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ORIGINAL ARTICLE

Prediction of short term outcome of pulmonary embolism: Parameters at 16 multi-detector CT pulmonary angiography

Mohamed Mohamed Hefeda [a,*], **Magdy Mohamed Elmasry** [b]

[a] Radiology Department, Tanta University, 2, Elbandar Square, Elmahalla ElKobra, Egypt
[b] Tanta University, Egypt

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KEYWORDS

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Abstract *Purpose:* To evaluate the accuracy of computed tomography pulmonary angiography (CTPA) parameters, for predicting short-term mortality in patients with acute pulmonary embolism (PE).

Materials and methods: Thirty-two patients with proven PE had CT pulmonary angiography were included in the study. The clot burden using the Qanadli score (QS), and the right ventricular dysfunction (RVD) parameters were assessed on CT by calculating right ventricular/left ventricular (RV/LV) diameter ratios, interventricular septum abnormality, inferior vena cava contrast reflux, azygous vein and superior vena cava measures. Contrast density in pulmonary artery and descending aorta was evaluated for all patients. Patients were followed up for 30 days and then classified as survivors or non survivors.

Results: Thirty-two patients were included in the study, 23 (71.8%) of them were classified as survivors, and the other nine (28.1%) patients died within the first month (non survivors). There was a positive, but weak correlation between the Qanadli score and the short term mortality (P value = 0.05). There was a statistically significant relationship between the RV/LV ratio and PE-related mortality, with a P value < 0.001. Also, there was a good correlation between degree of IVC reflux and PE outcome ($P < 0.001$). The PA/AO diameter ratio, SVC diameter and azygous vein diameter showed no statistically significant difference between survivors and non survivors.

Conclusions: CTPA findings that may predict short term mortality are the high grades of inferior vena cava reflux, RV/LV diameter ratio more than 1.2, and clot burden >18 according to the Qanadli score and to a lesser degree the interventricular septum abnormality.

* Corresponding author. Tel.: +20 1224569391, +20 402257997.
E-mail addresses: mohamedhefeda@yahoo.com (M.M. Hefeda), Magdy.ry@hotmail.com (M.M. Elmasry).

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1. Introduction

Pulmonary embolism (PE) is a common and potentially fatal cardiovascular disorder. The short-term mortality of PE varies widely, ranging from less than 1% in hemodynamically stable patients to over 90% in patients who present with cardiorespiratory arrest (1).

Risk stratification for patients with acute pulmonary embolism (PE) is important to establish appropriate treatment and management (2). Computed tomographic (CT) pulmonary angiography has progressively been established as the frontline imaging modality for the diagnosis of PE, replacing ventilation-perfusion lung scintigraphy and pulmonary angiography (3–5).

Several investigators have attempted to determine prognosis from findings by computed tomography (CT). Authors of several retrospective studies have suggested right sided heart strain and embolic burden at CT as prognostic parameters (6,7).

The presence, location, and degree of obstruction of arterial clots can be scored according to four different scoring systems as proposed by Miller et al. (8), Walsh et al. (9), Qanadli et al. (10), and Mastora et al. (11).

Acute PE increases the pressure of the pulmonary arterial system and right ventricle (RV) resulting in RV dysfunction, which may progress to right heart failure and circulatory collapse (12,13). Patients with RV dysfunction have a higher mortality rate than those without, even if they are initially hemodynamically stable (13,14). Thus, the presence of RV dysfunction is a marker for adverse clinical outcome in patients with acute PE (13–15).

The purpose of this study was to assess the prognostic value of different parameters at multi-detector CT pulmonary angiography in prediction of short term mortality in patients with acute pulmonary embolism.

2. Materials and methods

2.1. Patients

From December 2012 through October 2013, thirty-two patients with proven pulmonary embolism (PE) were included in the study. They had been followed up for 30 days and then classified into survivors and non survivors. Only the CT with acute PE at initial presentation was included. History and physical emergency room notes, discharge summaries, and progress notes were retrieved for each patient. Information such as patient demographics (age, sex, and race), preexisting co-morbidities, and discharge disposition was obtained. Short-term death was defined as death within 30 days (16). Patients who could not be followed up for 30 days and patients with major health problem that may affect survival (massive myocardial infarction, cerebral infarction/hemorrhage, and renal failure, etc.) were excluded from the study.

