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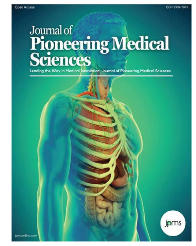

Role of CT Pulmonary Angiography in Clinically Suspected Cases of Acute Pulmonary Embolism: Correlation with Wells Score

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Abstract **Background:** Pulmonary embolism (PE) is the 3rd most frequent cause of cardiovascular death (30% of cases), following coronary artery disease and stroke. As most cases are caused by thrombotic occlusion, the condition is called pulmonary thromboembolism. **Objectives:** To determine the use and overuse of spiral computed tomography (CT) and CT pulmonary angiography (CTPA) in diagnosing the clinically suspected patients with PE. **Materials and methods:** This cross-sectional study enrolled 100 patients with clinically suspected PE in Shar Teaching Hospital, Sulaimaniyah City, Iraq, from December 2022 to October 2023. CT images were obtained and the axial, reformatted coronal and sagittal images were evaluated. Modified Wells Score (MWS) was calculated for cases and PE rule-out criteria (PERC) was calculated for those cases with a Well score ≤4. The D-dimer test was done randomly for 39 cases. **Results:** The cases comprised 63 females and 37 males aged 16-95 years. The most common symptoms evoking a suspicion of PE were dyspnea (87%), chest pain (26%), cough (14%) and fever (11%). Results revealed that 35% (n = 35) had PE and 65% (n = 65) had no PE. Most non-PE patients had normal CT (16%, n = 16), followed by pneumonia (11%, n = 11), heart failure (9%, n = 9), pleural effusion (6%, n = 6), atelectasis/pulmonary hypertension (PHTN) (5%, n = 5), fibrosis/lung mass (4%, n = 4), collapse (3%, n = 3), bronchiectasis and LAP (1%, n = 1). Most cases (n = 55) had MWS ≤4 (1 PE) and 45 cases had >4 (34 PE). PERC rule was positive in 33 cases (1 PE) and negative in 22 cases (no PE). **Conclusions:** CTPA was negative in most cases with MWS of ≤4, while in combined strategy (MWS ≤4+negative PERC), CTPA was negative in all cases. Therefore, utilizing the combined strategy could safely exclude PE without additional imaging.

Key Words Pulmonary Angiography, Acute Pulmonary Embolism, Wells Score, Rule Out Criteria

INTRODUCTION

Pulmonary Embolism (PE) occurs when emboli from venous thrombi migrate and block pulmonary arteries [1]. If PE is left untreated or undetected, PE can be fatal in up to 30% of cases [2]. Acute PE is linked to right ventricular dysfunction, resulting in arrhythmia, hemodynamic collapse and shock [3]. Individuals who survive PE may develop post-PE syndrome, which is chronic thrombotic remnants in the pulmonary arteries, persistent right ventricular dysfunction, poor quality of life, and/or chronic functional restrictions [2].

Non-thrombotic PE (NTPE) is the embolization of various cell types (adipocytes, hematopoietic, amniotic, trophoblastic or tumour), bacteria, fungi, foreign material or gas into the pulmonary circulation [4]. For many radiologists, NTPE is problematic since it presents nonspecific or odd imaging findings in the context of little or unusual clinical symptoms [4]. The prognosis of PE is determined by the degree of blockage and the hemodynamic implications of PE. Understanding the pathophysiology aids in risk stratification and treatment planning. Even though the natural course of thrombus is resolution, a subgroup of patients has chronic residual thrombus, which contributes to the post-PE syndrome [5].

Sudden chest pain and breathing difficulty, especially chest pleuritic pain, may suggest PE. Symptoms like cough, hemoptysis, tachypnea, tachycardia and hypoxia can also be present. However, these are common symptoms in general practice and Emergency Departments (ED) and most patients won't have PE [6]. Modified Wells Score (MWS) is a risk stratification tool and clinical decision rule used to evaluate the likelihood of acute PE in patients whose history and examination show that acute PE is a diagnostic possibility. It can be used with a negative D-dimer to rule out PE and prevent imaging [7].

