Prognostic Value of CT Pulmonary Angiography Parameters Prediction Short Term Outcome in Patients with Acute Pulmonary Embolism

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ABSTRACT:

BACKGROUND:

Risk stratification for patients with acute pulmonary embolism (PE) is important to create applicable treatment and management. Computed tomography pulmonary angiography (CTPA) is the first-line imaging method for assessment of patients PE. The different parameters of this modality can be used as predictors for survival in those patients.

AIMS:

This study aimed to assess the value of some parameters of CTPA as predictors for short-term mortality in patients with acute PE.

PATIENTS AND METHODS:

This is a prospective study which included a total of 30 adult patients with acute PE diagnosed with CTPA. Patients' demographic and clinical data were recorded. Patients were followed up for 30 days after first diagnosis, and the survival rate was recorded. The CTPA parameters including the diameter of pulmonary artery (PA), ascending aorta (AO), superior vena cava (SVC) and inferior cava (IVC), right ventricle/ left ventricle diameter ratio, PA/AO ratio, inferior vena cava reflux as well as bowing of interventricular septum and clot burden according to Qanadli score (QS) were analyzed and compared between survivals and non-survivals.

RESULTS:

The 30-day survival rate in the present study was 73.33%. None of included demographic factors was significantly associated with the survival rate, while only the presence of abnormal coagulation, as comorbidity, was significantly associated with reduced survival rate. Four CTPA parameters were found to be significantly decreasing the survival rate. These were RV/LV over 1.2 (OR=19.0, 95%CI= 2.54-141.93), followed by IVC reflux (OR= 10.56, 95%CI=1.61-69.12), PA/AO ratio over 1.0 (OR= 12.6, 95%CI= 1.07- 148.13), and QS over 18 (OR=6.33, 95%CI= 1.0 to 40.07).

CONCLUSION:

CTPA findings that may predict the short term mortality were RV/LV diameter ratio more than 1.2, the high grades of IVC reflux, PA/AO ratio over 1.0 and QS >18. However, most of these parameters are non-specific for PE.

KEYWORDS: CT pulmonary angiography, acute pulmonary embolism.

INTRODUCTION:

Acute venous thromboembolism (VTE), which includes deep-vein thrombosis (DVT) and acute pulmonary embolism (PE), is a leading cause of cardiovascular mortality, exceeded only by stroke and myocardial infarction [(1)]. Untreated, PE confers a high mortality, especially in the presence of right ventricular (RV) impairment. In an acute PE event arrhythmia or massive RV failure, or a combination of the two, can cause acute haemodynamic collapse leading to inadequate arterial blood flow to organs and, ultimately, death. Even after successful acute PE treatment, up to 10% of PE survivors will die within 1 year [(2)].

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PE survivors can develop post-PE syndrome, with a higher risk of developing recurrent PE and functional impairments [3]. Within the post-PE syndrome, two specific conditions have been described: chronic thromboembolic vascular disease (CTED) and chronic thromboembolic pulmonary hypertension (CTEPH). CTED has been defined as functional impairment due to chronic thromboembolic remains in the pulmonary artery tree without pulmonary hypertension. CTEPH is defined as a mean pulmonary artery pressure of ≥25 mmHg, a pulmonary capillary wedge pressure of ≤15 mmHg and the presence of multiple chronic or organized occlusive thrombi in the pulmonary artery tree after at least 3 months of anticoagulant treatment [4].

CTPA is the gold standard in the diagnosis of PE replacing the conventional angiography [5]. RV dysfunction and extent of pulmonary artery (PA) obstruction at CT are useful prognostic parameters [6]. Another strength of the CTPA-based model is that physicians can calculate the score using the CT images alone, and do not need to retrieve information from the patient's medical record (e.g., laboratory results and echocardiography). The CTPA-based scores can be calculated by radiologists, which may help referring physicians make immediate management decisions, in addition to prompt communication of the diagnosis of PE, which should improve the patient's outcome [43]. There are several CT findings related to RV dysfunction, and right ventricle/ left ventricle (RV/LV) diameter ratio has been evaluated for predicting the prognosis of acute PE [8]. Overall, the RV/LV ratio is an independent predictor or has additive value in the prediction of PE-related death [9]. Furthermore, the RV/LV diameter ratio and pulmonary vascular obstruction score are important parameters to evaluate RV dilatation which is associated with significant mortality in PE [10].