2.2. Pulmonary CTA

All scans were obtained using a commercially available 16-MDCT scanner (Somatom emotion 16, Siemens Medical Solutions). Patients were examined in a supine position with both arms extended above the head. A frontal scout view was acquired at 120 kVp and 50 mA. The angiography scan was obtained in a caudocranial direction during a single inspiratory breath-hold. The scan volume ranged from the level of the right diaphragm to a level just above the aortic arch. A standard collimation of 0.75 mm was used with a gantry rotation speed of 0.5 s and a pitch factor of 1.1. Patients were scanned with a kilovoltage of 100 kVp and a tube current level of 200 mA (100 mAs) as the reference value.

Vessel opacification was provided by intravenous administration of 125 ml of ioversol (Optiray 350; Tyco Health/Mallinckrodt, St. Louis, MO) at a rate of 4–5 ml/s.

Injections were given automatically using a commercially available injector (Injektron CT2, Medtron). Individual contrast optimization was based on bolus tracking (CARE Bolus, Siemens) in the right ventricle using a trigger level of 100 H. For measuring early contrast enhancement, a series of dynamic monitoring scans was obtained at 2-s intervals using a low-dose protocol (100 kVp; 20 mAs; slice thickness, 4.5 mm). Bolus tracking was started 4 s after injection of the contrast agent had started. Furthermore, an additional delay of 7 s was added after bolus tracking before diagnostic pulmonary CTA.

For further postprocessing, thin-slice reconstruction was performed with a slice thickness of 1 mm, an increment of 0.7 mm. Final image analysis was performed on axial images and on coronal maximum intensity projections (MIPs) with slice thicknesses of 3 and 6 mm, respectively.

2.3. Image analysis

2.3.1. Clot burden

Current study quantified the vascular obstruction index (i.e., the percentage of vascular obstruction of the pulmonary arterial tree caused by PE) by using the scoring system of Qanadli et al. (10). In brief, this index is defined as the number of segmental artery branches that are blocked and corrected by a factor of one for partial blockage or a factor of two for completely obstructive PE. With this scoring system, the highest possible score is 40 (thrombus completely obstructing the pulmonary trunk), which corresponds to a 100% obstruction index (Table 1).

2.3.2. CT signs of right heart dysfunction

CT signs used to assess function of the right heart included the ratio of right ventricle diameter to left ventricle diameter (RV/LV ratio), ratio of main pulmonary artery diameter to ascending aorta diameter (PA/AO ratio), superior vena cava diameter and interventricular septum morphology. Diameters (minor axes) of the right and left ventricles were measured on the axial CT image of the heart at their widest point (Fig. 1) (usually the image showing the atrioventricular valves) between the inner surface of the free wall and the surface of the interventricular septum (17). The RV/LV ratio was calculated. The diameters of the main pulmonary artery and the ascending aorta were measured on the transverse image at which the right pulmonary artery is in contiguity with the main pulmonary artery (7). The PA/AO ratio was calculated. The diameters of the superior vena cava and azygos vein were measured on the transverse CT image where the azygos vein reaches the superior vena cava (17). Morphology of interventricular septum was considered normal (Fig. 2c) (convex toward the right

Table 1 The Qanadli score adapted from Qanadli et al. (10).

No. of arteries assessed	Score	Maximum score
10 segmental arteries in each lung (n = 20)	0 – No thrombus observed 1 – Partial occlusion 2 – Total occlusion	40

ventricle), flattened, or bowing (convex toward the left ventricle) (17).

2.3.3. IVC reflux

The severity of reflux of contrast medium into the IVC or hepatic veins was graded using axial images into six categories according to a previously published scale (18): (1) no reflux into IVC; (2) trace of reflux into IVC only; (3) reflux into IVC but not hepatic veins; (4) reflux into IVC with opacification of proximal hepatic veins; (5) reflux into IVC with opacification of hepatic veins down to the mid-portion of the liver; and (6) reflux into IVC with opacification of distal hepatic veins.

2.3.4. Pulmonary artery and aortic enhancement

For the ratio of the descending aorta enhancement to main pulmonary artery enhancement, Hounsfield unit (HU) of pulmonary artery was measured at the widest area as possible of main pulmonary artery on a trans-axial CT image from where the main pulmonary artery branches to the left and the right pulmonary arteries, and the Hounsfield unit (HU) of the descending aorta was measured from the same level.

