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Added Value of Dual Energy CT Angiography in Assessment of Pulmonary Embolism

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ABSTRACT

Background: Pulmonary embolism (PE) is a common clinical condition being third on the list of cardiovascular causes of death. Computed tomography angiography (CTA) is considered the first-line imaging modality for suspected acute PE. Dual-energy computed tomography (DECT) has made it possible to simultaneously obtain angiographic CT imaging and pulmonary perfusion maps. The aim was to identify role of DECT angiography in diagnosing pulmonary embolism. **Objective:** This study aimed to evaluate accuracy of iodine perfusion maps in diagnosing pulmonary embolism using DECT scanner. To detect location of the small pulmonary emboli using iodine maps (segmental, sub segmental).

Methods: This cross-sectional study was conducted at Radiology Department, Zagazig University Hospitals. This study included 18 cases with pulmonary embolism. The duration of the study ranged from 6-12 months.

Results: Regarding per CT angiography findings, the current study showed that nine (50%) patients had pulmonary embolism at right lung, 7 (38.9%) patients had pulmonary embolism at left lung and found in both lungs in two (11.1%) patients. Pulmonary embolism was found in upper lobe in 44.4% patients, at lower lobe in 27.8% patients, at main pulmonary artery in 16.7% patients and at middle lobe in 11.1% patients. Regarding level of pulmonary embolism, Subsegmental level was the most common found (44.4%) followed by segmental level in 38.9% patients. 10 (55.6%) were occlusive, and 8 (44.4%) were non-occlusive. Regarding distribution of the studied patients concerning matched defect on iodine map, 8 (44.4%) patients had matched defect on iodine map.

Conclusion: The iodine maps have an important effective role in detection of pulmonary embolism.

Key words: Dual energy CT angiography, Conventional CT angiography, Pulmonary embolism.

INTRODUCTION

Pulmonary embolism (PE) is blood clot that occurs in lung, it is common and potentially fatal disorder as it can damage part of lung due to restricted blood flow and decreased oxygen level in the blood. So early diagnosis is effective and improves the chance of survival. PE is the third most common acute cardiovascular disease after myocardial infarction and stroke and it leads to thousands of deaths each year because it often goes undetected. Early diagnosis and treatment of PE are essential for optimizing clinical outcomes [(1)].

In some cases, a pulmonary embolism can be difficult to diagnose, this is especially true if you have an underlying lung or heart condition, such as emphysema or high blood pressure [(2)]. To detect the cause, patient should do one or more investigation such as: chest X-ray, pulmonary angiography, CT, MRI, duplex venous ultrasound, venography, ECG and D-dimer test but all cannot detect size and site of small blood clot exactly in some cases [(3)].

As the treatment of pulmonary embolism depends on the size and location of the blood clot, we tend to try to use dual energy CT angiography using iodine maps in diagnosing PE [(2)]. Dual energy CT angiography is the current reference standard for the detection of PE**,** allowing visualization of contrast material within the pulmonary vasculature using iodine maps and has been shown to be comparable to conventional angiography for diagnosis of PE. Dual-energy (DE) CT angiography allows differentiation of materials based on their energy absorption characteristics and has been proposed as a method to aid in the detection of PE in the lungs, the pattern of iodine enhancement at DE CT angiography has been shown to correspond to lung blood volume at planar scintigraphy and single photon-emission CT [(1)].

The objectives of the study were to identify role of DECT angiography in diagnosing pulmonary embolism. To evaluate accuracy of iodine perfusion maps in diagnosing pulmonary embolism using DECT scanner. To detect location of the small pulmonary emboli using iodine maps (segmental, sub segmental).

PATIENTS AND METHODS

This cross-sectional study was performed in the period from July 2020 to May 2021 in Zagazig University Hospitals and was conducted on thirty patients having renal masses previously diagnosed with ultrasound and/or computed tomography, referred to the Radiology, Urology and Oncology Departments. These patients included (13) females and (17) males, their ages ranged from 3 years to 72 years old.

Inclusion criteria: Age: all age groups (3-72 years old), sex: both sexes (males & females), and patient consent to enter the study.

Exclusion criteria: Renal insufficiency, and hemodynamic instability.

Collection of the recorded patient's data:

(1) Full history taking.
(2) Full clinical examination.

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(3) Investigations:

- Conventional CT angiography.
- Dual energy CT angiography.