AIMS OF THE STUDY:

This study aimed to assess the value of some parameters of computed tomography pulmonary angiography as predictors for short-term mortality in patients with acute pulmonary embolism.

PATIENTS AND METHODS:

This is a prospective study which was conducted at Al-Imamain Al-Kadhumain Medical city. The study included 30 adult patients 18 years of age or older who were admitted with acute PE over the period from March2019 December 2019. Informed written consent was taken from each patient before including in the study.

Inclusion criteria:

Adult patients with clinical, laboratory and CTPA evidence of pulmonary embolism, the diagnosis of PE on the CTPA was based on visualization of filling defects and cut-off within the contrast opacified pulmonary arteries down to their segmental branches on at least two subsequent scans. Eligible patients were followed up for 30 days post scanning either for hospital discharge or death.

Exclusion Criteria:

patients with major health problems that may affect survival such as myocardial infarction, cerebral infarction/hemorrhage and renal failure. Patients who could not be followed for enough time post scanning. Patients with a known hypersensitivity to the iodinated contrast medium.

Data Collection:

Each patient was subjected to full clinical history. The following data were recorded: Demographic characteristic (age, sex and body mass index), Risk factors for PE such as chronic lung disease, congestive heart failure, history of previous deep venous thrombosis.

Patients Preparation:

patients were asked to fast at least 4 hours. Normal kidney function was ensured. The patients were trained on the breath-hold required during the scanning process. A cannula (18-20 gauge) was inserted into the antecubital vein.

Computerized Tomographic Angiography:

examination done in supine position with both arms extended above the head. Non-ionic iodinated contrast (Iopromide (Ultravist) 370, Bayer, Berlin, Germany) in a dose of 1ml/kg body weight was injected via the antecubital cannula at a rate of 5 mL/s for vessel opacification. Normal saline was injected at the same rate prior and post contrast injection to examine the intravenous line for extravasation and wash out the contrast bolus respectively. A dual head injector (Merdad/ Bayer Germany) was used for the injection process (for both the contrast medium and normal saline).

Contrast-enhanced scans of the thorax were performed on 64-slice multidetector helical CT (Somatome definition AS, Siemens, Germany) provided with a rotation time of 0.5 second. Images were acquired from the lung apices to the level of the posterior costophrenic angles using the following parameters: 16mm*0.75mm collimation, pitch of 1.5 (table speed =18mm/s), 80–120 mAs depending on body habitus, and 120 kV.

Image acquisition was acquired using an automated bolus triggering technique when the level of enhancement in the pulmonary artery trunk exceeded 100HU. Images were reconstructed in 0.6mm slice thicknesses.

Image Analysis:

the images were transferred to the workstation (Siemens workstation (syngo)) for analysis which was performed by an experienced radiologist.

Clot Burden:

Qanadli scoring system was used in this study as follows: The percentage of obstruction={[Σ(n×d) 40]×100}. Where n = the number of segmental branches arising distally (minimum, 1; maximum, 20) and d = degree of obstruction (minimum, 0; maximum, 2). The arterial tree of each lung was assigned as 10 segmental arteries (3 to the upper lobes, 2 to the middle lobe and to the lingula, and 5 to the lower lobes). Values for n ranged from a minimum of 1 (one segment obstructed) to a maximum of 20 (obstruction of both the right and left pulmonary arteries). Values for d were assigned to provide information about the perfusion distal to the embolus. The maximum CT obstruction index was (20 segments×2), and the total Σ(n×d) product was divided by 40 and multiplied by 100.