The PE rule-out criteria (PERC) is another validated clinical tool that can be utilized in the ED for patients deemed low risk for PE but for whom the diagnosis is being considered to avoid further PE workup [8]. D-dimer testing is valuable in the evaluation of patients suspected of having PE, particularly in those with a low to moderate clinical probability of PE. A normal D-dimer can rule out PE and reduce the need for more invasive or costly diagnostic tests. Thus, a normal D-dimer makes acute thrombosis unlikely [9]. D-dimer levels are raised in acute thrombosis due to coagulation and fibrinolysis stimulation but have a limited positive predictive value, which is inadequate for confirming acute thrombosis [10].

CT pulmonary angiography (CTPA) is the preferred diagnostic tool for suspected PE due to its sensitivity, specificity (90%), quickness and high accuracy. It provides detailed pulmonary artery images, allowing precise detection of blood clots. It's effective in confirming PE and ruling it out to avoid unnecessary treatment [11]. It offers several significant advantages over alternative diagnostic tools that encompass direct visualization of thrombi, the capability to assess both mediastinal and parenchymal structures and the ability to diagnose various other clinical conditions [12]. Despite several theoretical worries about potentially dangerous risks of CT, like cancer from ionizing radiation, contrast-induced nephropathy [13] and anaphylactic reactions (0.1-0.7%) with mortality (1 out of 170,000 injections) [14], the use of CT is deemed reliable and essential in the diagnosis of PE. Accordingly, this study aimed to address the use and overuse of spiral CT scan /CTPA in the diagnosis of clinically suspected patients with PE.

METHODS

Study Design and Setting

This cross-sectional prospective study was done on 100 consecutive patients referred from the clinical wards as a suspected case of PE who underwent CTPA in the Radiology Department, Shar Teaching Hospital, Sulaimaniyah City, Iraq, from December 2022 to October 2023.

Inclusion Criteria

Inpatients (aged 16-95 years) referred from the clinical ward with PE who underwent MWS and PERC criteria, regardless of pregnancy, having cancer or high D-dimer.

Exclusion crit#eria

Patients with abnormal renal function test (serum creatinine ≥1.5 mg/dL) and previous allergic reaction to contrast media. Also, those with sub-optimal studies due to patient motion or other artefacts and those who underwent MWS or PERC criteria (because of lack of clinical information).

Procedure and Data Collection

A MWS with 2 titers (un-likely probability for PE ≤4, likely probability for PE >4) was calculated for all patients from data on the medical records (Table 1).

Clinically suspected cases of PE underwent MWS, of which clinicians in the ED assessed 21% and 79% had their scores calculated later by a radiologist. PERC rule was calculated for those patients with un-likely MWS (≤4) by the same radiologist (Table 2).

Moreover, all patients with clinically suspected PE underwent CTPA using a 64-slice Siemens CT scanner, following a standardized protocol of bolus tracking (putting the 100 HU ROI in below the carina at the level of the pulmonary trunk) or manually (scanning commences about 10-12 seconds after the contrast injection has started). The scans were done for patients in the supine position, with 0.625 mm or 1.0 mm slice thickness of 100-120 Kv and Auto mA. The iodinated intravenous contrast (Iopamidol, 370 mg/mL) was administered in an antecubital vein at a dose of 50-70 mL and a rate of 4-5 mL/second, followed by 20 mL normal saline. Finally, 39 patients were randomly selected to test for D-dimer.

Statistical Analysis

The Statistical Package for the Social Sciences (SPSS, IBM, Chicago, USA, version 27) was used for data analysis. The data were expressed as numbers and percentages for categorical data and Mean±standard deviation for numerical data. A p≤0.05 was considered significant, while a p≤0.001 was set as highly significant.