2.3.5. Statistical analysis

Results are expressed as the mean ± standard deviation for data distributed normally. Baseline characteristics and imaging parameters were analyzed by ANOVA and chi-squared test. A P value < 0.05 was considered significant. The data were analyzed using the Statistical Package for the Social Sciences (SPSS, version 15.0; SPSS, Inc., Chicago, IL, USA).

3. Results

One month follow up was completed for all patients. During this month, 9 patients died (non survivors), and death is mostly related to pulmonary embolism. The patients were accordingly classified into survivors and non survivors.

3.1. Baseline patient characteristics

Table 2 states the basal patient characteristics. Thirty-two patients were included in the study, 23 (71.8%) of them were

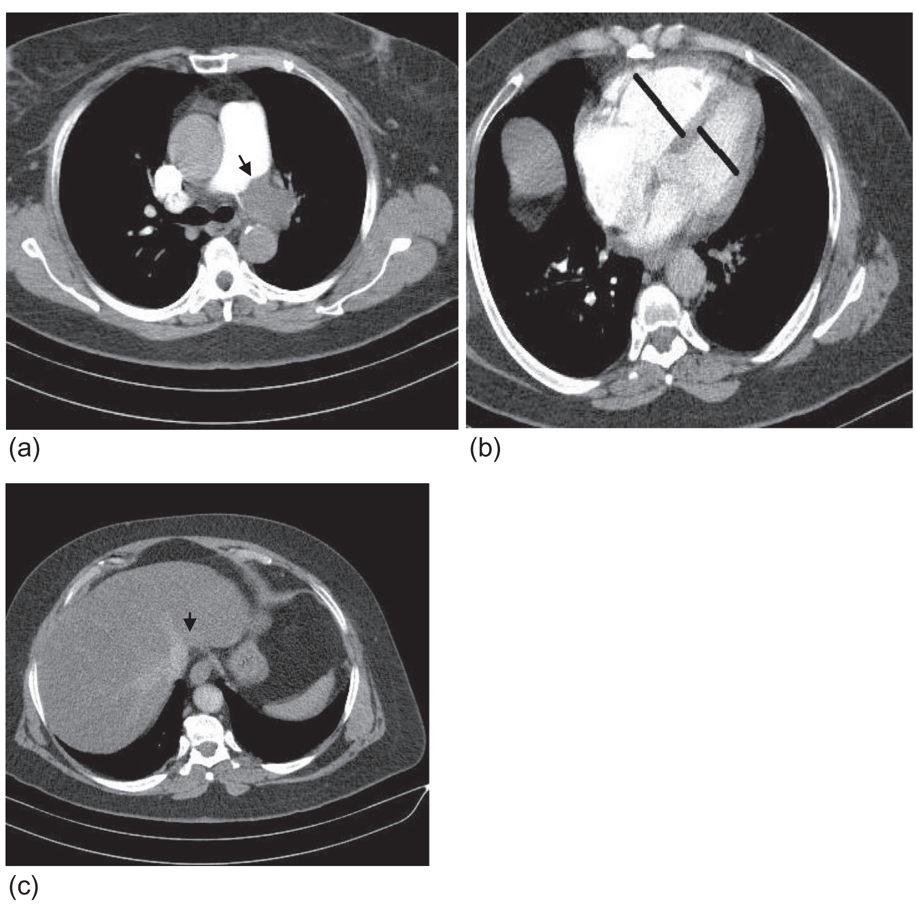

Fig. 1 CTPA of a female patient aged 45 years. (a) Large thrombus seen in the left main pulmonary artery, QS > 18. (b) RV/LV ratio >1.4, with flattening of the interventricular septum. (c) Significant reflux in the inferior vena cava and hepatic veins. The patient died on the 6th day.