Right Heart Dysfunction:

The following parameters were used for the assessment of right heart functions based on CT signs:

- Right ventricular diameter/ left ventricular diameter ratio (RV/LV). This was measured on the axial CT image of the heart at the widest point of the diameter.
- Main pulmonary artery diameter/ main ascending aorta diameter ratio (PA/AO). This was measured on the transverse image at which the right pulmonary artery in the continuity with the main pulmonary artery.
- Heart septum morphology: Normal (convex toward the right ventricle), Flattened (convex toward the left ventricle)

Inferior Vena Cava Reflux: The severity of reflux of contrast medium into the inferior vena cava (IVC) or hepatic veins was graded from the axial images according to six categories: 1 = no reflux into IVC; 2 = trace of reflux into IVC only; 3 = reflux into IVC but not hepatic veins; 4 = reflux into IVC and opacifying proximal hepatic veins; 5 = reflux into IVC and opacifying mid-part of hepatic veins; and 6 = reflux into IVC and opacifying distal hepatic veins.

All patients were followed up for 30 days, and the survival rate was recorded.

Statistical Analysis: The SPSS statistical package was used for all the statistical evaluations (SSPS Inc., Chicago, IL, USA). Data were summarized as mean ± standard deviation (SD) for the continuous variables and as number of individuals (percentage) for categorical variables. Comparison of continuous variables between survived and non-survived subjects using the independent student_s t-test, while the comparison between frequencies of categorical variables was done using the chi-square test. All the above analyses were considered significant at P value<0.05.

RESULTS:

Mean age and BMI of the patients were 52.74±8.39 years and 26.7±9.18 kg/m2 respectively, with 11(36.67%) males and 19(63.33%) females. The most prevalent comorbidity was DVT which observed in 18(60%) of the patients, followed by hypertension 11 (36.67%), Diabetes mellitus was observed in 8 (26.67%), Malignancy was observed in 6 (20%), Abnormal coagulation in 7 (23.33%). On the other hand, history of surgery, trauma and history of travel represented the least comorbidities observed in 13.33%, 10% and 6.67% of patients.

Computed Tomography Pulmonary Angiography Findings:

Mean PA, AO and SVC diameters were 29.58±3.22 mm, 32.56±4.45 mm and 22.53±3.05 mm respectively. Nine patients (30%) showed RV/LV ratio greater than 1.2, while only 4 patients (13.33%) had PA/AO ratio greater than 1.0. The majority of patients (83.33%) had normal inter-ventricular septum, whereas about one-fourth of the patients were suffering from IVC reflux. Mean clot burden was 18.9±10.7, and 7 patients (23.33%) had QS greater than 18. As seen in table 1.

Table 1: Computed tomography pulmonary angiography findings.

Variables	Mean± SD or No(%)
RV/LV ratio >1.2 ≤1.2	 9(30%) 21(70%)
PA diameter (mm)	29.58±3.22
AO diameter (mm)	32.56±4.45
PA/AO ratio >1.0 ≤1.0	 4(13.33%) 26(86.67%)
SVC diameter (mm)	22.53±3.05
Bowing of interventricular septum Positive Negative	 5(16.67%) 25(83.33%)
Inferior vena cava reflux Positive Negative	 7(23.33%) 23(76.67%)
Clot burden (QS)	18.9±10.7
QS >18 QS ≤18	7(23.33%) 23(76.67%)

QS = Qanadli score, AO = Aorta, PA = Pulmonary artery, RV = Right ventricle,SVC = Superior vena cava, LV = Left ventricle

Survival Rate

After 30 days follow up, 22(73.33%) patients survived versus 8(26.67%) did not survive. The death was mostly related to PE. Accordingly, patients were categorized into survivors and non-survivors.

