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Original article

OVERDIAGNOSIS OF ACUTE PULMONARY EMBOLISM DETECTED ON CTPA - A RETROSPECTIVE STUDY

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Abstract

Aim: To evaluate the prevalence of overdiagnosis of pulmonary embolism (PTE) by computed tomography pulmonary angiography (CTPA) and assess the clinical justification for CTPA use.

Methods: A retrospective study was conducted on 200 patients who presented with symptoms of PTE between 2023 and 2024. CTPA was performed, and results were analyzed to determine diagnostic yield and identify factors contributing to over diagnosis.

Results: Out of 200 patients, 22.5% were diagnosed with PTE, while 77.5% had negative results. Common symptoms included dyspnea (45%) and chest pain (42.5%). Elevated D-dimer levels were found in 92.5% of patients. For those with negative CTPA results, alternative diagnoses included pneumonia (29.03%) and pleural effusion (16.13%).

Conclusion: The study highlights a significant issue of overdiagnosis due to excessive reliance on CTPA. The low positive yield suggests overuse of this imaging modality, potentially driven by inadequate application of clinical decision rules and the D-dimer test. Recommendations include improving adherence to clinical guidelines and optimizing the use of diagnostic tools to reduce unnecessary imaging and radiation exposure.

Keywords: pulmonary thromboembolism, computed tomography pulmonary angiography, overdiagnosis, diagnostic yield, clinical decision rules, D-dimer

Introduction

Pulmonary thromboembolism (PTE) is a prevalent diagnosis among patients presenting to the emergency department and those hospitalized with acute symptoms. Long-term anticoagulation therapy is the standard treatment, aiming to reduce mortality and mitigate the morbidity associated with chronic pulmonary thromboembolism. Given the nonspecific clinical presentation of PTE, which can be easily mimicked by various other conditions, computed tomography pulmonary angiography (CTPA) has become the imaging modality of choice for further investigation[1].

CT pulmonary angiography (CTPA) is highly effective in identifying acute pulmonary emboli, typically revealing filling defects within the pulmonary vasculature. When viewed in the axial plane, the central filling defect caused by the thrombus is often surrounded by a thin rim of contrast, a feature commonly referred to as the "polo mint sign." Emboli can be occlusive or non-occlusive; in the latter case, a thin stream of contrast may be visible adjacent

to the embolus. Moreover, the embolus typically forms an acute angle with the vessel wall, distinguishing it from chronic emboli. The affected vessel may also exhibit enlargement[2].

CTPA can be performed rapidly in patients with suspected PTE and demonstrates high sensitivity and specificity[3-5]. The diagnostic accuracy of CTPA is well-documented, with sensitivity ranging from 96% to 100% and specificity between 89% and 98%[6].

However, the increasing frequency of CTPA utilization, coupled with a declining positive yield, raises concerns about the unnecessary consumption of medical resources and the exposure of patients - particularly pregnant women - to avoidable radiation[7-9]. To address this issue, clinical scoring systems such as the Wells and Geneva Scores have been developed to reduce the number of unwarranted CTPAs in patients with suspected pulmonary issues[10-12]. Despite their potential utility, these scoring systems are not consistently adhered to in clinical practice and may not accurately predict PE in certain populations, including critically ill patients[10-12].

Similarly, the D-dimer test is widely used to exclude PE, with a negative result being particularly valuable in high-risk patients[13-15]. Although effective as a screening tool, the D-dimer test has limitations, as its levels are influenced by age and can be elevated in conditions such as infection, trauma, and malignancy, even in the absence of PTE[15-17]. The risk of hemorrhage associated with anticoagulation therapy is also a significant concern. A large meta-analysis conducted in 2003 reported a 7% annual risk of major bleeding and a 0.4% incidence of fatal hemorrhage in patients receiving oral anticoagulation therapy for venous thromboembolism for more than three months[18].