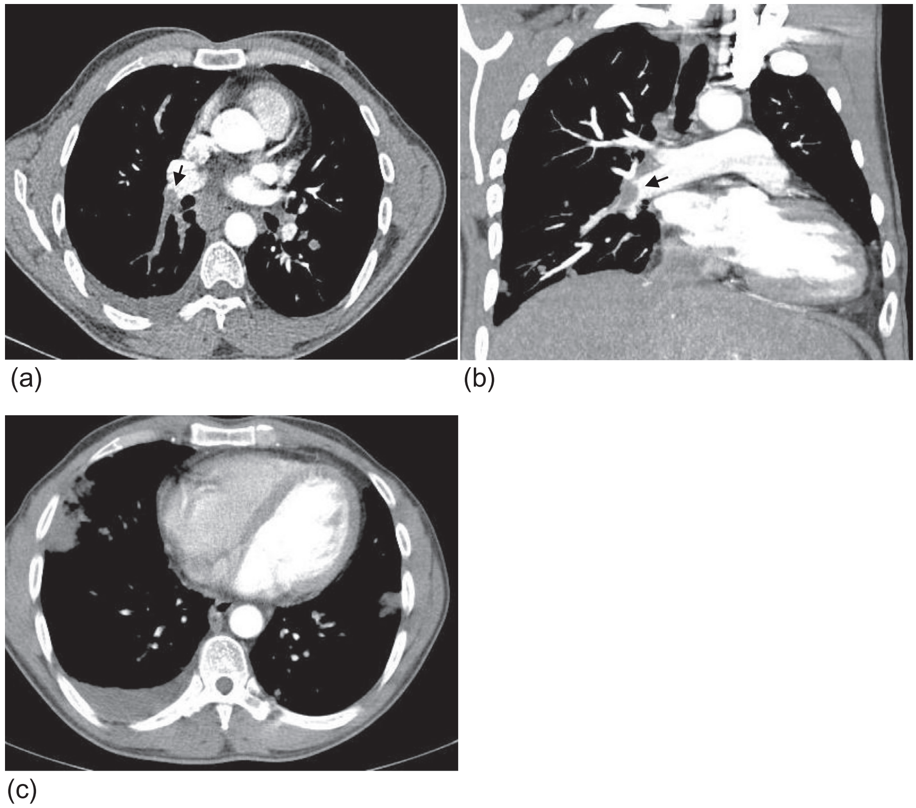

Fig. 2 CTPA of a male patient aged 55 years. (a, b) Thrombus seen in the inferior lobar artery, Qanadli score <18. (c) RV/LV ratio = 1, with normal interventricular septum. Small area of pulmonary infarction in the right lower lobe. The patient was a survivor.

Table 2 Patient characteristics of the study.

Parameters	Survivors (n = 23)	Non survivors (n = 9)	P value
Age	55.6 ± 9.5	58 ± 8.7	0.214
Male gender (%)	**15 (65.2)**	**6 (66.6)**	**0.651**
Smoking (%)	10 (43.4)	7 (77.7)	0.01*
Hypertension (%)	15 (65.2)	6 (66.6)	0.651
Diabetes (%)	7 (30.4)	3 (33.3)	0.55
CAD (%)	3 (13.04)	5 (55.5%)	0.001*
S creatinine (%)	0.9 ± 0.8	1.2 ± 1.4	0.61

* Significant <0.05.

Table 3 Relation ship between Qanadli score and patient outcome in the current study.

Q score	Survivors (n = 23)	Non survivors (n = 9)	P value
QS < 18	18	3	0.05
QS > 18	5	6	

classified as survivors, and the other nine (28.1%) patients died within the first month (non survivors). There was no significant difference between the two groups as regards age, gender, presence of hypertension, diabetes and the serum creatinine level. The presence of coronary artery disease was significantly higher in non survivors than survivors. Also, smoking was significantly higher in non survivors than survivors.

3.2. Clot burden

There was a positive, but weak correlation between the Qanadli score and the short term survival. Of 11 patients with QS > 18, 6 died within 30 days and 5 survived. On the other hand, of 21 patients with QS < 18, only 3 died within 30 days. (Table 3) (Figs. 3 and 4).

3.3. Right heart dysfunction parameters

In the current study, right heart dysfunction parameters were studied (Table 4). There was a statistically significant relationship between the RV/LV ratio and PE-related mortality, with a P value < 0.001. Also, the shape of the interventricular septum shows good correlation with outcome, 7/9 of the patients died during the 30 day period had abnormal septum. The PA/AO diameter ratio, SVC diameter and azygous vein diameter show no statistically significant difference between survivors and non survivors.

The degree of reflux into the inferior vena cava was classified as mild–moderate (grade I–III), and significant (grade IV–VI) There was a good correlation between degree of reflux and PE outcome ($P < 0.001$) (Table 4) (Fig. 1d).

3.4. Correlation between clot burden and signs of right ventricular dysfunction

RV/LV ratio was significantly higher ($P = 0.002$) in patients with QS > 18. The PA/AO ratio, SVC, AV were similar in survivor and non survivor groups. The Interventricular septal abnormality was greater in patients with QS > 18 points, P value 0.05 (Table 5).

