

Suboptimal implementation of diagnostic algorithms and overuse of computed tomography-pulmonary angiography in patients with suspected pulmonary embolism

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Abstract:

BACKGROUND: Majority of our computed tomography-pulmonary angiography (CTPA) scans report negative findings. We hypothesized that suboptimal reliance on diagnostic algorithms contributes to apparent overuse of this test.

METHODS: A retrospective review was performed on 2031 CTPA cases in a large hospital system. Investigators retrospectively calculated pretest probability (PTP). Use of CTPA was considered as inappropriate when it was ordered for patients with low PTP without checking D-dimer (DD) or following negative DD.

RESULTS: Among the 2031 cases, pulmonary embolism (PE) was found in 7.4% (151 cases). About 1784 patients (88%) were considered "PE unlikely" based on Wells score. Out of those patients, 1084 cases (61%) did not have DD test prior to CTPA. In addition, 78 patients with negative DD underwent unnecessary CTPA; none of them had PE.

CONCLUSIONS: The suboptimal implementation of PTP assessment tools can result in the overuse of CTPA, contributing to ineffective utilization of hospital resources, increased cost, and potential harm to patients.

Key words:

Compliance rate, computed tomography-pulmonary angiography overuse, D-dimer, pulmonary embolism

The estimated annual incidence of pulmonary embolism (PE) is about 70 cases per 100,000.^[1,2] This number almost doubled to 112 cases per 100,000 after implementing computed tomographic pulmonary angiography (CTPA) in PE evaluation.^[3] PE accounts up to 0.5% of all deaths in the United States (US),^[4] with a constant decrease in mortality rate over the past few decades.^[1,4-6]

With the advent of spiral computed tomography (CT), CTPA has become a method of choice in diagnosing PE, with a sensitivity and a specificity of 83% and 96%, respectively.^[7,8] This reliable diagnostic tool is capable of visualizing pulmonary vasculature with a detailed distribution of filling defects caused by pulmonary emboli.^[9] In addition, ancillary findings have been detected in several studies and found to be valuable in patient care.^[10-13] On the other hand, CTPA carries some concerning issues which might primarily affect patient safety. This includes ionizing radiation exposure, contrast-induced nephropathy (CIN), contrast-induced anaphylaxis, and dye extravasation.^[14] Furthermore, CTPA is an expensive and relatively time-consuming test which may potentially strain facility resources.

The current guidelines recommend assessing clinical pretest probability (PTP) as an initial step in approaching patients with suspected PE.^[7,14-16] Wells' criteria [Table 1] are by far one of the most well-established scoring systems used in estimating patients' PTP and stratifying individuals into "PE unlikely" and "PE likely" groups.^[17] Thus, PE can be safely ruled out in patients who are at a low risk for PE with negative D-dimer (DD) assay.^[15-19] Such practice will avert performing unnecessary CTPA and

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Table 1: Modified Wells' criteria

Features	Score (points)
Clinical signs and symptoms of DVT	3.0
No alternative diagnosis	3.0
Heart rate >100 beats/min	1.5
Immobilization ≥3 days or surgery in the previous 4 weeks	1.5
Previous DVT or PE	1.5
Hemoptysis	1.0
Malignancy with active treatment in the past 6 months or under palliative care	1.0
Pretest clinical probability	
PE unlikely	≤4.0
PE likely	>4.0

PE = Pulmonary embolism, DVT = Deep vein thrombosis

exposing patients to the risk of radiation and kidney injury. Unfortunately, numerous studies have reported a remarkable increase in using CTPA examination with a decrease in its positive yield rate.^[9,14,20-23]

At our tertiary teaching medical center, we noticed an increase in the overall negative testing rate of CTPA in PE workup. Hence, we conducted this study to investigate whether or not CTPA is overused, and assessment of PTP of PE using modified Wells criteria and DD is underutilized.

Methods

Study design and data collection

We conducted our study at the Detroit Medical Center (DMC), which has a total of 1100 beds and an average of 250,000 emergency room visits annually. The Institutional Review Board of Wayne State University, to which DMC is affiliated, has approved the study.

We performed a retrospective chart review on all patients who underwent CTPA for suspected PE during a 6-month period from January 1, 2011 to June 30, 2011 at our institution. The collected data included patient demographic features (coded identifier, age, gender, and race), presenting complaints, comorbidities, physical examination findings, and laboratory results.

Our investigators reviewed the documented notes for each patient and retrospectively calculated PTP of PE at the time of ordering CTPA. Subsequently, they reported the initial diagnostic testing (DD versus CTPA) in PE evaluation for each case.