Given these considerations, minimizing the misdiagnosis of PTE is crucial. The literature has extensively documented common artifacts that may lead to false-positive PTE diagnoses[19-21]. Furthermore, the lack of a universally accepted reference standard for PTE diagnosis complicates the assessment of pulmonary CTPA's accuracy in routine clinical practice.

Aim

The study aimed to assess the rate of overdiagnosis of pulmonary thromboembolism (PTE) by clinicians and to evaluate the clinical indications for performing pulmonary CTPA at the University Clinic for Pulmonology and Allergology in Skopje.

Materials and methods

This study retrospectively analyzed 200 patients who presented with clinical symptoms suggestive of pulmonary thromboembolism (PTE) at the University Clinic for Pulmonology and Allergology in Skopje during the one-year period from 2023 to 2024. Following initial clinical evaluation, pulmonary CT angiography (CTPA) was indicated and subsequently performed using a 128-slice PHILIPS INCISIVE CT scanner, adhering to the standard protocol for PTE assessment.

For the CTPA procedure, 60-80 ml of iodine-based contrast medium, with a concentration of 350 to 370 mgI/ml, was intravenously administered, followed by a 40 ml saline flush. The contrast agent was delivered at a rate of 3-4 ml/second using an automatic injector. The scan was initiated automatically once a threshold of 150 Hounsfield Units (HU) was reached, with a total scanning time of 7-8 seconds. Key imaging parameters included a rotation time of 0.5 seconds, maximum tube current (mAs), and a voltage setting of 120 kVp. The acquisition of data in 1 millimeter or sub-millimeter sections facilitated detailed evaluation of pulmonary vasculature, extending to the sixth branching order, thereby enhancing the detection of segmental and subsegmental pulmonary emboli.

To maintain the integrity of the study, patients with chronic pulmonary embolism or those undergoing follow-up CTPA were excluded. The CTPA scans were independently

interpreted by two general radiologists, one with 1.5 years of experience and the other with 11 years of experience; however, their interpretations were not compared for this analysis.

Clinical data, including patient demographics (sex, age), CTPA outcomes (positive or negative findings), and characteristics of the detected emboli (unilateral/bilateral involvement and specific localization), were obtained from the National Electronic Medical Records System (Moj Termin). Descriptive statistics were utilized to analyze these parameters across the study cohort.

Results

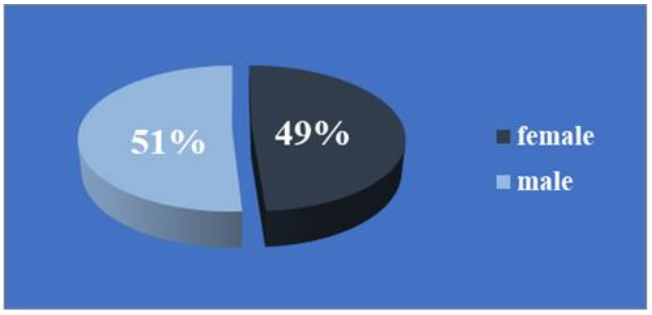

Fig. 1. Gender Distribution of the Study Population

Gender distribution within the study cohort is illustrated in ***Figure 1***. Of the total participants, 49% were female, while 51% were male. The mean age of female participants was 59.20 years, with a standard deviation of ±1.50 years, and an age range spanning from 16 to 60 years. In comparison, male participants had a mean age of 58.12 years, with a standard deviation of ±1.41 years, and their ages ranged from 60 to 89 years. The overall age range for all participants extended from 16 to 89 years, resulting in a combined mean age of 58.65 years (±1.03 years) for the entire cohort, as detailed in Table 1.