Demographic Characteristics and Short-term Survival in Patients with PE:

For statistical purpose, age was categorized into ≥ 45 years and < 45 years. Likewise, BMI index was categorized into ≥25 kg/m^{2}and <25 kg/m^2. None of the three included demographic characteristics (age, gender and BMI) had a significant association with the short-term survival in patients with PE. Rather, survivors and non-survivors showed comparable proportion of these parameters (Table 23).

Table 2: Association of demographic characteristics with the short-term survival in patients with PE.

Variables	Survivors (n=22)	Non-survivors (n=8)	P-values
Age, years ≥45 <45	 15(68.18%) 7(31.82%)	 6(75%) 2(25%)	0.719
Gender Male Female	 6(27.27%) 16(72.73%)	 5(62.5%) 3(37.5%)	0.077
BMI, kg/m^2 ≥25 <25	 13(59.09%) 9(40.91%)	 5(62.5%) 3(37.5%)	0.886

Different Comorbidities and Short-term Survival in Patients with PE

The presence of abnormal coagulation showed a significantly higher percent among non-survivors than survivors (50% versus 13.67%). Other illnesses such as DM and history of surgery although more frequent among non-survivors than survivors, the different did not reach significant levels as shown in table 3.

Table 3: Association of different comorbidities with short-term survival in PE patients.

Variables	Survivors (n=22)	Non-survivors(n=8)	P-values
Deep venous thrombosis	14(63.64%)	4(50%)	0.50
Hypertension	8(36.36%)	3(37.5%)	0.954
Diabetes mellitus	4(18.18%)	4(50%)	0.081
Malignancy	4(36.36%)	2(25%)	0.68
Abnormal coagulation	3(13.67%)	4(50%)	0.037
History of surgery	1(4.55%)	3(37.5%)	0.257
Trauma	2(9.09)	1(12.5%)	0.783
History of travel	1(4.55%)	1(12.5%)	0.440

CTPA Findings and Short-term Survival in Patients with PE: 4 main findings were found to be significantly increased in non-survivors than survivors (Table 4). Six patients (75%) among non-survivors showed RV/LV ratio >1.2 (Figure1A and 1B) compared to 3 patients (13.64%) among survivors. Likewise, PA/AO ratio >1.0 was observed in 3 patients (37.5%) and 1 patient (4.55%) of non-survivors and survivors respectively. IVC reflux (Figure 1 C) was positive in 5(62.5%) of non-survivors compared to 2(9.09%) of survivors. Percent of non-survivor patients with Qanadli score of greater than 18 (Figure 1) was significantly higher than that of survivors (4 patients (50%) versus 3 patients (13.64%) which was reflected in mean clot burden between the two group (20.72±11.7 versus 18.24±8.2.

Table 4: Association between CTPA findings and short-term survival in patients with PE.

Variables	Survivor(n=22)	Non-survivor n=8)	p-value
RV/LV ratio >1.2 ≤1.2	 3(13.64%) 19(86.36%)	 6(75%) 2(25%)	0.001
PA diameter (mm)	29.1±3.4	30.9±4.2	0.402
AO diameter (mm)	32.1±4.4	33.8±4.7	0.309
PA/AO diameter ratio >1.0 ≤1.0	 1(4.55%) 21(95.45%)	 3(37.5%) 5(62.5%)	0.019
SVC diameter (mm)	22.41±4.1	22.86±3.9	0.448
Bowing of interventricular septum Positive Negative	 2(9.09%) 20(90.91%)	 3(37.5%) 5(62.5%)	0.065
Inferior vena cava reflux Positive Grade 2 Grade 3 Negative	 2(9.09%) 2(100%) 0(100%) 20(90.19%)	 5(62.5%) 3(60%) 2(40%) 3(37.5%)	0.007
Clot burden (QS)	18.24±8.2	20.72±11.7	0.029
QS >18 ≤18	 3(13.64%) 19(86.36%)	 4(50%) 4(50%)	0.037