RESULTS

Sociodemographic of the Patients

The mean age was 55.1±19.6 years, with an age range of 16 to 95 years and the majority were >60 years (n = 42, 42%). Most patients were females (63%) and 37% were males.

Chief Complaints and Risk Factors of the PE

The most abundant complaints of the patients were shortness of breath (87%), chest pain (26%), cough (14%) and fever (11%). Regarding the risk factors, bedridden is prevalent in 36%, cigarette smoking in 28%, recent surgery in 22%, obesity in 16%, cancer in 10%, deep vein thrombosis/enlarged veins in the legs (varicose veins) in 9%, family history of blood clotting in 5%, a history of recent pregnancy in 5% and oral contraceptive use in 1% (Table 3).

Comparison of MWS to D-dimer and CTPA

The MWS of 55 patients was ≤4 and 45 were >4. Interestingly, 80% (n = 44) of those with MWS of ≤4 were not tested D-dimer, while among those who tested (20%, n = 11), 16.4% (n = 9) were negative and only 3.6% (n = 2) were positive. On the contrary, 37.8% (n = 17) of those with MWS of >4 were not tested for D-dimer, while among those who tested, 2.2% (n = 1) were negative and 60% (n = 27) were positive (p<0.001). Notably, 98.2% (n = 54) of those with MWS of ≤4 had no PE, while 1.8% (n = 1) had PE. On the other hand, 24.4% (n = 11) of those with MWS of >4 had no PE and 75.6% (n = 34) had PE (p<0001) (Figure 1, 2, Table 4).

Comparison of PERC to D-dimer and CTPA

Regarding PERC, 33 patients were positive and 22 were negative. Among positive cases, 75.8% (n = 25) had not done the D-dimer test, while among those who tested, 18.2% (n = 6) were negative and 6% (n = 2) were positive. Among negative PERC cases, 86.4% (n = 19) had not done

Table 1: Modified Wells Score (MWS) criteria

Predictor	Score
DVT clinical signs and symptoms (minimal leg swelling and pain with deep vein palpation)	3
A different diagnosis is less likely than PE	3
Heart rate >100 beats/minute	1.5
≥3 consecutive days of immobility or surgery in the past 4 weeks	1.5
A history of objectively diagnosed PE or DVT	1.5
Hemoptysis	1
Cancer (current therapy, treatment within the last 6 months, or palliative)	1

Table 2: Pulmonary embolism rules out criteria (PERC)

Age <50 years
Heart rate <100 beat per minute
Oxygen saturation >95% on room air
No unilateral leg edema
No hemoptysis
No recent trauma or surgery that required hospitalization in the previous 4 weeks
No prior history of venous thromboembolism
No use of exogenous estrogen

Table 3: Clinical characteristics of the study samples

Variable	Frequency (%)
Complains	
Shortness of breath	87 (87)
Chest pain	26 (26)
Cough	14 (14)
Fever	11 (11)
Risk factors	
Bed redden	36 (36)
Cigarette smoking	28 (28)
Recent surgery	22 (22)
Obesity	16 (16)
Cancer	10 (10)
Deep vein thrombus	9 (9)
Enlarged veins in the legs (varicose veins)	9 (9)
Family history of blood clotting disorders	5 (5)
History of recent pregnancy	5 (5)
Oral contraceptive pills	1 (1)

Table 4: Comparison of modified wells score (MWS) to D-dimer and computed chromatography pulmonary angiography (CTPA)