Table 1. Age Distribution, Central Tendency, and Range by Gender

Age distribution	Mean	Median	SD	Min	Max
Female	59.20	62.5	1.50	16	60
Male	58.12	60	1.41	60	89
Total	58.65	60	1.03	16	89

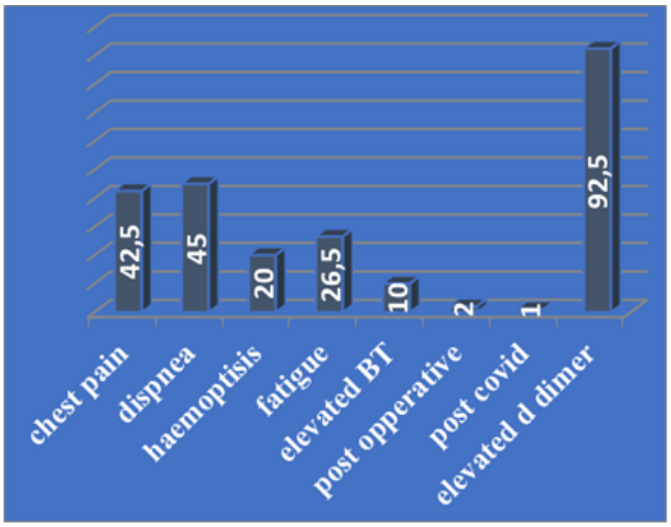

Fig. 2. Presentation of predominant symptoms

The symptom presentation within the studied cohort varied significantly, as illustrated in Figure 2. Dyspnea was the most frequently reported symptom, affecting 45% of patients. Chest pain was the second most common symptom, reported by 42.5% of participants. General fatigue was observed in 26.5% of cases. Hemoptysis, though less prevalent, was noted in 20% of patients. Elevated body temperature was recorded in 10% of the cohort. Additionally, a small percentage of patients (2%) with a history of recent surgery and 1% with recent COVID-19 infection were identified. Elevated D-dimer levels, a notable diagnostic marker, were detected in 92.5% of patients.

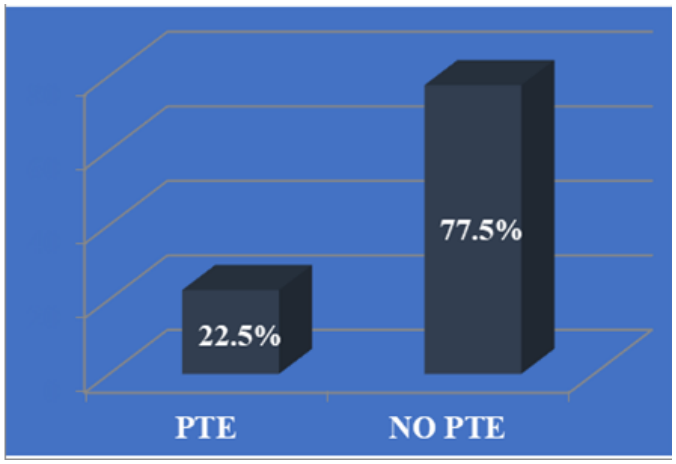

Fig. 3. Pulmonary Embolism Findings on CTPA

Figure 3 depicts the distribution of pulmonary embolism (PTE) findings based on computed tomography pulmonary angiography (CTPA). Among the study population, 22.5% of patients exhibited positive radiological evidence of pulmonary artery opacification defects, indicating the presence of pulmonary embolism. Conversely, 77.5% of the CTPA scans did not reveal any signs of pulmonary embolism.