QS = Qanadli score, AO = Aorta, PA = Pulmonary artery, RV = Right ventricle, SVC = Superior vena cava, LV = Left ventricle

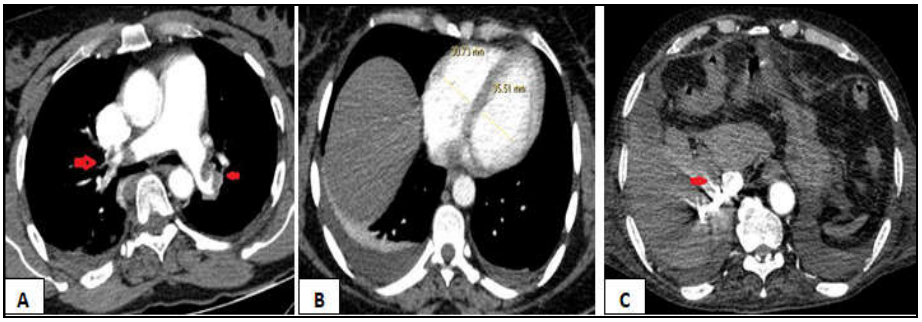

Figure 1: A: CTPA of non-survivor 68 years old male presented with chest pain and dyspnea in which RV/LV ratio >1.2 and QS >18. B:CTPA of survivor 55 years oldmale presented with chest pain in which RV/LV ratio <1.2 and QS <18. C: CTPA of non-survivor 60 old male presented with chest pain and dyspnea showing reflux of contrast in IVC (arrow).

Predictors of Death in Patients with PE:

All factors (comorbidities and CTPA Findings) that demonstrated a significant association with survival were entered in a multivariate logistic regression model to find out the odds ratio predictors for death in PE patients (Table 5). The most powerful predictor in this regard was RV/LV over 1.2 (OR=19, 95%CI= 2.54 to 141.93), followed by inferior vena cava reflux (OR= 10.56, 95%CI=1.61 to 69.12). PA/AO ratio over 1.0 came third (OR= 12.6, 95%CI= 1.07 to 148.13), while both the presence of abnormal coagulation and QS over 18 had the same power (OR=6.33, 95%CI= 1.0 to 40.07).

Table 5: Predictors of death in patients with PE.

Variables	Odds ratio (OR)	95% confidence intervals (CI)
Presence of abnormal coagulation	6.33	1.0 to 40.07
RV/LV ratio over 1.2	19.0	2.54 to 141.93
PA/AO ratio over 1.0	12.6	1.07 to 148.13
Inferior vena cava reflux	16.67	2.17 to 128.18
QS over 18	6.33	1.0 to 40.07

DISCUSSION:

The present study aimed to evaluate the role of CTPA parameters as predictors of survivals in patients with PE. The 30-day survival rate in the present study was 73.33%. In accordance with this result is an Egyptian study including 32 patients with PE. The 30-day survival rate was 71.88% versus 28.12% death [(11)]. However, the present rate was much lower than many previous studies worldwide such as that reported in Germany (89.3%)[(12)], USA (89%) [(13)] and Italy (85.8%) [(14)], these variation between the current study and most other international studies can be explained by several factors, the most important of which are the difference in the patients samples, difference in demographic characteristics of the patients (especially age), and the presence of comorbidities.

According to the current study, none of included demographic factors was significantly associated with survival rate. Furthermore, out of 8 comorbidities, only the coexistence of abnormal coagulation was significantly associated with reduced survival rate. Different studies worldwide revealed different risk factors for death in patients with PE. These results were similar to previously reported studies [(15, 16)].