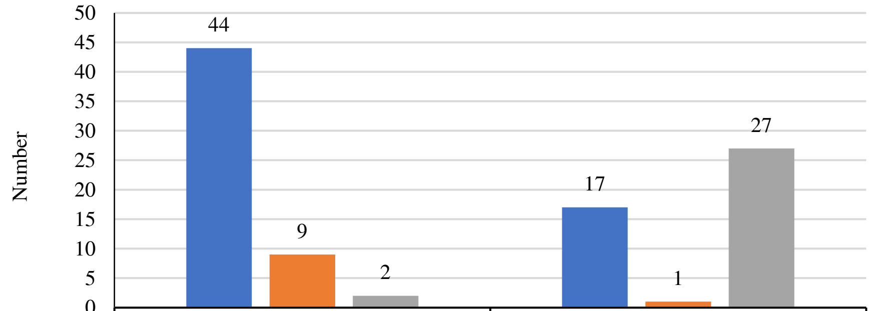
Variable	MWS frequency (%)		p-value
	≤4 score (un-likely)	>4 score (likely)	
D-dimer			
Not done (n = 61)	44 (80)	17 (37.8)	<0.001**
Negative (n = 10)	9 (16.4)	1 (2.2)	
Positive (n = 29)	2 (3.6)	27 (60)	
CTPA			
Negative PE (n = 65)	54 (98.2)	11 (24.4)	<0.001**
Positive PE (n = 35)	1 (1.8)	34 (75.6)	
Total	55 (100)	45 (100)	

**Highly significant difference using Chi-square test, PE: Pulmonary embolism

Table 5: Comparison of pulmonary embolism rule out (PERC) to D-dimer and computed chromatography pulmonary angiography (CTPA)

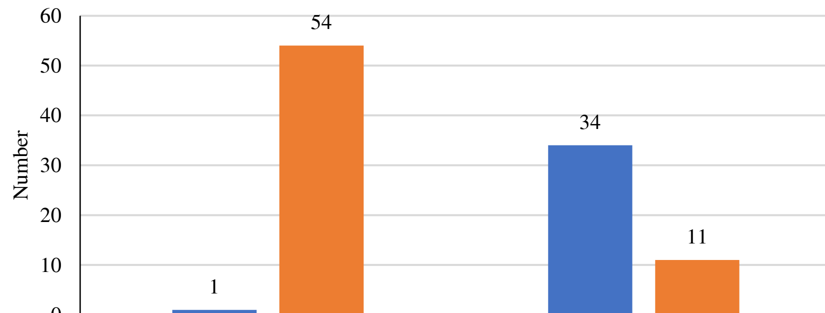
Variable	PERC Frequency (%)		p-value
	Positive	Negative	
D-dimer			
Not done (n = 44)	25 (75.8)	19 (86.4)	0.431
Negative (n = 9)	6 (18.2)	3 (13.6)	
Positive (n = 2)	2 (6.0)	0 (0.0)	
CTPA			
Negative PE (n = 54)	32 (97)	22 (100)	0.41
Positive PE (n = 1)	1 (3.0)	0 (0.0)	
Total	33 (100)	22 (100)	

D-dimer, while among those who had done the test; 13.6% (n = 3) were negative and 18.2% (n = 3) were positive (p = 0.431). Regarding PERC and CTPA comparison, 97% (n = 32) of positive PERC had no PE and only 3% (n = 1) had PE. On the other hand, 100% (n = 22) of negative PERC had no PE (p≥0.05) (Figure 3, 4, Table 5).



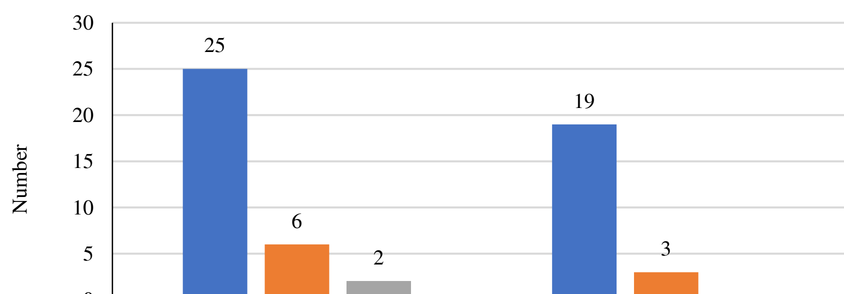
	<=4 score	> 4 score
Note done	44	17
Negative	9	1
Positive	2	27

