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The Role of CT Angiography in Diagnosing Patients Suspected to Pulmonary Embolism

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ABSTRACT

Pulmonary embolism (PE) is a blockage of the main pulmonary artery or one of its branches by a substance that has travelled from elsewhere in the body through the bloodstream (embolism). Pulmonary embolism (PE) is the third most common cause of cardiovascular related mortality. Numerous diagnostic tools have been utilized in order to improve diagnosis and prompt appropriate treatment. Since the first introduction of Computed Tomography (CT) angiography in the setting of PE diagnosis algorithm, it has rapidly become as the first choice among imaging techniques. However, still there is long way to improve the abilities and lowering the possible hazards and problems. The purpose of this review is to evaluate and summarize the role of imaging tools in diagnosis of PE in suspected patients, with particular focus on CT angiography. We studied different areas related benefits, disagreements and challenges in utilizing CT angiography in the setting of PE diagnosis algorithm. Although CT angiography is still the imaging of choice in rule-outing PE in suspected patients, there are areas of uncertainty in the field of over-diagnosing of CT angiography and consequent over-treatment.

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Introduction

The term Venous Thromboembolism (VTE) covers two relative incidences of Deep Vein Thrombosis (DVT) as well as Pulmonary Embolism (PE). In cardiovascular diseases, VTE posed the third position of the most frequent with 0.1-0.2 percent overall annual incidence (1, 2).

One of the most critical clinical scenarios of VTE is acute PE. It is hard to estimate PE prevalence and/or incidence in which it may remain asymptomatic for years and diagnosed as an incidental finding and in other hand, their first presentation could be sudden death (2-4). However it is estimated that over 317000 deaths were due to VTE in a 454.4 million population in Europe. Of these, only 7% were diagnosed as PE before they had been died (2).

VTE is considered to increase with age, as its risk approximately doubled following each decade after 40 years old. However its annual incidence in children is about 0.05 and 0.014-0.049 percent in hospitalized patients and large groups of community of children, respectively (5-8).

Diagnosis of pulmonary embolism

On the basis of guidelines, the cornerstone of management of PE is based on differentiating a "confirmed PE" in which evidences indicate probability of PE is high enough to initiate a specific treatment, and "excluded PE" in which the risk of PE is as low as the specific treatment could be withhold (9). There are numerous diagnostic tools with variable indications and contraindication and also variable sensitivity and specificity ranges including clinical probability (mostly on the basis of Wells score), D-dimer testing, lung scintigraphy, pulmonary angiography, magnetic resonance angiography, echocardiography, compression venous ultrasonography and Computed Tomography (CT-angiography) (9). In this review, we are going to specifically focus on CT-angiography as the imaging modality of choice in PE diagnosis.

Computed tomographic pulmonary angiography

For decades, invasive angiography of pulmonary arteries considered as "gold standard" for PE diagnosis.

However, gradually with introduction of Multi-Detector Computed Tomographic (MDCT) angiography, which was less invasive than

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conventional angiography with equivalent diagnostic value (10), CT angiography gained the first position for diagnosis PE in suspected patients. Its high spatial and temporal resolution let us to examine arterial vasculature down to pulmonary segmental level (11-13).

In PIOPED II trial (14), declare the relationship between clinical probability and predictive value of MDCT in PE diagnosis. Overall sensitivity and specificity of MDCT was calculated 83% and 96%, respectively. However, as clinical probability of PE on the basis of the Wells rule increased from low to moderate and especially to high, negative predictive value for PE decreased dramatically (96%, 89%, and 60% respectively).

On the other hand, the positive predictive value was obviously higher (92–96%) as the clinical probability getting higher from 58% in low probable patients to 92-96% in high or intermediate probability of PE (14). Some studies demonstrate that MDCT could be used in as the only imaging test in PE-suspected patients.

For example, In Perrier study (15), 756 consecutive patients with high probability for PE and also non-high probable patients but with a positive Enzyme-Linked Immunosorbent Assay (ELISA) D-dimer test were examined with lower extremities sonography and MDCT. The results showed only 0.9% of patients with a proximal DVT in lower limbs, had negative MDCT for PE (15).

