

# Diagnostic implications of computed tomography pulmonary angiography in patients with pulmonary embolism

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#### Abstract:

**INTRODUCTION:** Pulmonary embolism (PE) is a serious cardiovascular and pulmonary complication worldwide. We aimed to assess the implications of different computed tomography pulmonary angiography (CTPA) parameters in patients with acute PE.

**METHODS:** A retrospective observational study to include patients presented with clinical suspicious of PE who underwent CTPA was conducted. Patients' demographics, clinical presentation, risk factors, laboratory investigations, management, and outcome were analyzed. Computed tomography findings included clot burden (Qanadli score [QS]) and right ventricular dysfunction (RVD) parameters.

**RESULTS:** A total of 45 patients with radiologically confirmed diagnosis of PE were included in the study; of these patients, 8 (17.8%) died during the hospital course. Patients who died were 13 years older than those who survived, and the mortality rate was significantly higher in patients with cancer. The two groups were comparable for cardiovascular parameters. The mean clot burden (QS) was  $19.5 \pm 11.3$  points and 53% of patients had QS >18 points. Obesity (52.4% vs. 12.5%;  $P = 0.01$ ), hypertension (54.4% vs. 23.8%;  $P = 0.03$ ), and median D-dimer levels (7.8 vs. 3.4;  $P = 0.03$ ) were significantly higher in patients with QS >18. Among right ventricular (RV) dysfunction parameters, only higher RV/left ventricular (LV) ratio ( $P = 0.001$ ) and bowing of interventricular septum ( $P = 0.001$ ) were associated with higher QS. A significant positive correlation was found between RV short axis ( $r = 0.499$ ,  $P = 0.001$ ), RV/LV ratio ( $r = 0.592$ ,  $P = 0.001$ ), and pulmonary artery (PA) diameter ( $r = 0.301$ ,  $P = 0.04$ ) with the PA clot burden. Receiver operating characteristic curve for clot burden showed a cutoff value of 17.5 points to accurately predict RV dysfunction.

**CONCLUSIONS:** Clot burden >18 is associated with RV dysfunction in patients with acute PE. Echocardiography and RVD parameters showed no correlation with in-hospital deaths. CTPA has clinico-radiological implications for risk stratification in PE patients. As the sample size is small, our findings warrant further larger prospective studies.

#### Key words:

Computed tomography angiogram, pulmonary embolism, right ventricular dysfunction, thromboembolism

Pulmonary embolism (PE) is a serious cardiovascular and pulmonary condition with mortality ranging from 2% to 7% worldwide, even after thromboprophylaxis.<sup>[1]</sup> It is the third most common cause of cardiovascular death, after myocardial infarction and cerebrovascular stroke.<sup>[2]</sup> Regardless of the advancement in thromboprophylaxis, diagnosis, and treatment, PE remains an important determinant of in-hospital complications and outcome.<sup>[3]</sup> In some cases with acute massive PE, severe hemodynamic compromise and systemic hypotension causes sudden death secondary to circulatory collapse and heart failure.<sup>[4,5]</sup> This occurs due to increased pulmonary vascular resistance with high pulmonary arterial and right ventricle (RV) pressure which overwhelms the RV failure.<sup>[6]</sup> Risk stratification of patients with acute PE is crucial for early diagnosis and appropriate selection of the treatment.<sup>[7]</sup>

Echocardiography is a useful diagnostic and prognostic tool for RV dysfunction which is considered as an independent predictor of short-term outcome of PE.<sup>[8]</sup> Moreover, computed tomography pulmonary angiography (CTPA) has become the modality of choice for the

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diagnosis of PE as it offers a multiplanar view for the assessment of pulmonary vessels to the subsegmental levels.<sup>[9,10]</sup> RV dysfunction and extent of pulmonary artery (PA) obstruction at computed tomography (CT) are useful prognostic parameters.<sup>[11]</sup> Patients with RV dysfunction and PE have a high mortality rate, and hence, RV dysfunction is considered as a poor prognostic marker.<sup>[8]</sup> Furthermore, the RV/left ventricular (LV) diameter ratio and pulmonary vascular obstruction score are important parameters to evaluate RV dilatation which is associated with significant mortality in PE.<sup>[12,13]</sup> In addition, the presence of RV dysfunction indicates a high risk of recurrent or fatal PE.