Figure 1: Comparison between Modified Wells Score (MWS) and D-dimer test result



	<=4 score	> 4 score
PE	1	34
No PE	54	11

Figure 2: Comparison between Modified Wells Score (MWS) and computed chromatography pulmonary angiography (CTPA)



	PERC Positive	PERC Negative
Note done	25	19
Negative	6	3
Positive	2	0

Figure 3: Comparison between pulmonary embolism rule out criteria (PERC) to D-dimer result

CTPA results

Among patients, 35% (n = 35) had PE and 65% (n = 65) had no PE and most of them were normal (16%, n = 16), followed by pneumonia (11%, n = 11), heart failure (9%, n = 9), pleural effusion (6%, n = 6), atelectasis/ PHTN (5%, n = 5), fibrosis/lung mass (4%, n = 4), collapse (3%, n = 3), with bronchiectasis and lymphadenopathy (LAP) (1%, n = 1 each) (Figure 5-9, Table 6).

DISCUSSION

CTPA is a first-choice valuable diagnostic imaging technique in suspected patients of acute PE as it is widely

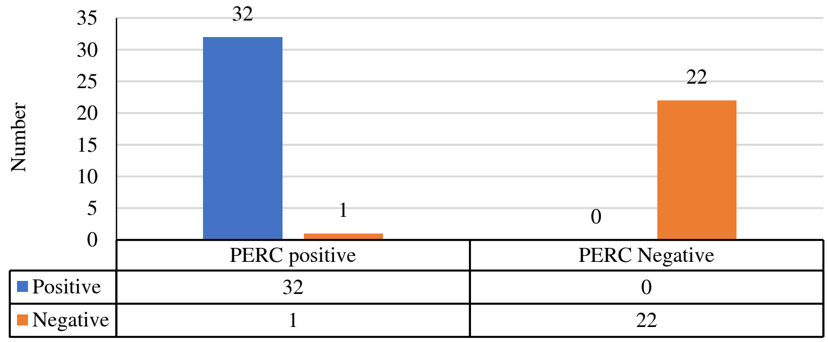


Figure 4: Comparison between pulmonary embolism rule out criteria (PERC) to computed chromatography pulmonary angiography (CTPA)

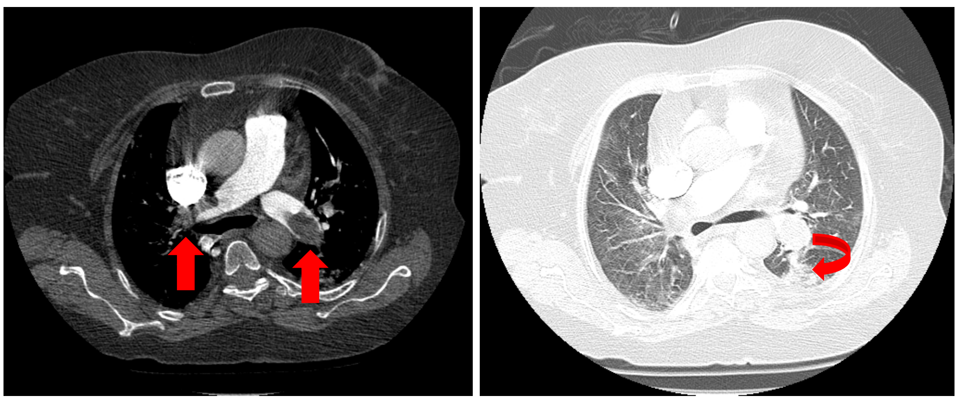


Figure 5: A 75 years old female with multiple myeloma has bilateral filling defects in the pulmonary arteries (red arrows) with lung infarction in superior segment of left lower lobe (curved arrow)

