Original Article

Evolution Role of Imaging Techniques in Diagnosis and Management of Pulmonary Embolism

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Abstract

Background: Pulmonary embolism (PE) is a common cause of mortality from cardiovascular disease, preceded only by myocardial infarctions and cerebrovascular accidents. The diagnostic challenge of pulmonary emboli divides into missing the emboli or overuse of imaging before initiating needed therapy. PE can be misdiagnosed and inevitably fatal in vulnerable populations when untreated. **Objectives:** In this paper, we focused on diagnostic imaging in pulmonary embolism patients, and only relevant studies were discussed. **Methodology:** PubMed database was used for articles selection. The papers on imaging modalities and pulmonary embolism detection were obtained and reviewed. **Conclusion:** Pulmonary embolism is a fatal disease when identified late and improperly managed. Further intensive work is required in the field of pulmonary embolism imaging. The approach for diagnosis and rapid management of fatal diseases has changed during the last 50 years. The advent of new radio-pharmaceuticals and optimized radiosensitive tracers would be an advantageous addition to current imaging modalities.

Keywords: Pulmonary Embolism, Imaging Modalities, Venous thromboembolism

Introduction

Increasing urbanization in many developing countries by modification of lifestyle has confronted them with the challenge of doubling illnesses [1]. During the last ten years, the incidence of cardiovascular diseases has been increasing substantially in the world [2, 3]. The people with a history of cardiovascular disease are exposed to the high risk for suffering from complications such as hypertension [4], atherosclerosis [5], and pulmonary embolism (PE) [6]. PE is a common cause of mortality and among cardiovascular diseases, it is preceded only by myocardial infarctions and cerebrovascular accidents. It has a major impact on the population with the European guidelines reporting an annual incidence rate of pulmonary embolism of approximately 0.5 to 1.0 per 1,000 inhabitants [7]. Pulmonary embolism falls under the spectrum of venous thromboembolism and was described for the first time two centuries ago, by Virchow. He also described its triad of hypercoagulability, endothelial injury, and hemodynamic stasis and the triad was named after him. During this Virchow's era, a pulmonary embolism was fatal and remained that way until the early 1960s when the clinical trial on heparin was initiated [8]. Pulmonary embolism diagnosis is challengeable due to many factors, like missing the emboli entirely, and/or overuse of imaging modalities before initiating needed therapy. As a result, pulmonary embolism is, more often than not, misdiagnosed or diagnosed late, with fatal consequences when unmanaged or late therapy, and death rates reaching up to 30% [9, 10]. Our aim in this paper was to identify the diagnostic approach of a pulmonary embolism with the comparison of current imaging

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modalities as published in recent literature, and we shed light on the other aspects of pulmonary embolism such as pathophysiology, clinical factors, and management.

Methodology

PubMed database was used for article selection, and the following keys were used in the mesh ("Pulmonary Embolism" [Mesh] and "Diagnostic Imaging" [Mesh]). In regards to the inclusion criteria, the articles were selected based on the inclusion of one of the following topics; pulmonary embolism pathophysiology, ventilation-perfusion, imaging evaluation, and diagnosis. Exclusion criteria were all other articles that did not have one of these topics as their primary endpoint.

Discussion

Venous thromboembolism (VTE), which includes both deep vein thrombosis (DVT) and pulmonary embolism (PE) can occur due to many factors, and generally, they can be classified in the Virchow's triad (hypercoagulability, endothelial injury and hemodynamic stasis). Common risk factors include age, previous history of VTE, pregnancy, long flight hours, immobilization, and cancer. Unfortunately, up to 30% of cases of PE still develop idiopathically and the physician cannot pinpoint any risk factors. In the clinical setting, the majority of patients with PE tend to complain primarily of sudden-onset or worsened resting dyspnea as well as progressive (exercise-induced) dyspnea. Other presentations include chest pain similar to the angina of ischemic origin (sharp, stinging, and occasionally related to respiratory excursions), cough, hemoptysis, and syncope. Unfortunately, some of the patients may present as a silent PE (i.e. with no symptoms), and only with DVT upon presentation. Generally, patients with pulmonary embolism often present with pleuritic rather than central chest pain. Some Important clinical features that can be found are loud pulmonary second sound, S3 and S4 gallop, and cyanosis [11]. Other signs that can be seen are tachypnea, tachycardia, and hypotension which is noted in serious cases and may lead to cardiac arrest and/or shock. The location of the embolism may be a factor in the presentations' complain; for example, extensive central PE may present with rapidly progressive dyspnea along with a major hemodynamic instability. However, minor embolisms occluding peripheral branches produce minimal symptoms or present as a lung infarction syndrome [12].