3.5. Ratio of pulmonary artery enhancement to descending aorta enhancement

In the current study, there was no significant relation between the degree of enhancement in the descending aorta and the pulmonary artery (Table 6).

The IVC reflux had sensitivity 66.6%, specificity 79.2% in prediction of short term mortality. The RV/LV ratio had sensitivity 77.7% and specificity 65.2% (Table 7).

4. Discussion

In the current study, there was no significant difference in age, sex, hypertension, diabetes mellitus, and renal function among survivor and non survivor groups. The presence of coronary artery disease and previous history of smoking were significantly higher among non survivors than survivors.

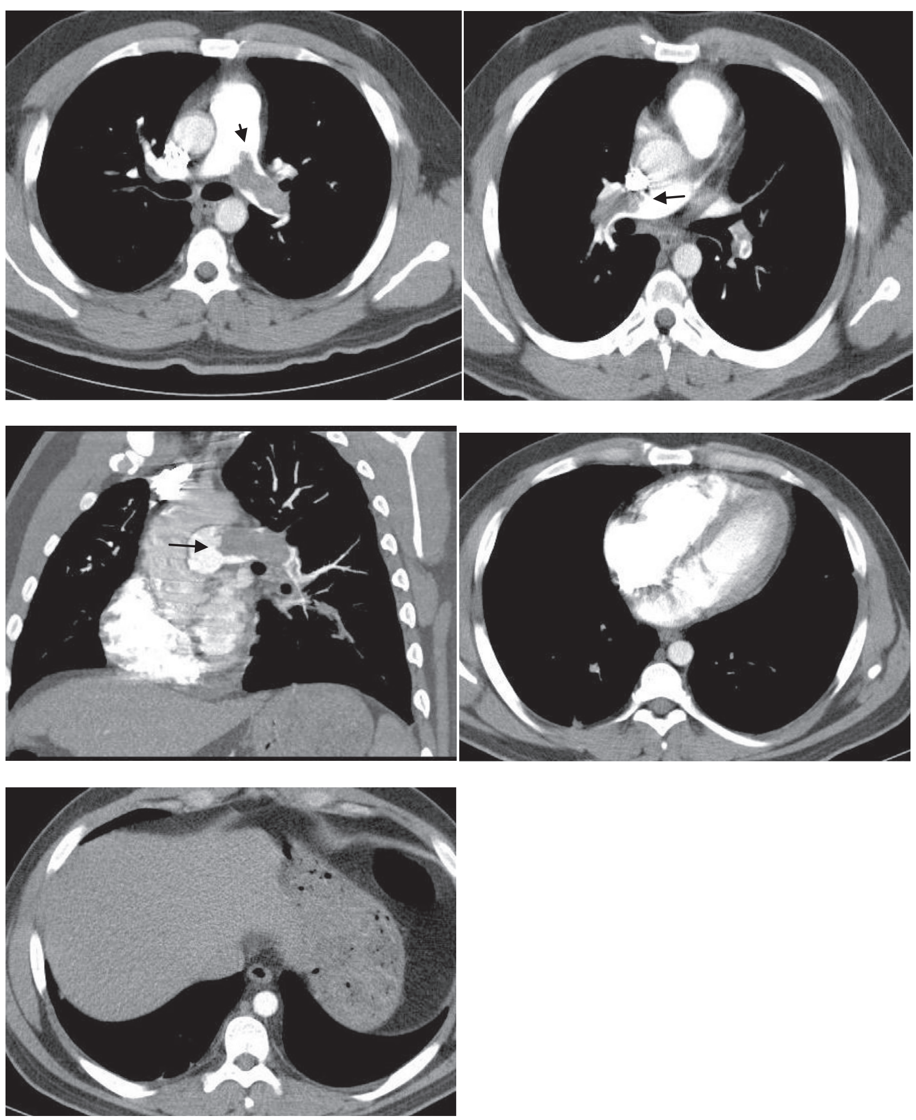

Fig. 3 CTPA of a female patient aged 42 years. (a–c) Large thrombi seen in the left and right pulmonary arteries. Qanadli score >18. Dilated main pulmonary artery relative to the ascending aorta is seen. (d) RV/LV ratio >1.2, with flattening of the interventricular septum. (c) No IVC reflux. The patient was a non survivor, died on the second day.