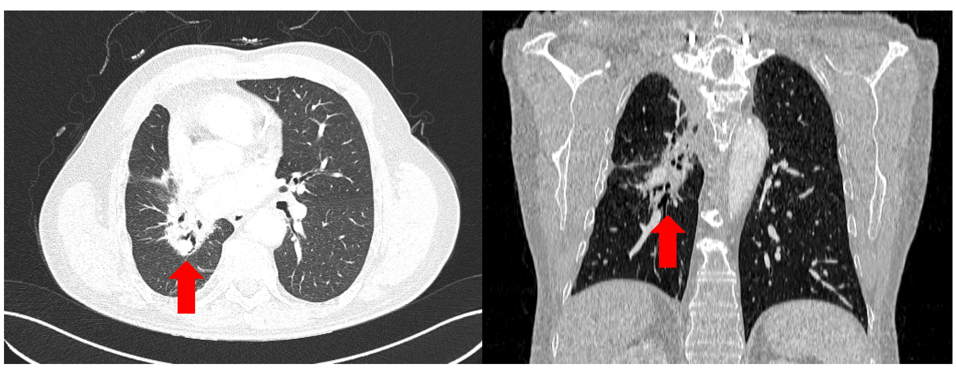


Figure 6: A 57 years old male patient with bronchiectasis in right upper lung lobe (red arrows)

Table 6: Computed chromatography pulmonary angiography results

Variable	Frequency (%)
Pulmonary embolism	35 (35.0)
Pneumonia	11 (11.0)
Heart failure	9 (9.0)
Pleural effusion	6 (6.0)
Atelectasis	5 (5.0)
Pulmonary hypertension	5 (5.0)
Fibrosis	4 (4.0)
Lung mass	4 (4.0)
Collapse	3 (3.0)
Bronchiectasis	1 (1.0)
Lymphadenopathy	1 (1.0)

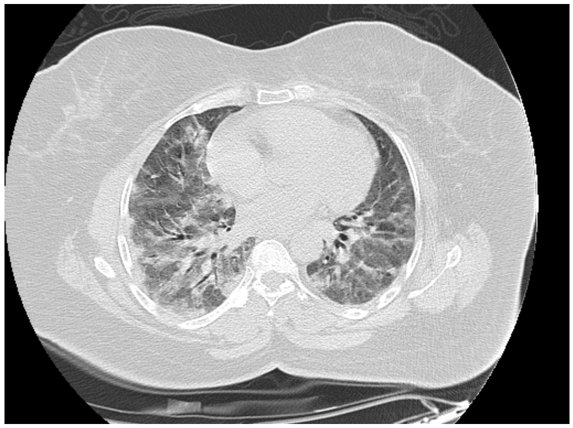


Figure 7: Axial computed tomography (CT) scan lung window for a 55 years old female patient demonstrated extensive diffuse bilateral ground glass opacities, the patient is treated for pulmonary edema and the CT finding is resolved.

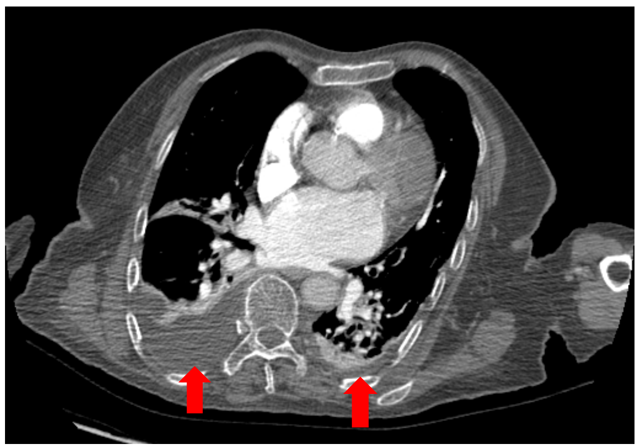


Figure 8: Axial computed tomography (CT) scan pulmonary window for 85 years old female demonstrating mild right and minimal left pleural effusion (red arrows) with adjacent pulmonary atelectasis