Patients that performed CT angiography of the chest received intravenously 120 ml contrast. Contrast material was infused at 3.0–4.0 ml/sec. A region of interest was placed over the pulmonary artery at the level of the carina (central venous access) and infused via a peripheral intravenous catheter injection. First, the location, level, and type (occlusive vs non-occlusive) of PEs on conventional CT angiograms was recorded then iodine maps were reviewed for defects suggestive of PE. Last, CT angiograms were reviewed to detect additional PEs suggested by the iodine map. Consensus reviews were performed for examinations with PEs. The confidence interval of percentages was calculated by using the Clopper-Pearson method.

Dual energy CT angiography procedures:

Image reconstruction and iodine map generation:

The contrast-enhanced dual-energy CT images were reconstructed using an iterative dual-energy reconstruction kernel at 1-mm thickness with sinogram-affirmed iterative reconstruction. The dual-energy CT iodine maps were generated using the lung analysis with default blending by using a 128-channel CT system. DE CT-PA was performed for all participants by using a dual-source CT system. All patients received 70 mL of iopamidol (370 mg/ml iodine) via an antecubital vein at 4 ml/sec by a power injector. Following contrast injection, 30 ml of saline was administered. During the scan, patients held their breath on inspiration. Pulmonary trunk attenuation was tracked by a bolus-tracking technique. Image acquisition was triggered manually once attenuation in the pulmonary trunk reached 100 Hounsfield units (HU). Radiation exposure was estimated from the dose-length product (DLP) to obtain the subtraction CT iodine maps, arithmetic subtraction of the pre-contrast image from the contrast-enhanced image was performed using the 100-kV dual-energy CT acquisition after motion correction. The dual-energy iodine map was color coded for presentation to the readers.

Image analysis and assessment:

Consensus reviews were performed. DE CT angiograms were retrospectively reviewed. All radiologists were blinded to the clinical report. A junior thoracic radiologist first reviewed CT angiograms for the presence of PE (cutoff of contrast opacification in a pulmonary artery, visualization of thromboembolic clot). If a PE was present, the location, level (main, lobar, segmental, or subsegmental pulmonary artery), and extent (occlusive vs non-occlusive) of PE was recorded. PEs were classified as occlusive if no contrast material was visualized distal to the clot. For each examination, the iodine map was reviewed after review of the CT angiogram. Image quality on the iodine maps was recorded as either excellent (no artifacts), good (minor artifacts), moderate (still able to assess iodine distribution), or poor (impossible to assess iodine distribution). The iodine map images were then reviewed for the presence of any defect. Iodine map defects were characterized as either consistent with PE not consistent with PE if they appeared to be caused by tumors or consolidations or band-like defects consistent with artifact, often due to cardiac motion or beam hardening from contrast material within the superior vena cava or innominate vein. For examinations with iodine map defects characteristic for PE, CT angiograms were re-reviewed to determine if iodine map defects corresponded to any CT angiogram findings.

Conventional CT angiography (CCTA) procedures:

CCTA examination:

All CCTA examinations were performed using MDCT scanner. Patients were examined in a supine position, and both arms were extended above the head. All CCTA data were acquired in the craniocaudal direction from the lung apex to the costophrenic angles during a single breath-hold (inspiration). The bolus-tracking technique was used in the main pulmonary artery with a trigger attenuation threshold of 50 HU. Total 40 ml of contrast agent was injected. First, 12 ml contrast agent and 18 ml saline were injected simultaneously at a flow rate of 4 ml/sec using a dual-head power injector to compensate for a delay time of 7 sec when the table moved from the bolus-tracking level to the lung apex. Then, the rest 28 ml contrast agent were injected followed by a constant saline flush of 30 ml at a flow rate of 5 ml/sec.

Image analysis and radiation exposure dose:

The CCTA data were transferred to an external workstation. The quantitative analysis was performed by a radiologist. The CT attenuation in the nine arteries was measured using ROI that was slightly less than the selected artery: the pulmonary trunk, left pulmonary artery, right pulmonary artery, both upper lobe arteries, both lower lobe arteries, right middle lobe artery and left lingual artery. The average value was calculated as the mean CT attenuation. The average standard deviation in the three regions (left, middle and right) with a ROI area of 20 mm^2 in front of the chest at the right pulmonary artery slice was measured as the background noise. The CT value of the bilateral paravertebral muscle was measured, and the mean value was calculated as the background CT attenuation. The signal-to-noise ratio (SNR) was calculated as the mean CT attenuation/the background noise. The contrast-to-noise ratio (CNR) was calculated as follows: (mean CT attenuation-background CT attenuation)/background noise.

The subjective image quality analysis and the diagnosis of PE were performed by radiologists who were blinded to the clinical features and the CCTA protocols.