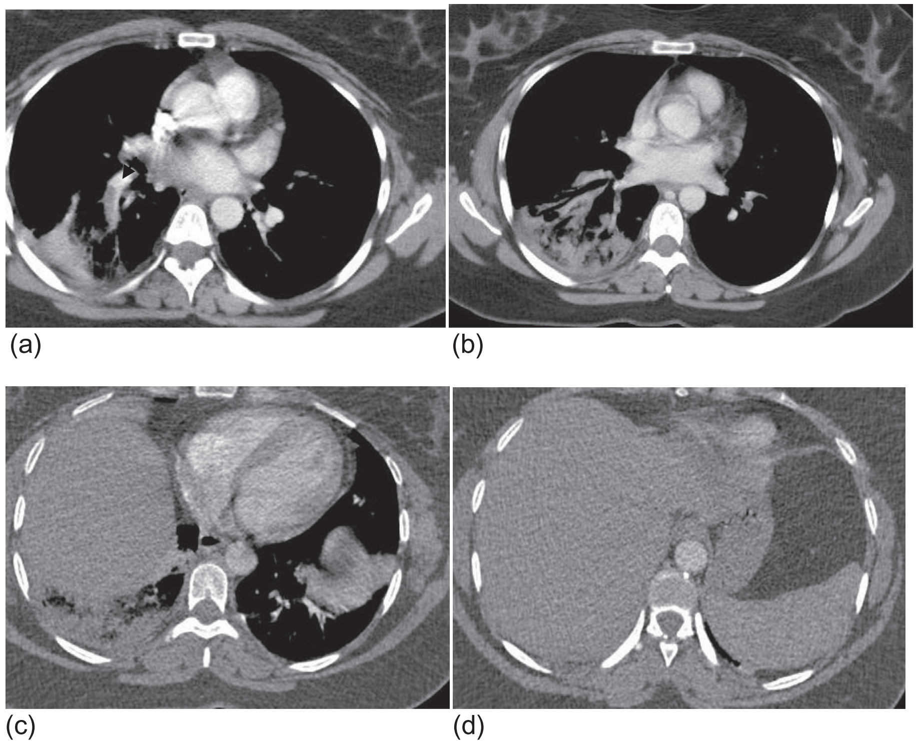

Fig. 4 CTPA of a female survivor patient aged 55 year, with thrombus in the right inferior lobar artery, Qanadli score < 18, wedge shaped infarction in the right lower lobe, RV/L V ratio < 1, normal interventricular septum and no IVC reflux.

Table 4 Relation between right ventricular dysfunction parameters and patient outcome in the study group.

Parameters	Survivors (n = 23)	Non survivors (n = 9)	P value
RV/LV			
> 1.2	8 (34.7)	7 (77.7)	< 0.001*
< 1.2	15 (65.2)	2 (22.2)	
Interventricular septum			
Normal	12 (47.8)	2 (22.2)	0.01*
Flattened	11 (39.1)	5 (55.5)	
Bowed To left	0	2 (22.2)	
PA/AO ratio			
> 1.0	10 (43.4)	5 (55.5)	0.42
< 1.0	13 (56.5)	4 (44.4)	
SVC diameter**	17.2 ± 5.2	18.4 ± 4.9	0.61
Azygous vein**	9.1 ± 3.8	9.8 ± 3.2	0.66
IVC reflux			
Grades 1–3	19 (82.6)	3 (33.3)	
Grades 4–6	4 (17.4)	6 (66.6)	< 0.001*

* Significant < 0.05.
** Value = mean ± standard deviation. RV/LV: right ventricle/left ventricle ratio; PA/AO: pulmonary artery/aorta ratio; SVC: superior vena cava; IVC: inferior vena cava.

Clot burden score using MDCT is important because the direct visualization of the clot within the pulmonary artery is an accurate method of diagnosing PE. Also, determination of the degree of vascular obstruction helps in the stratification of patient risk and enables treatment monitoring (10,19).

There are various systems described in the literature to assess the pulmonary tree and calculate clot burden scores (8–11). Our study used the Qanadli score, as it was considered the easiest to calculate.

The literature shows mixed results in the usefulness of the PA obstruction index as a predictor of RVD and mortality. Qanadli et al. found that a CT obstruction score of 40% or greater correlates well with RV dilatation (10). Later, Van der Meer et al., reported an 11.2-fold increased risk of short term mortality for patients with an obstruction index of 40% or higher (7). In a study that included 48 patients, Bazeed et al. reported a significant difference in the PA obstruction index between survivors and non-survivors (P value < 0.001)

Table 5 Correlation between the QS and right ventricular dysfunction parameters.