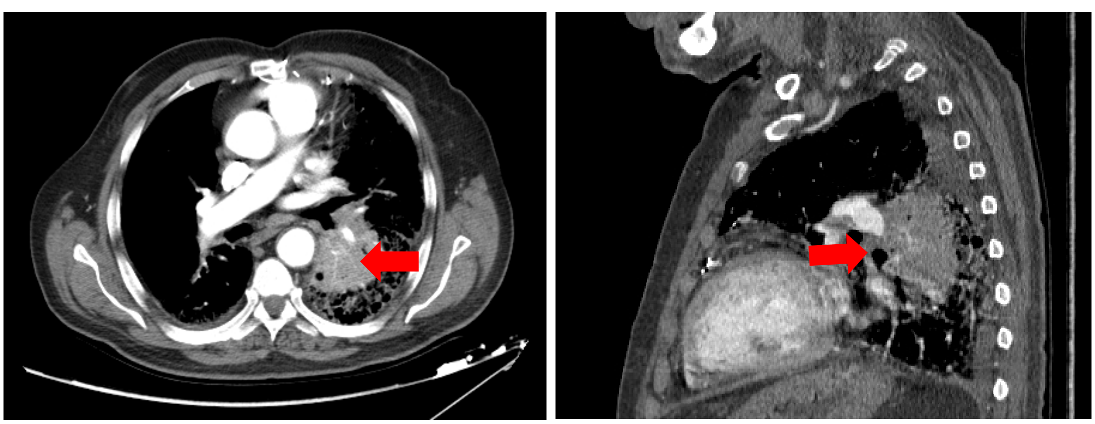


Figure 9: Axial and sagittal computed tomography (CT) scan pulmonary window for 83 years old male demonstrated large mass in the superior segment of left lower lobe (red arrows), later on it proved to be malignant round blue cell tumor by biopsy

available and non-invasive [15]. There are concerns about risks of CTPA overuse, including those from contrast and radiation [16], that can be solved by validated risk stratification tools like MWS and PERC and the high negative predictive D-dimer test [17]. Therefore, this study explored the association between MWS, PERC and D-dimer results and the presence of PE by CTPA in clinically suspected patients.

In this study, 35% of clinically suspected cases had PE, while 65% did not. The PE prevalence is consistent with

Prabhu and Ashwini [18] who reported 38% PE cases after conducting CTPA without considering MWS, PERC or D-dimer test; Qanadli *et al.* [19] who found PE in 34% cases who underwent CTPA and Dalen *et al.* [20] who reported 35% PE in clinically suspected cases; however, the prevalence of PE is lower than that reported by Bhagat *et al.* [21] (53%). These disparities may be attributed to differences in D-dimer testing; in the Indian study, 80% of cases underwent the D-dimer test with a 78% positive rate [21], whereas in this study, the D-dimer test was performed on 39% of cases, with only 29% positive rate.

Moreover, this study revealed the diagnostic capability of spiral CT in identifying various clinical conditions rather than PE, including pneumonia (n = 11), cardiovascular disease (n = 9), pleural effusion (n = 6), atelectasis/PHTN (n = 5 each), pulmonary fibrosis/lung mass (n = 4 each), lung collapse (n = 3) and LAP/bronchiectasis (n = 1 each). At the same time, the test was standard in 16 patients. These findings are by Lee *et al.* [22], who found that out of 96 cases, 39 cases did not have any other diagnosis. In comparison, the remaining 57 cases were diagnosed with atelectasis/pneumonia (n = 22), malignancy (n = 3), congenital heart disease/PHTN/pericardial effusion (n = 2 each), with pulmonary nodules/rib fractures/right atrial thrombus/fat embolism (n = 1 each). Similarly, Kavanagh *et al.* [23] studied 102 patients, 85 had no PE and 21 were normal, while 64 cases had other diseases, such as emphysema (21%), consolidation (18%), pleural effusion (12%), atelectasis (8%), pulmonary fibrosis/bronchogenic neoplasm (5% each), mediastinal LAP (2.5%) and pulmonary metastasis/arterio-venous malformation/pulmonary tuberculosis (1 case each).