In van Belle study, patients with either a high PE probability on the basis of Wells rule or a positive D-dimer test, were examined by MDCT and followed for three months. These authors declared that the risk of thromboembolic incidences in patients with negative CT who left untreated was as low as 1.1% in the following 3 months (16).

In a Canadian study, Anderson evaluate 1417 PE-suspected patients with either a 4.5 or greater Wells score or a positive D-dimer test with ventilation/perfusion (V/Q) scan or CT-angiography, randomly. They demonstrated in 3-month follow-up period, among patient with a negative CT only 1.3% (7 of 531) of patients had a DVT and only one patient suffered a thromboembolic event (17). Consequently they specify a 1.5% risk of thromboembolic event in patient with suspected PE in which assessed only by CT-angiography as an imaging modality (17).

The above results were further confirmed by a European study of Righini in which 1819 clinically suspected PE patients were randomized to assess by a D-dimer and CT-angiography strategy or D-dimer, CT-angiography and venous compression ultrasonography (CUS) of lower limbs. Results showed no difference between these two arms of study as the thromboembolic risk was 0.3% in both groups in 3-month follow-up. These results demonstrated combine D-dimer and CT-angiography strategy is sufficient enough to exclude PE (18).

Areas of uncertainty

However, still there are areas of uncertainty in using CT-angiography. One of these challenges is isolated sub-segmental PE which is found in 4.7% and 9.4% of patients using single-detector or multi-detector CT-angiography, respectively (19). As the positive predictive value of Ct-angiography is relatively low in the levels below segmental level (20), it is recommended to utilize CUS in these cases in order to rule out DVT and define if it is necessary to initiate treatment (9). However, initiating treatment in cases with sub-segmental PE and without DVT is basically upon clinical probability and other possible comorbidities (9).

Some authors suggest adding CT-venography in combination to CT-angiography to improve its ability to diagnose contemporary DVT in a single procedure.

As in PIOPED II trial, combining these two modalities was associated with 7% increase in sensitivity (83% to 90%) with the same specificity of 95% (14, 21). It should keep in mind that adding CT-venography add further amount of irradiation and therefore limit its use especially in young women (22).

As it was found that CT-venography and CUS had similar clinical value in symptomatic patients with DVT (21), it seems using sonography could be a wise substitute. Another controversial situation in this field is finding incidental PE with 1-2% frequency in all thoracic CT scans. These incidental findings were mostly found in patients with cancer, paroxysmal atrial fibrillation, heart failure and history of atrial fibrillation (23–26). It is controversial whether initiate anti-coagulant therapy in these asymptomatic or even unsuspected patients for PE. However, it is accepted in overall that anti-coagulant therapy should be initiated in cancer patients and also in those with clots at the lobar or more proximal level (27).

Finally, some authors believe that introduction of CT angiography as a diagnostic tool in PE-suspected patients has led to over diagnosis (28). It was observed in a study with randomized comparison that nevertheless V/Q scanning less frequently diagnoses PE than CT-angiography; outcomes in a 3-month follow-up were even between two groups (17).

Additionally, although there is an 80% increase in PE diagnosis after using CT in United States, no significant change was observed in mortality rate due to PE (29, 30).

Conclusion

Pulmonary embolism is potentially life threatening and undoubtedly rapid diagnosis and treatment could improve disease prognosis. Therefore rapid and reliable diagnostic tools are the simple needs in this setting.

After introduction of CT-angiography, it rapidly becomes the first choice in imaging modalities due to its high sensitivity and specificity. Also some authors claimed that it could be used as the only imaging modality in PE-suspected patients. However, every method has its advantages and disadvantages. Although

so many lives have been saved in this way, but many are harmed due to over-diagnosis and/or overtreatment.

Additionally it should be mentioned that CT angiography is still weak in diagnosing sub-segmental pulmonary emboli. On the other hand, it is not completely defined which small emboli need be treated and improve outcomes.

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