	QS < 18 (n = 21)	QS > 18 (n = 11)	P
RV/LV ratio	1.08 (±0.47)	1.58 (±0.33)	0.002*
PA/AO ratio	0.85 (±0.16)	0.98 (±0.17)	0.215
SVC diameter (mm)	18.3 (±4.9)	19.4 (±3.8)	0.143
AV diameter (mm)	9.6 (±2.67)	10.1 (±2.2)	0.41
IVS abnormality (%)	57.1%	72.7%	0.005*

* Significant <0.05. Value = mean ± standard deviation. QS: Qanadli score; RV/LV: right ventricle/left ventricle ratio; PA/AO: pulmonary artery/aorta ratio; SVC: superior vena cava; AV: azygous vein; IVS: interventricular septum.

Table 6 Relationship between ratio between pulmonary artery enhancement and aortic enhancement and patient outcome in the current study.

	Survivors (n = 23)	Non survivors (n = 9)	P value
DAE/MPAE	0.64 ± 0.27	0.55 ± 0.18	0.15

*Significant <0.05. DAE: descending aortic enhancement; MPAE: main pulmonary artery enhancement. Mean ± standard deviation.

Table 7 Statistical analysis of different parameters for predicting short-term death. Due to PE.

Parameters	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
QS score	66.6	78.2	54.5	85.7
RV/LV	77.7	65.2	46.6	88.2
Interventricular septum	77.7	52.1	38.8	100
PA/AO ratio	55.5	56.2	33.3	76.4
IVC reflux	66.6	79.1	60	86.3

QS: Qanadli score; RV/LV: right ventricle/left ventricle ratio; PA/AO: pulmonary artery/aorta ratio; IVC: inferior vena cava.

(20). Also in a recent study (21), included 81 patients, the obstruction index showing significant risk factors for mortality (P < 0.001). Another study revealed a higher obstruction index in patients who had poor prognosis (22). Also, Huang and Fei (23), found that the severity of the obstruction index using CTPA significantly correlated with the blood gas values. In the current study; QS showed positive correlation with short term mortality (P value = 0.05, sensitivity = 66.6% and specificity = 78.2%). On the other hand, Ghaye et al. (24), Araoz et al. (16) and Collomb et al. (17) found PA clot load scores to be a poor predictor of mortality in patients with acute PE. While PA clot load scores can be an indicator of the severity of the current episode of PE or treatment effectiveness, it seems that they cannot be used as a predictor of RV failure and death of the patient (25) (Fig. 5).

The marked controversy in the literature may be explained by the fact that pulmonary vascular resistance is not only related to mechanical obstruction by the intravascular clot load but can be further increased by the release of vasoactive agents; reflex PA vasoconstriction and systemic arterial hypoxemia occurring during PE (26–28). Furthermore, PA clot load scores do not take into account clots located in small peripheral PAs (29). Finally, PA clot load scores do not take into account possible unresolved previous episodes of PE, emphysema, or other restrictive pleuro-parenchymal disease (17).

Right ventricular dysfunction (RVD) is the most common cause of short-term mortality in patients with acute pulmonary embolism (PE) (30). The pathophysiology of RVD in PE is thought to be due to a sharp increase in the right ventricular (RV) after-load caused by mechanical pulmonary arterial obstruction and pulmonary vasoconstriction (31). Previous studies have reported that RV failure, is a more accurate indicator of the severity of PE than the degree of obstruction at angiography or scintigraphy (32,33).

Several studies have proposed an increased RVD/LVD ratio as a predictor of short-term mortality after PE (17,24,34–36). Lim et al. (37) found a RVD/LVD ratio of greater than 1 measured on axial sections indicative of RV strain at pulmonary CTA, whereas others have proposed a threshold ranging 1–1.5 (16,17,38,39). In the current study, we used a threshold of 1.2, with a highly significant difference ($P \leqslant 0.001$) between survivors and non survivors. However, other previous studies failed to prove any association between mortality and increased RV/LV ratio (16,35,40). The reason for this discrepancy in the literature could be partially due to the difference in the RV/LV ratio measurements (e.g., standard axial view of the heart versus reconstructed four-chamber