We relied on the independent interpretation of CTPA imaging reported by in-house board-certified chest radiologists to divide the CTPA results into positive or negative for PE. DD assay in our medical center was measured in micrograms per milliliter (µg/mL) using enzyme-linked immunosorbent assay. DD value was considered positive in our laboratory when it exceeds 0.58 µg/mL.

Outcome

The primary outcome of the study was to assess the compliance with evidence-based guidelines in approaching patients with

suspected PE. Noncompliance was considered when CTPA was ordered without checking DD or following negative DD in "PE unlikely" group.

The secondary outcome of this review was to estimate the rate of CIN which was defined as an increase in serum creatinine more than 0.5 mg/dL or more than 25% from its baseline level, 48–72 h postcontrast exposure.^[24,25] We calculated the prevalence rate of CIN in our sample after excluding the patients with end-stage renal disease (ESRD) who were on dialysis management.

Statistical analysis

Statistical analyses were performed using the Statistical Package for the Social Sciences software version 18. We applied Chi-square and Fisher's exact tests to compare between the categorical variables (e.g., gender, race, elements of Wells' criteria, and CTPA results), whereas we used an unpaired *t*-test to determine the difference among continuous variables (e.g., age and Wells scores). All *P* values were two-sided, considering values <0.05 as statistically significant.

Results

We reported 2136 consecutive CTPA scans performed at the DMC during a period of 6 months. We excluded 96 cases secondary to unavailable proper documentations, and nine cases because of repeating CTPA due to intravenous (IV) contrast extravasation. A total of 2031 cases of CTPA have been retrospectively analyzed. Almost half of them (1001 cases, 49%) were from emergency department (ED), while the rest (1030 cases, 51%) were inpatients. PE was diagnosed in 151 out of 2031 cases (7.4%); 63 were ED patients and 88 were inpatients.

Our sample had a female (64%) and African-American (AA) (86%) predominance, with a mean age of 54 years (range 18–101). The cardinal complaints leading to ordering CTPA were dyspnea (45%) and chest pain (34%). Tachycardia was the most frequent component of Wells' criteria among patients with diagnosed PE (60%). The average of Wells scores was significantly higher in PE-positive cases compared with PE-negative ones; 4.06 versus 1.78, respectively ($P < 0.0001$) [Table 2].

Based on Wells scores, we categorized 1784 patients (88%) into "PE unlikely" group and 247 patients (12%) into "PE likely" group. There was no significant difference in patients' demographics between these two groups [Table 3]. However, PE was remarkably more prevalent in "PE likely" group compared with "PE unlikely" one; 30% versus 4%, respectively ($P < 0.0001$) [Figure 1].

In 1784 cases of "PE unlikely" group, physicians conducted CTPA instead of ordering DD as the first test in 1084 cases (61%); out of those, 1039 CTPA scans (96%) came back negative for PE. Such noncompliance rate was even significantly higher in the inpatient cohort (65%) compared with ED one (57%) ($P < 0.001$). Yet, both of them showed a remarkable nonadherence rate to the current guidelines. Moreover, we reported 78 cases from "PE unlikely" group where CTPA was performed in spite of negative DD assay. All of those CTPA scans had normal pulmonary vasculature [Figure 2].

Finally, DD was unnecessarily ordered in 68 cases from “PE likely” group; definitive diagnostic imaging would have been the appropriate next step in such patients with a high clinical PTP for PE [Figure 3].

The kidney function was assessed post-CTPA in 1322 patients in our sample. After excluding those with ESRD (80 cases), CIN was found in 94 out of 1242 cases (7%); none of them required continuous renal replacement therapy.

Discussion

Positive yield rate of computed tomography-pulmonary angiography

CTPA confirmed the presence of PE in 7.4% of our patients (2031 cases). Moore *et al.*^[26] performed a meta-analysis of 23 studies and found that positivity rates of CTPA ranged between 13% and 42% with an overall PE prevalence average

of 27%. Thereafter, several worldwide reviews reported lower diagnostic yield rates of CTPA studies. Over the past decade, positivity rates of CTPA reported in the US have ranged between 8% and 10% on average,^[11,14,21-23,27-37] whereas such rates are slightly higher (14–16%) in studies performed outside the US.^[10,20,38-44] Reasons for this low diagnostic yield of CTPA in the US are not clear. However, nonadherence to guidelines and legally protective practice adopted by some physicians are likely to be the culprit.