Complications and its Pathophysiology

The most notable complication in pulmonary embolism is sudden pulmonary hypertension, however, this may not reflect the morphological severity because large emboli may present as a hemodynamically minor PE and vice versa. This may be due to compensatory mechanisms in lungs and heart, and this was noted in people with no comorbidities that they can sustain normal status even with 30% to 50% pulmonary bed obstruction before developing pulmonary hypertension. As a result of pulmonary hypertension, the right ventricular overload will increase, resulting in dilatation, right heart failure, sub-endocardial RV ischemia, and possibly even infarction. This right ventricular sudden failure may result in the sudden death of the patient through pulseless electrical activity or asystole. Another complication is a decrease in left ventricular (LV) filling, which can lead to hypotension and may present in the clinical setting as syncope or cardiogenic shock. However, if the patient survives the complications, pulmonary hypertension along with systemic vasoconstriction can preserve systemic blood pressure and thus organ function. The respiratory insufficiency usually seen in PE may be due to low cardiac output or due to the ventilation/perfusion mismatch. This mismatch is caused by low or no blood going to the alveoli due to the emboli blocking the blood circulation. This will result in a higher ratio (V/Q > 0.8) creating a shunt, and hence the gas exchange may never happen. Consequently, the capillary blood in this shunt area will have gas concentrations of oxygen and carbon dioxide close to venous blood values. And this mismatch cannot be fixed with higher O2 supplements, and the oxygen saturation will drop as well, even with 100% O2. This mismatch can be measured via ventilation-perfusion studies and can aid in diagnosis [13-15].

Clinical Classification

Clinically, patients with PE can be divided into an acute massive, acute submissive, acute small, sub-acute massive, and chronic thromboembolic pulmonary hypertension. Further classification based on risk into high, intermediate and low can be done using the risk stratification markers [11]. Furthermore, both classification systems depend on hemodynamic impact (mainly RV dysfunction) as the main prognosis factor, with patients with symptomatic RV dysfunction being massive/high-risk. Asymptomatic dysfunction and/or RV overload are submissive/intermediate-risk, and normal RV function is small/low-risk [12]. Even though thrombotic PE is the most typically talked about, there are non-thrombotic PEs. These generally include foreign body embolization, septic emboli, fat or air embolism, amniotic fluid embolism, and tumorous mass embolization. All of these may present in the same manner as thrombotic PE or with symptoms and signs related to the emboli origin (e.g. fever in septic emboli). Thus, they usually are diagnosed by the same methods with extra tests for confirmation of the source and treated according to the type of the emboli [12]. In addition, imaging studies may show a full or relative morphological closure affecting the classification.

Clinical Approach to Diagnosis and Management

Imaging modalities, along with D-dimer test, ECG, Echo, and to a lesser degree NT-proBNP are done for diagnosing and management. For example, in 10% of patients with PE, and specifically those with a massive disease, an ECG finding of S1Q3T3 is found and is known as McGinn-White sign [15]. Diagnosing the PE is not enough since deciding how severe it is (based on hemodynamic impact), makes a major difference in the management of this disease. A general

approach to these patients includes deciding their PE probability using risk factor scores (modified Well's score). Then, the score will show either, a likely possibility that will need immediate radiology modality to be done in order to exclude or diagnose PE. The second probability is the unlikely possibility of PE which a simple D-dimer test is enough to rule it out safely if it comes back negative [14]. The treatment approach in these patients include thrombolysis, anticoagulants (including unfractionated heparin, low-molecular-weight heparin, direct thrombin inhibitors, factor Xa inhibitors, and warfarin), catheter embolectomy, and even surgery (e.g. embolectomy and IVC filter), that may all be done depending on the severity and the patients' status [16].