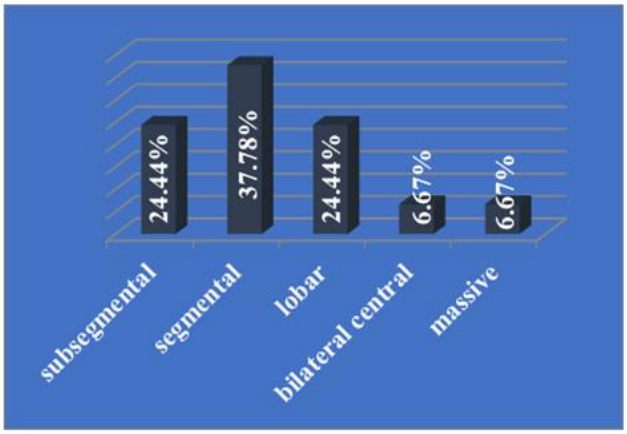

Fig. 4. Distribution of emboli based on location

The anatomical distribution of emboli, as shown in ***Figure 4***, was categorized as follows: 24.44% of emboli were located in the subsegmental arteries, 37.78% in the segmental arteries, and 24.44% in the proximal lobar arteries. Additionally, 6.67% of the emboli were classified as either bilateral proximal or massive, reflecting their more extensive involvement.

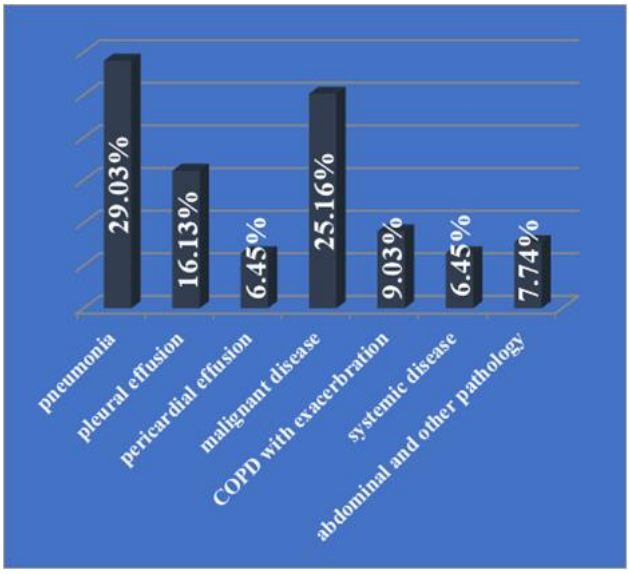

Fig. 5. Distribution of Common Differential Diagnoses in Negative CTPAs

In all the 155 patients who underwent CTPA (Computed Tomography Pulmonary Angiography) and had negative results for pulmonary embolism, a range of alternative diagnoses were considered. The distribution of these differential diagnoses is shown in Figure 5. The most common alternative diagnosis was pneumonia, identified in 29.03% of patients. Pneumonia is a frequent cause of chest symptoms that mimic those of pulmonary embolism, such as pleuritic chest pain and dyspnea. The presence of infectious infiltrates, as seen on imaging, is a key differentiator from thromboembolic events. Pleural effusion was the next most common finding, occurring in 16.13% of cases.

Pleural effusion can present with symptoms similar to those of a pulmonary embolism, including shortness of breath and pleuritic pain, making it a significant consideration when CTPA results are negative. Pericardial effusion, found in 6.45% of patients, also represents a critical differential diagnosis. It may manifest with chest pain, dyspnea, and other symptoms that overlap with those of pulmonary embolism, particularly when the effusion is large enough to cause hemodynamic compromise. Malignant diseases were identified in 25.16% of cases, underlining the importance of considering neoplastic processes when evaluating patients with unexplained chest symptoms and a negative CTPA. Malignancies can lead to a variety of paraneoplastic syndromes, including pleuritic pain and systemic symptoms, which may be mistaken for pulmonary embolism. Chronic obstructive pulmonary disease (COPD) with exacerbation accounted for 9.03% of the differential diagnoses. COPD exacerbations can mimic the clinical presentation of a pulmonary embolism, particularly when there is an acute worsening of dyspnea and chest discomfort. Systemic diseases with pulmonary involvement were noted in 6.45% of patients. These conditions can include a wide array of autoimmune or inflammatory disorders that affect the lungs, often leading to symptoms like dyspnea and chest pain, which can be confused with those of a pulmonary embolism. Lastly, abdominal and other non-thoracic conditions, although less common, were diagnosed in 7.74% of cases. These conditions can sometimes present with referred pain or atypical symptoms that initially raise suspicion for a pulmonary embolism. These findings emphasize the importance of considering a broad differential diagnosis when evaluating patients with negative CTPA results. Accurate identification of these alternative diagnoses is crucial for guiding appropriate management and ensuring optimal patient outcomes.