Our study helps in assessing the clinicians’ practice at one of the academic tertiary centers in Detroit metropolitan area. Surprisingly, the rate of positive CTPA in our institution was found to be less than the national average, suggesting a significant overuse of this test.

Compliance rate and avoidable computed tomography-pulmonary angiography

Majority of the physicians in this study (61%) did not check DD level prior to ordering CTPA for “PE unlikely”

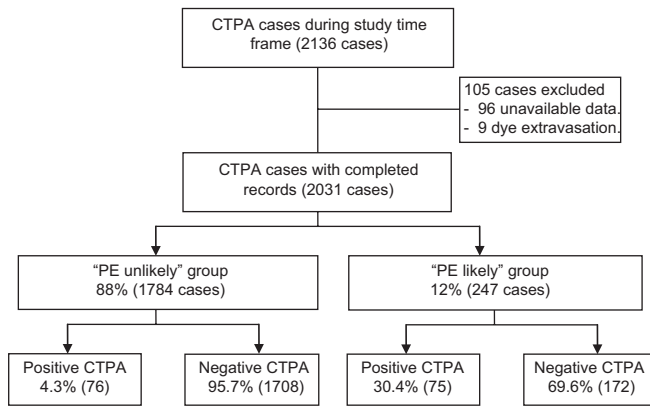


Figure 1: Stratifying the patients who underwent CTPA to “PE unlikely” and “PE likely” groups based on Wells’ criteria. CTPA=Computed tomographic pulmonary angiography, PE=Pulmonary embolism

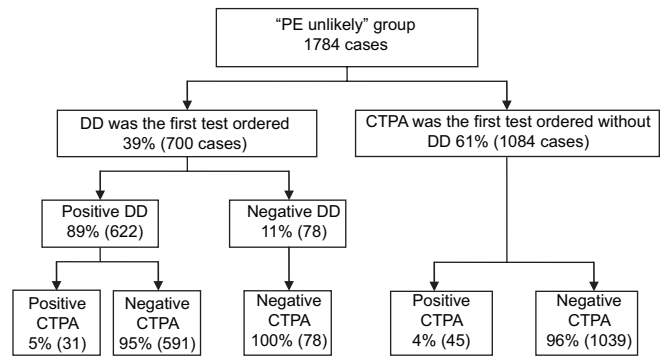


Figure 2: “PE unlikely” group based on modified Wells’ criteria (score ≤4). PE=Pulmonary embolism, CTPA=Computed tomographic pulmonary angiography, DD=D-dimer

Table 2: Patients’ demographics and Wells’ criteria comparison between patients with pulmonary embolism and those without pulmonary embolism

	All patients	CTPA results		P
		Positive CTPA	Negative CTPA	
Total n	2031	151	1880	
Age (years), mean±SD	54±17	59±19	53±17	<0.0001
Male gender, n (%)	723 (36)	64 (42)	659 (35)	0.0836
African-American, n (%)	1744 (86)	130 (86)	1614 (86)	1.00
Emergency room, n (%)	1001 (49)	63 (42)	938 (50)	0.0588
Dyspnea, n (%)	909 (45)	77 (51)	832 (44)	0.0949
Chest pain, n (%)	697 (34)	39 (26)	658 (35)	0.0251
Syncope, n (%)	76 (4)	6 (4)	70 (4)	1.00
Cough, n (%)	22 (1)	1 (0.7)	21 (1)	0.7188
DVT symptoms and signs, n (%)	93 (4.6)	26 (17)	67 (4)	<0.0001
Heart rate >100, n (%)	958 (47)	91 (60)	867 (46)	0.0009
Recent immobilization or surgery, n (%)	601 (30)	84 (56)	517 (28)	<0.0001
History of VTE, n (%)	258 (13)	34 (23)	224 (12)	0.0001
Hemoptysis, n (%)	50 (2.5)	2 (1)	48 (3)	0.1556
Malignancy, n (%)	235 (12)	25 (17)	210 (11)	0.0257
Wells score, mean±SD	1.95±1.84	4.06±2.37	1.78±1.68	<0.0001

CTPA = Computed tomographic pulmonary angiography, VTE = Venous thromboembolism, DVT = Deep venous thrombosis, SD = Standard deviation