Ethical consent:

An approval of the study was obtained from Zagazig University Academic and Ethical Committee. Every patient signed an informed written consent for acceptance of the study. This work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Statistical analysis

The collected data were coded, processed and analyzed using the SPSS (Statistical Package for Social Sciences) version 22 for Windows® (IBM SPSS Inc., Chicago, IL, USA). Data were tested for normal distribution using the Shapiro Walk test. Qualitative data were represented as frequencies and relative percentages. Chi square test (χ^2) was used to calculate the difference between two or more groups of qualitative variables. Quantitative data were expressed as mean ± SD (Standard deviation). Independent samples t-test was used to compare between two independent groups of normally distributed variables (parametric data). P value < 0.05 was considered significant.

RESULTS

Table (1) showed clinic-demographic characteristics in the studied patients. The age of patients ranged from 27 to 85 years with a mean of 50.89 ± 19.87 years. Regarding gender, half (50%) patients were males and 9 (50%) patients were females with male to female ratio of 1: 1. Three (16.7%) patients were smokers. As regards to chronic diseases, 5 (27.8%) patients were hypertensive, 4 (22.2%) patients were diabetics and two (11.1%) patients had dyslipidemia.

Table (2) illustrated distribution of the studied patients as per pulmonary embolism data. Nine (50%) patients had pulmonary embolism at right lung, 7 (38.9%) patients had pulmonary embolism at left lung and found in both lungs in two (11.1%) patients. Pulmonary embolism was found in upper lobe in 44.4% patients, at lower lobe in 27.8% patients, at main pulmonary artery in 16.7% patients and at middle lobe in 11.1% patients. Regarding level of pulmonary embolism, subsegmental level was the most common found (44.4%) followed by segmental level in 38.9% patients.10 (55.6%) were occlusive, and 8 (44.4%) were non-occlusive.

Table (3) illustrated distribution of the studied patients as regards matched defect on Iodine Map. 8 (44.4%) patients had matched defect on Iodine Map.

Table (4) showed comparison between CT angiograms and iodine maps. Among the 10 occlusive pulmonary embolism found on CT angiograms, 8 (80%) had a matched defect on iodine maps and 2 (20%) did not. In comparison, 8 (80%) of the 8 non-occlusive PEs found on CT angiograms had not matched defect on iodine maps. Receiver operating characteristic (ROC) analysis was performed to determine diagnostic value of dual energy CT angiography for assessment of pulmonary embolism. By using ROC-curve analysis, Dual Energy CT Angiography can determine pulmonary embolism with excellent accuracy (90.0%). The sensitivity, specificity, PPV and NPV was 100%, 80%, 83.33% and 100% respectively (p < 0.001) as shown in table (5).

Table (1): Distribution of clinic-demographic characteristics among the studied patients

Parameters		Studied patients (No.=18)	
		No.	%
Age (years)	**Mean ± SD**	50.89 ± 19.87	
	Median	47.0	
	Range	27.0- 85.0	
Gender	**Male**	9	50.0%
	Female	9	50.0%
Special habits as Smoking	**No**	15	83.3%
	Yes	3	16.7%
Diabetes mellitus	**No**	14	77.8%
	Yes	4	22.2%
Hypertension	**No**	13	72.2%
	Yes	5	27.8%
Dyslipidemia	**No**	16	88.9%
	Yes	2	11.1%

SD: standard deviation,

Table (2): Distribution of the studied patients as per CT angiography findings

Parameters		Studied patients (No.=18)	
		No.	%
Site	**Bilateral**	2	11.1%
	Left	7	38.9%
	Right	9	50.0%
Location	**Lower lobe**	5	27.8%
	Main	3	16.7%
	Middle lobe	2	11.1%
	Upper lobe	8	44.4%
Level of pulmonary embolism	**Lobar**	1	5.6%
	Main	2	11.1%
	Segmental	7	38.9%
	Subsegmental	8	44.4%
Extent of pulmonary embolism	**Nonocclusive**	8	44.4%
	Occlusive	10	55.6%

Table (3): Distribution of the studied patients as regards matched defect on iodine map

Parameters		Studied patients (n=18)	
		No.	%
Matched defect on iodine map	**No**	10	55.6%
	Yes	8	44.4%

Table (4): Comparison between CT angiograms and iodine maps

		Matched Defect on Iodine Map		Not Matched on Iodine Map		p-value
		No.	%	No.	%	
Extent of pulmonary embolism	Non-occlusive	0	0.0%	8	80.0%	0.001
	Occlusive	8	100.0%	2	20.0%	

Table (5): Validity of dual energy CT angiography in comparison with conventional CT angiography for assessment of pulmonary embolism