Imaging Modalities

In the modern era of imaging, the approach to diagnosis is achieved through clinical suspicion, DVT investigation through D-dimers and Doppler, and pulmonary ventilation-perfusion scintigraphy or computerized tomographic angiography [7]. Computerized tomography pulmonary angiography (CTPA) is utilized in modern institutions to diagnose a pulmonary embolism and is often considered as the first line. While CT pulmonary angiography successfully performs its diagnostic role, there are several issues that require addressing. Its higher radiation dose, hypersensitivity risks that may result in contrast-induced renal injury, radiation medium-induced solid tumors, the difficulty of interpretation without consultant or specialist help and technical faults are all aspects that halter the management and diagnosis process. However, recently there have been some steps made into making CTPA used only when needed, and sequential pretest using several clinical probability scores (CPSs) is done and had helped in reducing the need for CTPA by up to 30% [17, 18].

In a major survey distributed across France, Australia and Canada, the evaluation of a pulmonary embolism in institutions was largely dependent on single photon emission contrast tomography (SPECT), however, the interpretation criteria were oddly inconsistent [19]. This modality, however, did not have as good results as CTPA. Nevertheless, another study concluded that ventilation-perfusion SPECT had a more outstanding outcome when combined with low-dose non-contrast CT compared to SPECT alone [20]. Another modality that is used sometimes in a special population, mainly cancer patients (which are at high risk of a pulmonary embolism), is non-contrast SPECT. This modality helps in revealing additional important findings and accurately diagnose embolism in these special patients [21]. SPECT usage in the diagnostic approach of a pulmonary embolism has shown recently higher definitive results regarding diagnosis, yet further studies are required for its validation as a standard technique and incorporation into the standard protocol for pulmonary embolism management [22].

Recently, hybrid imaging of pulmonary vasculature consisting of CT modalities and scintigraphy, as well as others has been suggested. Studies have shown that combined perfusion and ventilation studies with low dose CT had significantly high sensitivity and specificity regarding diagnosis [22, 23]. One study investigated lung perfusion by hybrid SPECT with CT as a modality for diagnosis of a pulmonary embolism and showed significantly higher sensitivity and specificity when compared to non-hybrid techniques [23, 24]. Moreover, excluding the existence of a pulmonary embolus can be safely based upon a perfusion SPECT with radiograph [22, 23]. Another important vulnerable population is pregnant patients and PE is a leading cause of mortality in this group. Hence, accurate diagnosis and fast management are essential to save both the mother and child. Fortunately, current protocols state that CT pulmonary angiography and pulmonary scintigraphy can be applicable to exclude the disease during pregnancy [22, 25]. Nevertheless, clinically it is better to use the D-dimer test with modified Well's score before carrying on with the imaging techniques as a precaution to the unnecessary imaging complications and radiation's risk [25, 26].

A recent radiologic modality that has been suggested for diagnosis includes ventilation-perfusion PET. And even though this test showed advantageous results, it is still within the developmental stages, and further studies are needed. However, this scan remains one of the most important and newer imaging techniques that make a case for substituting the ones commonly used. These new modalities can help the clinician in even higher accurate diagnosis and subsequent well-timed management of an otherwise missed and mortal condition [20, 27].

Conclusion

Pulmonary embolism is a fatal disease especially when identified late and improperly managed. Diagnosis of PE is the most challenging part of this disease, and thus the most important step for any clinician suspecting it. As a result, radiological investigations and imaging is the most researched topic in this disease and still remains the field needing the most intensive work. The approach for diagnosis and rapid management of an otherwise fatal disease has fortunately changed during the last 50 years, providing a much needed faster diagnosis and thus earlier intervention. Moreover, with the advancement of new radio-pharmaceuticals and optimized radiosensitive tracers, a further advantageous addition to current imaging modalities has been added. However, there is still a need for further studies, and more clinical trials to be carried out before these new breakthroughs being added to the international protocols regarding the management of pulmonary embolism.

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