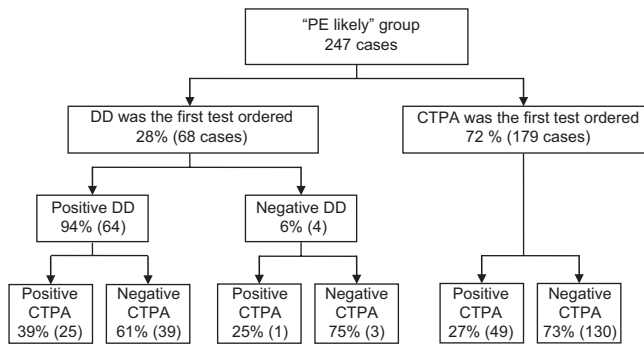


Figure 3: “PE likely” group based on modified Wells’ criteria (score >4). PE=Pulmonary embolism, CTPA=Computed tomographic pulmonary angiography, DD=D-dimer

Table 3: Patients’ demographics and positivity rate of computed tomographic pulmonary angiography comparison between “pulmonary embolism unlikely” and “pulmonary embolism likely” groups

	PE unlikely	PE likely	P
Total number, n (%)	1784 (88)	247 (12)	
Age (years), mean±SD	53±17	55±18	0.1589
Male gender, n (%)	626 (35)	97 (39)	0.2291
African-American, n (%)	1530 (86)	214 (87)	0.7705
Emergency room, n (%)	876 (49)	125 (51)	0.6354
Positive PE in CTPA, n (%)	76 (4)	75 (30)	0.0001

PE = Pulmonary embolism, CTPA = Computed tomographic pulmonary angiography, SD = Standard deviation

patients. This percentage reflects a significant nonadherence to evidence-based guidelines for PE workup. The elevated noncompliance rate might be attributed to unfamiliarity with scoring systems to estimate PTP of PE, lack of knowledge, the fear of malpractice litigation, or using CTPA as a diagnostic tool in assessing the thorax looking for an alternative diagnosis.

Similar retrospective studies have been performed in the US to oversee the compliance with the current guidelines. Significant nonadherence rates (46–73%) were reported at different institutions where the physicians did not order DD test as the first step in PE workup for “PE unlikely” patients.^[23,28-31] This rate was found to be lower in a small study performed in New Zealand (23%).^[40] Crichlow *et al.*^[31] obtained DD samples from 72 patients who did not get DD assay prior to CTPA from “PE unlikely” group; 16 of them (22%) had negative DD and normal CTPA.

Moreover, there were 78 cases (4%) in our sample where CTPA was ordered in spite of negative DD in patients with low PTP; none of them had PE. According to the current guidelines, those CTPA scans are considered unnecessary and should be avoided. Multiple studies showed that the rates of ordering CTPA in “PE unlikely” patients with negative DD ranged between 5% and 18%.^[23,28-31] Yin *et al.*^[33] reviewed all DD tests performed on 1056 patients with low-intermediate probability of PE and found 111 cases (11%) where CTPA was ordered despite negative DD; all of them were negative for PE.

Our study shows a disturbing pattern of CTPA overuse that could have been easily avoided with the implementation of recommended diagnostic algorithms.

Risks of ordering unnecessary computed tomography-pulmonary angiography

CTPA is the most reliable imaging modality to diagnose PE in the current medical practice.^[7] Nevertheless, it is costly and can potentially cause serious problems.

Ionizing radiation exposure is one of the major drawbacks of using CT imaging. Mayo *et al.*^[45] reported that the effective dose of conventional CTPA is 9.0 mSv. However, this dose was measured by Hurwitz *et al.*^[46] and found to be 19.9 ± 1.38 mSv, which is significantly higher than what was previously reported. Sarma *et al.*^[47] estimated the radiation exposure of CTPA to be equivalent to 750 postero-anterior chest radiographs given together at one time. The highest radiation doses during CTPA are absorbed by liver, skin, esophagus, heart, breast, and lungs.^[46,48] This kind of radiation exposure has been linked to an increased risk of cancer, especially in younger ages.^[46,49,50] Estimated relative risks for breast and lung cancer incidences were 1.002–1.011 and 1.005–1.022, respectively.^[46] In addition, Brenner and Elliston^[51] estimated the lifetime attributable cancer death risk in 45-year-old adults who underwent a full-body CT test to be around 0.08%. Thus, appropriate use of CTPA is warranted to avoid unnecessary radiation exposure, especially in women and young patients.^[52]