In the current study, the 4 CTPA findings were found to be significantly decreased the survival rate. These were RV/LV > 1.2 (OR=19.0, 95%CI= 2.54 to 141.93), followed by IVC reflux (OR= 10.56, 95%CI=1.61 to 69.12), PA/AO ratio > 1.0 (OR= 12.6, 95%CI= 1.07 to 148.13), and QS > 18 (OR=6.33, 95%CI= 1.0 to 40.07). These results are partially in accordance with an Egyptian study in which the authors recruited 32 patients with PE and investigated the role of several CTPA parameters as predictors for 30-day survivals. Out of six included parameters, each of a RV/LV ratio, inter-ventricular septal bowing and IVC reflux was significantly associated with survival rate [11]. A number of studies have suggested an augmented RV/LV ratio as a poor predictor factor of short-term death after PE [17, 18, 19, 20]. Lim et al. [21]established that a RVD/LVD ratio of over 1 calculated on axial sections is suggestive of RV strain, whereas others have assumed a threshold ranging 1–1.5 [22, 23].

The other important factor for anticipating short term mortality in the current study was reflux of the dye in the IVC, which was significantly associated with poor outcome. Such a result was completely in agreement with an American study included 260 patients in which IVS, IVC contrast reflux, and RV/LVD ratio were measured on axial sections. On multivariate analysis (adjusted for clinical and demographic risk factors), IVC contrast reflux (OR= 2.57) as well as interventricular septum bowing (OR=2.07) were predictive of adverse outcome [24]. In contrast, Collomb et al. [17] reported that IVC contrast reflux was not significantly associated with severe PE and short-term outcome. That is because reflux of contrast medium into the IVC is an indirect sign of increased RV pressure and tricuspid valve insufficiency [25].

The third important CTPA parameter as predictor for survival in PE patients in the present study was PA/AO ratio greater than 1.0. In agreement with this result is the study of Furlan et al. [51]. Similar finding was also reported by Sen et al. [26]. However, many other studies reported poor association between this CT sign and short-term survival rate in PE patients [11, 27, 28], while Park et al. [29] showed that PA/AO did not differ significantly between survivors and non survivors PE patients and may not be likely to predict the prognosis.

The final CTPA parameter which was significantly associated with survival rate in the present study was QS (also known as pulmonary artery obstruction index). These results are in line with many earlier studies that reported strong correlations between semi-quantitative scores of clot burden and short-term mortality[14, 30, 31], whereas other studies failed to show a significant correlation between the Qanadli score and short-term mortality [17, 32, 33]. The disagreement among different studies 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 augmented by the discharge of vasoactive agents; a vasoconstrictor, such as serotonin which appears to play an important role in determining pulmonary vasoconstriction (i.e., reflex vasoconstriction) [34, 35].Furthermore, PA clot burden scores do not take into account clots located in small peripheral PAs or possible unresolved previous episodes of PE, emphysema, or other restrictive pleuro-parenchymal disease[22].

In the present study, the inter-ventricular septal bowing was markedly increasing in non-survived patients compared with the survived patients although the significance exceeded the acceptable limit. Similar results were reported by Araoz et al. [22]and Hafeda and Al-Misry[11]. Conversely, Van der Meer et al.[36],Ghaye et al. [18]and Aviram et al. [37] did not find this sign to be predictive of death from acute PE. The inter-ventricular septum, which normally bows toward the RV, may shift toward the LV related to increased right heart pressure with severe pulmonary arterial obstruction [38]. However, septal bowing is not specific for PE and can be found in numerous disorders resulting in increased pulmonary artery pressure. Kang et al. [24] suggested that the abnormal position of interventricular septum was overall predictive of adverse events but not of 30-day death, while Collomb et al. [17] reported that such a sign strongly predicts admission to the intensive care unit (ICU).

CONCLUSION:

CTPA findings that may predict the short term mortality were RV/LV diameter ratio more than 1.2, the high grades of IVC reflux, and QS>18 and inter-ventricular septum abnormality. However, most of these parameters are non-specific for PE. Demographic characteristics of the patients had negligible effect on the short-term survival rate, while only abnormal coagulation of possible comorbidities was significantly associated with reduced survival rate

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