have also reported similar results [20].

In recent decades V/Q scintigraphy has been overtaken by CTPA for diagnosing PE [21], ^{99m}Tc-MAA RNV, which usually combined with lung perfusion scan, has also been underestimated. In fact, V/Q scintigraphy is as good as CTPA in ruling out PE [22-24]. Sometimes patients are over diagnosed as PE, by detecting smaller pulmonary emboli on CTPA exams that might not be of clinical significance. Furthermore, V/Q scintigraphy has much lower radiation exposure dose than CTPA. The radiation exposure associated with multidetector CT is about 7-30mSv depending on device and protocol. Breast radiation by using 4-slice CTPA is also varying from 20 to 60mSv. Comparatively, a full V/Q study delivers only 0.28 to 0.9mSv [24, 25]. It is difficult to ignore this enormous 65- to 250-fold difference between the 2 procedures. As some physicians appeal to continue including V/Q scintigraphy in PE diagnosis [26-28], attention should be paid to the combination of ^{99m}Tc-MAA RNV and perfusion scan in evaluating patients with suspected PE and DVT.

In conclusion, our study demonstrated that there is a high incidence of DVT detected by ^{99m}Tc-MAA RNV in patients with suspected PE. The prevalence of DVT was higher in patients with PE than in patients without PE. Pulmonary embolism was more likely to occur in patients with proximal DVT, and more embolic lung segments were detected in patients with proximal DVT. It is the opinion of the authors that it is necessary for patients with suspected PE to perform ^{99m}Tc-MAA RNV simultaneously when lung perfusion scintigraphy is performed.

The authors declare that they have no conflicts of interest.

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