IV iodinated contrast media used in CTPA have a variety of potential adverse effects, which might be severe enough to cause fatal consequences.^[50] These side effects became less common after developing nonionic low-osmolality contrast materials (1–3%).^[53] However, severe adverse reactions are still possible (0.03%) with a mortality rate of 1–3 per 100,000 cases of contrast use.^[53] Such reactions include urticaria, nausea, vomiting, bronchospasm, and dyspnea. Life-threatening allergic manifestations, such as angioedema and anaphylactic shock, may occur.^[50] Furthermore, extravasation of IV contrast can induce local skin irritation and image failure. This often leads to repeating CTPA and exposing patients to more radiation. The extravasation can occur in 0.1–0.9% of the patients, especially those with vascular diseases.^[50] Wang *et al.*^[54] reviewed 69,657 computed tomography scans with IV contrast and reported 475 extravasation events (0.7%). Similarly, in our study, nine cases (0.4%) had repeated CTPA because of image failure secondary to contrast extravasation.

Moreover, CIN is one of the most serious nonallergic adverse effects to IV contrast agents. On contrary to anaphylactoid reaction, CIN is dependent on the injected dye dose. It is defined as an increase in serum creatinine more than 0.5 mg/dL or more than 25% than its baseline level, within 2–7 days postcontrast exposure.^[55] Nash *et al.*^[56] described CIN as the third most frequent cause (11%) of hospital-acquired acute kidney injury cases. In a prospective cohort performed on 174 patients who underwent CTPA, Mitchell *et al.*^[35] reported a CIN incidence rate of 14% of the cases. This percentage was as high as 25% in a retrospective review performed by Reagle *et al.*^[34] on 925 patients who underwent CTPA. In our study,

two-thirds of cases (65%) had their kidney function checked after contrast exposure, with a CIN rate of 7%.

Finally, air embolism, seizure, pulmonary edema, and cardiac arrhythmias have also been reported as rare but serious nonanaphylactoid complications of IV contrast.^[50]

Therefore, minimizing unnecessary CTPA scans will improve patients' safety and protect them from potential harm due to unnecessary radiation exposure and contrast media injection, while reducing cost and possibly hospital length of stay.

Suggestions

We have made some suggestions to improve our physicians' compliance with the recommended guidelines. Periodic targeted educational sessions for medical staff are perhaps helpful in keeping physicians aware of the available evidence-based literature and updated trials. Furthermore, the electronic medical records (EMRs) system can be employed to guide clinicians to auto-calculate the probability scores for patients with suspected PE. This will facilitate the utilization of diagnostic algorithms and minimize the nonsystematic approach in PE evaluation. Drescher *et al.*^[36] found that implementing the computerized decision support system improved the diagnostic yield of CTPA, although it was poorly applied by physicians. Similarly, Roy *et al.*^[57] reported a significant improvement in decision-making during PE approach by following a computerized handheld decision-support system. Moreover, the widely used current DD cutoff point carries a high false-positive rate (95% in our study) leading to a significant number of negative CTPA [Figure 2]. In our cohort, using age-adjusted DD cutoff levels in patients older than 50 years may have changed the interpretation from a "positive" to a "negative" DD test in 13 cases, corresponding to 3.4% of those patients, and potentially avoided conducting a significant number of CTPA studies.

Study limitations

The retrospective nature of our study resulted in assessing PTP of PE by research personnel instead of decision-making physicians who evaluated the patients. Besides that, our researchers relied on electronic data documented prior to CTPA images to collect the variables which might not be properly reported in physicians' notes. However, the investigators were instructed to search for each element of Wells' criteria among the best well-documented data to assess PTP, before reviewing CTPA results.

In addition, we studied all patients who underwent CTPA during that time frame, but we did not include patients with suspected PE who did not have CTPA. Adding those patients could have provided a better assessment of physicians' compliance with the current guidelines. Nevertheless, we suspect that this group of patients is small and may not have significantly affected our study result.

Although our sample size is large, it is still limited to a single institution in Detroit area. Besides that, AA race was predominant in this study (86%), which can be attributed to the normal ethnical distribution of Detroit metropolitan area. However, we did not find a significant difference in DD values and PE prevalence between AA and non-AA groups.

Conclusions

The suboptimal implementation of clinical probability assessment tools can result in the overuse of CTPA, contributing to ineffective utilization of hospital resources, increased cost, and potential harm to patients. We believe that this practice is widespread and not limited to our institution. Further multicenter studies are needed to confirm whether this disturbing pattern is widespread. Implementing validated guidelines will optimize the use of CTPA, while helping with better allocation of resources and cost containment. Subsequent prospective trials are important to assess the efficacy of the suggested EMR-guided algorithms and targeted staff education sessions.

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Conflicts of interest

There are no conflicts of interest.

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