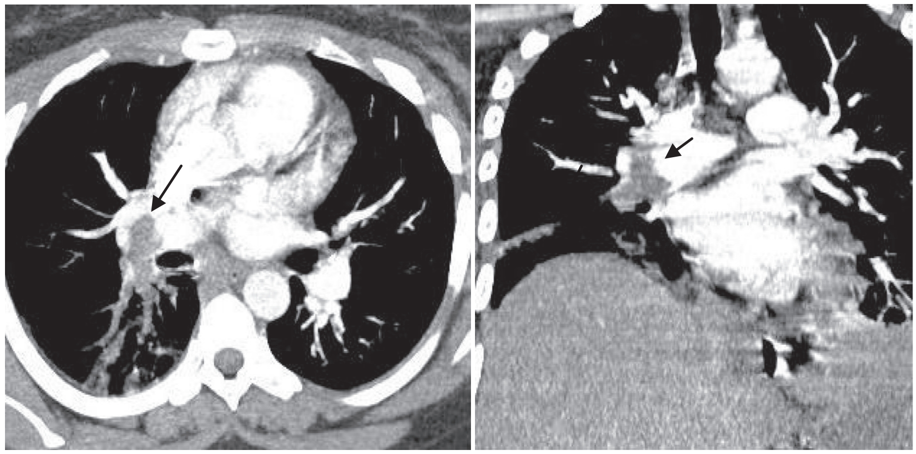

Fig. 5 CTPA of a male patient aged 51 years. Large thrombus seen in the right main pulmonary artery and inferior pulmonary arteries, Qanadli score <18. The patient was a non survivor, died on the first day.

view) and diversity of CT acquisition (different CT scanner geometry).

The other important parameter for predicting short term mortality in this study was reflux of the dye in the inferior vena cava, which associated with poor outcome. Kang et al. (41) in a study that included 260 patients found that the inferior vena cava contrast reflux associated with poor outcome (HR: 2.57; $P = 0.001$). Reflux of contrast medium into the IVC is an indirect sign of tricuspid valve insufficiency, frequently observed in right heart failure (33). Nevertheless, Collomb et al. (17) on the other hand, found this sign not differentiate patients with severe PE from patients with non-severe PE, although the prevalence of IVC reflux in their study was somewhat smaller (12%).

The interventricular septum, which normally bows toward the RV, may shift toward the LV related to increased right heart pressure with severe pulmonary arterial obstruction (42). Septal bowing is not specific for acute PE and can be found in numerous disorders resulting in increased pulmonary artery pressure. In the literature, controversy predominates regarding the significance of interventricular septum abnormality in prediction of short term mortality. On the one hand, Araoz et al. (35) and Collomb et al. (17) reported that ventricular septal bowing strongly predicted admission to the ICU. On the other hand, Araoz et al. (16) and Van der Meer et al. (7) did not find this sign to be predictive of death from acute PE.

In the current study, there was a positive correlation between the IVS abnormality and the short term mortality ($P = 0.01$). Ventricular septal bowing detected with CT may be a predictor, but it may not be a very powerful one (35).

No significant association between the diameters of the superior vena cava, the azygos vein diameters and short-term mortality in the current study, in agreement with a recent report by Furlan et al. (43). However, two other studies reported that the mean diameter of the azygos vein and superior cava vena was higher in non survivors than in survivors (24,34).

In accordance with the previous report by Park et al. (44), the ratio of the descending aorta enhancement to main pulmonary artery enhancement showed no significant difference between survivors and non survivors, and we are in agreement with the previous report that the ratio of descending aortic enhancement to main pulmonary artery enhancement proposed by the authors may not be likely to predict the prognosis.

This study has potential limitations, the number of cases is relatively limited because we excluded from the study, patients we could not follow up for full 30 days (11 patients), patients with renal failure (2 patients), patients with concomitant myocardial infarction (2 patients) and patients with cerebral infarction (3 patients). Also, we did not correlate the results of CTA with echocardiographic findings. Another important limitation is that we did not use ECG gated CTPA. Non-ECG-gated pulmonary CTA is inevitably inaccurate for measuring the ventricular chamber size because the images are acquired in different phases of the cardiac cycle. Also Inter-observer variation was not included in the study.

5. Conclusion

CTPA findings that may predict the short term mortality are the high grades of inferior vena cava reflux, RV/LV diameter ratio more than 1.2, and clot burden >18 according to the Qanadli score and to a lesser degree the interventricular septum abnormality.

Conflict of interest

None.

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