In this study, an MWS clinical probability was calculated for all cases based on information from medical records (79% assessed by the radiologist and 21% by the clinician in the medical ward). Among cases, 55% were “PE-unlikely” (n = 1, 1.8%) and 45% were “PE-likely” (n = 4, 75.6%) on CTPA. In another two comparable studies by Singh *et al.* [7] and Page [24], PE was detected in 12.1% of patients that were classified as “PE-unlikely” in each study, while in patients with “PE-likely”; PE presented in 37.9% and 37.1%, respectively. Consistent with these findings, we also revealed a highly significant association ($p<0.001$) between patients who had “PE-likely” and frequent detection of PE on CTPA. The same association was observed between patients who had “PE-unlikely” and negative CTPA for PE ($p<0.001$).

In the present study, 39% of patients underwent a D-dimer test, of which 11% were “PE-unlikely” and 28% were “PE-likely”. In contrast, Geersing *et al.* [25] stated that the D-dimer test was done for all cases with “PE-unlikely” (45.5% of 598 cases). Notably, this study shows that 80% of those with an MWS of ≤4 did not undergo the D-dimer test, even when indicated according to the MWS criteria. This raises concerns about potential misclassification during pretest scale calculation, possibly leading to unnecessary CTPA. On the other hand, 61% of our cases did not undergo a D-dimer test before CTPA and 10% had PA despite a negative D-dimer result, indicating potential overuse of this diagnostic tool. Similar patterns were found by Alhassan *et al.* [26] where 61% of patients didn't have a D-dimer assay before CTPA and 9.8% had PA despite a negative D-dimer result.

In the current study, the PERC rule was calculated for low-risk patients to PE (those with MWS of ≤4; 55/100 cases), among them, 22 cases met PERC rule criteria (PERC-) and all had negative CTPA results. This indicates that the PERC- rule exhibits significant sensitivity in ruling out PE in low-risk patients or those with MWS of ≤4. These findings are consistent with that of Dachs *et al.* [27], where 48/213 patients meeting the PERC rule criteria also had negative CTPA, demonstrating 100% sensitivity and negative predictive value for the PERC rule. Additionally, Clarke *et al.* [28] included 1150 patients, 65 had a PERC score of 0 (PERC-), 64 had a negative scan for PE and one had a possible small sub-segmental PE that resulted in a negative predictive value of 99%. The sensitivity of the PERC rule in their study was approximately similar to this finding, highlighting the consistency and reliability of the PERC rule in excluding PE in low-risk patients.

Lastly, our findings emphasize the combined strategy and the clinical relevance of the MWS, PERC, D-dimer and CTPA in diagnosing PE. The MWS and PERC effectively stratify patients' risk, while the D-dimer test aids in further refining this risk assessment that was done for 39 cases only. Moreover, CTPA is a pivotal diagnostic tool for confirming or ruling out PE, as evidenced by the marked difference in CTPA outcomes between the MWS categories. These results are in line with Ceriani *et al.* [29], who found that different clinical decision rules had similar accuracy in assessing clinical probability and Pasha *et al.* [30], who demonstrated that PE can be safely excluded by a low clinical probability assessment, as well as a negative D-dimer result [31]. Sometimes, the referring clinician or physician did not provide all the required information for the MWS or PERC rule; however, we could get the clinical information directly from the patients.

CONCLUSIONS

Utilizing the combined strategy (MWS of ≤4 with negative PERC rule and/or negative D-dimer test) could safely exclude PE without additional imaging. When selecting patients for CTPA, clinicians should do an adequate clinical evaluation and utilize the MWS and PERC rules and the D-dimer test to avoid overusing CTPA and minimize unjustified exposure of patients to radiation and intravenous contrast administration.

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