Parameters	Dual Energy CT Angiography
Cutoff value	>1.0
AUC (95% CI)	0.900 (0.667 - 0.990)
Sensitivity	100.0%
Specificity	80.0%
PPV	83.33%
NPV	100.0
Accuracy	90.0%
P value	**<0.001**

PPV= Positive predictive value, NPV= Negative predictive value, AUC= Area under curve

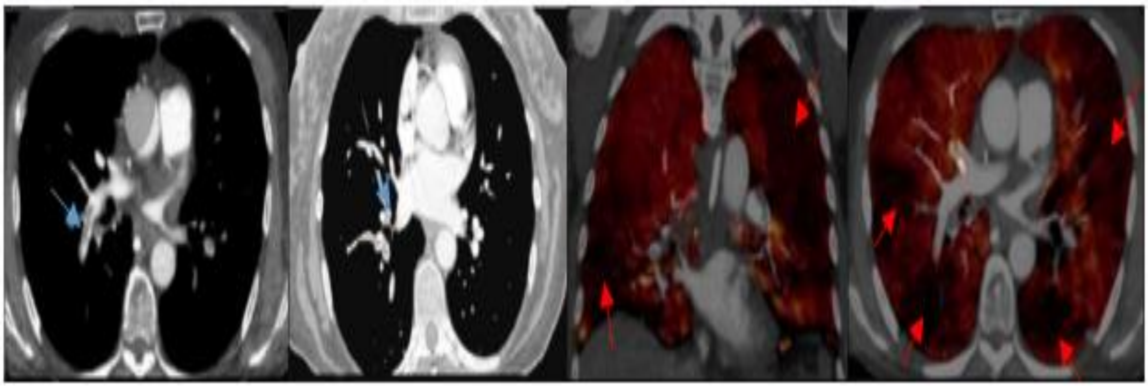

Figure (1): Female 55 years old presented to emergency room with severe chest pain dyspnea, sweeting, tachycardia patient was suspected for pulmonary embolism after exclusion of other causes CT pulmonary angiography showed insufficient contrast in branches of left pulmonary artery (blue arrow). Iodine mapping showed bilateral filing defect (red arrow).

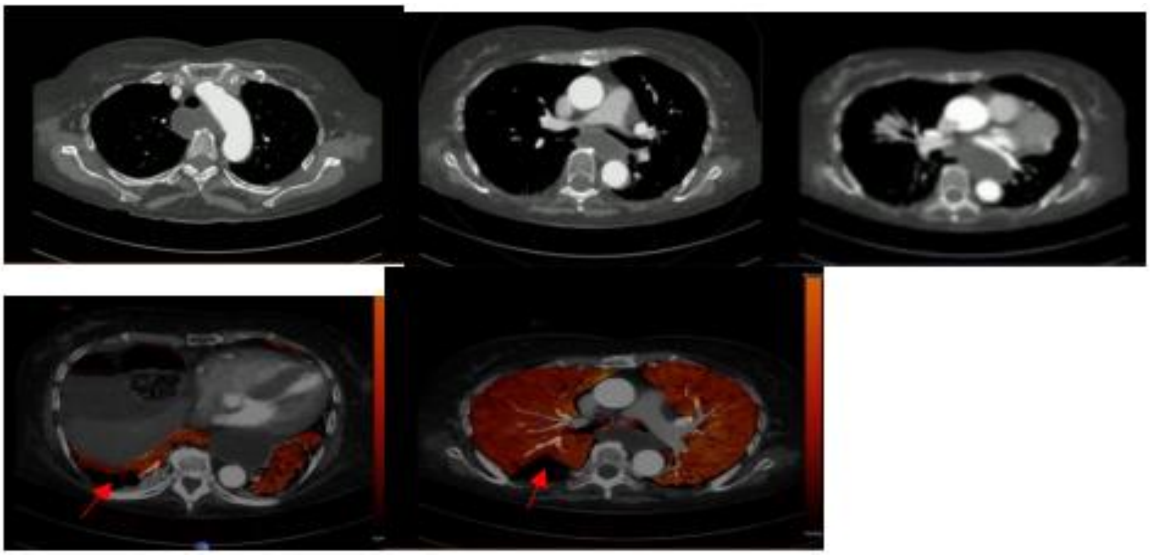

Figure (2): Female patient 50 years old suffering from chest pain normal CT angiography iodine mapping showing wedge shape filling defect at right lower lobe (red arrow).

Figure (3): 55 years old patient went under bone biopsy from pelvis and new large mass at lower abdomen huge hematoma noted at CT scan (yellow arrow) CT angiography normal iodine mapping showing filling defect at lingula (red arrow).