Discussion

Pulmonary thromboembolism (PTE) remains a significant diagnostic challenge due to its nonspecific clinical presentation, which overlaps with various other conditions. As a result, the use of pulmonary CT angiography (CTPA) has become increasingly prevalent as the first-line imaging modality for suspected PTE. However, the results of our study underscore a critical issue in current clinical practice: the potential overuse of CTPA leading to overdiagnosis.

Our study, conducted at the University Clinic for Pulmonology and Allergology in Skopje, revealed that out of 200 patients who underwent CTPA for suspected PTE, a substantial proportion were ultimately found to have no evidence of embolism. This aligns with findings from other studies, which have reported similar trends of high CTPA utilization with relatively low positive rates[22,23]. In our cohort, only 22.5% of patients had a positive CTPA, indicating a substantial number of negative scans. This low positive rate raises concerns about the appropriateness of CTPA indications and highlights the need for more stringent criteria when selecting patients for this imaging modality.

Several factors contribute to the overuse of CTPA. Clinicians may rely heavily on CTPA due to its high sensitivity and specificity, often bypassing clinical scoring systems such as the Wells or Geneva Scores, which are designed to stratify PTE risk and guide imaging decisions[24]. Despite their proven utility, these scoring systems are underutilized in practice, particularly in emergency settings where time pressures and diagnostic uncertainty may prompt immediate imaging[25,26]. Additionally, the D-dimer test, which can effectively rule out PTE in low to moderate-risk patients, is often not fully integrated into the diagnostic pathway, leading to unnecessary CTPA referrals[27]. Our study reinforces these observations, as the clinical indications for CTPA in our patient population often lacked rigorous adherence to established guidelines.

The implications of CTPA overuse extend beyond the immediate diagnostic context. The unnecessary radiation exposure, particularly in vulnerable populations such as pregnant women and young patients, is a significant concern. Moreover, the economic burden associated with high CTPA utilization is nontrivial, adding strain to healthcare resources without commensurate clinical benefits. This issue is compounded by the potential for incidental findings on CTPA, which can lead to further testing, anxiety, and even unnecessary interventions[28].

Our findings also raise the issue of inter-observer variability in CTPA interpretation. Although our study did not compare the reports from the two radiologists involved, the existing literature suggests that variability in CTPA interpretation can contribute to both false-positive and false-negative diagnoses[29]. This variability underscores the importance of experience and training in accurately diagnosing PTE, as well as the potential value of double reading in complex cases.

In light of these findings, there is a pressing need to optimize the use of CTPA in suspected PTE. This can be achieved through more rigorous application of clinical decision rules, enhanced use of the D-dimer test, and ongoing education of clinicians on the appropriate indications for CTPA. Additionally, further research is needed to explore alternative diagnostic strategies that could reduce reliance on CTPA, such as combining clinical assessment with non-imaging tests in selected patient populations[30].

Conclusion

In conclusion, our study highlights a concerning trend of overdiagnosis of pulmonary thromboembolism by the excessive use of CTPA at the University Clinic for Pulmonology and Allergology in Skopje. The findings suggest that a significant proportion of CTPA scans are performed in the absence of stringent clinical indications, resulting in low positive rates and unnecessary exposure to radiation and healthcare costs. To mitigate these issues, it is

imperative to reinforce adherence to established clinical guidelines, optimize the use of diagnostic tools such as the D-dimer test, and ensure that CTPA is reserved for patients with a high pretest probability of PTE. By addressing these challenges, we can improve the accuracy of PTE diagnosis, reduce the incidence of overdiagnosis, and enhance the overall quality of care for patients with suspected pulmonary embolism.

Conflict of interest statement. None declared.

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