DISCUSSION

Regarding per CT angiography findings; the current study showed that nine (50%) patients had pulmonary embolism at right lung, 7 (38.9%) patients had pulmonary embolism at left lung and two patients (11.1%) had in both lungs. Pulmonary embolism was found in upper lobe in 44.4% patients, at lower lobe in 27.8% patients, at main pulmonary artery in 16.7% patients and at middle lobe in 11.1% patients. Regarding level of pulmonary embolism, subsegmental level was the most common found (44.4%) followed by segmental level in 38.9% patients. 10 (55.6%) were occlusive, and 8 (44.4%) were non-occlusive. While in the study of **Chen *et al.*** [(4)], two hundred eleven computed tomography pulmonary angiography (CTPA) examinations were positive for PE, giving a CTPA positive yield rate of 15.9% (95% CI (13.93–17.87). One hundred and thirteen (8.1%) CTPA were considered indeterminate, and eleven were considered non-diagnostic (0.8%). Among the 211 CTPA positive for PE, 67 (32%) were proximal emboli, 98 (47%) were segmental emboli and 44 (21%) were subsegmental emboli.

In conclusion, in this retrospective study done in a Canadian academic tertiary center, they reported a positive rate of 15.9% for PE detection with CTPA, which is above the generally accepted lower threshold of 10% for the yield of CTPA. Also, **Weidman *et al.*** [(5)] reported that a total of 372 PEs were found in 147 of 1144 (12.8%; 95% CI: 10.9%, 15.1%) CT angiograms. Among these 372 PEs, 20 (5.4%) were in a main pulmonary artery, 76 (20.4%) were at the lobar level, 149 (40.1%) were at the segmental level, and 127 (34.1%) were at the subsegmental level; 40.9% (152) were occlusive, and 59.1% (220) were non-occlusive.

In the study in our hands, regarding distribution of the studied patients concerning matched defect on iodine map, 8 (44.4%) patients had matched defect on iodine map. **Pontana *et al.*** [(6)] describing iodine map defects in 14 of 17 occlusive PEs (82%) versus five of 51 non-occlusive PEs (10%). **Thieme *et al.*** [(7)] found defects on iodine maps in 42 of 44 (95%) occlusive PEs and only two of 44 (5%) were non-occlusive PEs. Prior studies have found the extent of perfusion defects on iodine maps to correlate with the Qanadli CT angiography obstruction index, which has independently been shown to correlate with PE severity as measured by pulmonary artery pressure and oxygen saturation [(8)].

Regarding comparison between CT angiograms and iodine maps, the present study showed that among the 10 occlusive pulmonary embolisms found on CT angiograms, 8 (100%) had a matched defect on iodine maps and 2 (20%) did not. In comparison, 8 (80%) of the 8 non-occlusive PEs found on CT angiograms had not matched defect on iodine maps.

In the study of **Weidman *et al.*** [(5)], thirty-three of 1144 (2.9%) iodine maps in 33 of 1035 (3.2%) patients had peripheral wedge-shaped defects suspicious for PE without a corresponding finding on CT angiograms. Of these 33 patients, 18 (54.5%) were treated with anticoagulation due to concurrent PE in an alternate location or other clinical indication. 20 (60.6%) died within a 6-month follow-up period and two (6.1%) died within 14 days of the DE CT angiography examination (both of these patients had PEs detected elsewhere with CT angiography and were treated with anticoagulation. **Jawad *et al.*** [(9)] stated that automatic perfusion defect volume (PDvol) (DECT assessed perfusion defect volume) had a weak correlation ($r = 0.47$, $p = 0.02$) and semiautomatic PDvol ($r = 0.68$, $p < 0.001$) had a moderate correlation to obstruction score in patients with confirmed acute PE, while only semiautomatic PDvol (r = 0.43, p = 0.03) had a weak correlation with the RV/LV diameter ratio. Their data indicate that PDvol assessed by DECT software technique may be a helpful tool to assess the severity of acute PE when compared to obstruction score and RV/LV diameter ratio.

In a study conducted by **Im *et al.*** [10] in both CTPA and DECT groups, right to left ventricle diameter ratio ≥ 1 was associated with an increased risk of all-causes of death within 30 days (hazard ratio: 3.707, p < 0.001 and 5.573, p < 0.001, respectively). However, C-statistics showed no statistically significant difference between the CTPA and DECT groups for predicting death within 30 days (C-statistics: 0.759 vs. 0.819, p = 0.117).

Furthermore, **Zhang *et al.*** [11] showed the higher sensitivity of the DECT iodine map in PE detection in rabbits in comparison with conventional CTPA (89% and 67%, respectively).

CONCLUSION

The iodine maps have an important effective role in detection of pulmonary embolism.

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