To date, four scoring systems have been proposed by different investigators to determine the presence, location, and degree of obstruction of arterial clots in patients with PE.<sup>[14]</sup> Among them, Qanadli PE index<sup>[13]</sup> is easy to calculate, identify complete or partial obstruction due to proximal clot, and thus provides information about the residual pulmonary perfusion. The clot burden score has significant prognostic and therapeutic potential as it facilitates direct visualization of the clot within the PA with a standard reproducible score to quantitate the improvement after therapeutic intervention.<sup>[13,14]</sup> There are few clinical studies from the Middle East to evaluate the role of CTPA for diagnosis and prognosis of PE.<sup>[14-16]</sup> The aim of this study is to assess the diagnostic implications of different CT parameters, and to correlate the clot burden, cardiovascular measurements, and clinical presentation of patients with acute PE.

## Methods

We conducted a retrospective observational study of fifty consecutive patients presented with a clinically suspected PE and underwent CTPA. Patients were identified from the radiology database, and the relevant clinical information was retrieved from the medical records at Hamad General Hospital between May 2011 and February 2015. Clinically suspected patients with PE who were not confirmed by CT imaging were excluded from the study. Images from 16- or 64-slice multidetector CT angiography were reviewed in 45 patients, after excluding patients in whom images were not available on the database or in whom poor image quality precluded accurate assessment. Clinical presentation, preexisting comorbidities, radiologic imaging, detailed notes for in-hospital course, and discharge summaries were reviewed for each patient. Data collection included patient demographics (age, sex, and nationality), clinical presentation and predisposing factors, laboratory investigations (D-dimer testing, coagulation profile), Doppler ultrasound, finding of echocardiography (ejection fraction [%], RV wall hypokinesis and pulmonary arteries dilation) and CTPA, management, hospital length of stay, complications, and outcome. Patients were followed up for routine clinical care as per the standard practice. The plasma D-dimer concentrations were measured at the clinical laboratory, Hamad General Hospital, using a well-validated commercial assay used for routine D-dimer testing. The normal range of plasma D-dimer concentration in our hospital laboratory is 0–0.55 mg/L. Coagulation profile includes protein S deficiency, protein C deficiency, hyperhomocysteine, antithrombin III deficiency, and antiphospholipid syndrome. PE was defined radiologically as the presence of an endoluminal central filling defect partially

or completely occluding the pulmonary arteries.<sup>[17]</sup> The RV dysfunction refers to the presence of RV hypokinesis, explained by a qualitative evaluation of the RV wall motion.<sup>[18]</sup>

## Computed tomography pulmonary angiography

The occurrence of PE was confirmed by CTPA examination. In brief, all patients were examined using Siemens SOMATOM Sensation (Siemens AG, Munich, Germany) 16- or 64-slice machine. For all examinations, kV was set as 100, collimation of 0.6, rotation time of 0.5 s, slice thickness of 5 mm, and pitch of 1.0. Nonionic intravenous contrast (100 ml of Omnipaque 350 mg/ml) was injected at a rate of 4.0–5.0 ml/s. Pulmonary arterial phase bolus tracking through main pulmonary trunk was carried out followed by aortic phase immediately following pulmonary arterial phase. (In pregnant patients, only pulmonary arterial phase was performed.) Moreover, three-dimensional reconstruction was performed, if indicated.

## Imaging analysis

### Clot burden

Qanadli *et al.*'s<sup>[13]</sup> scoring system was used to quantify the vascular obstruction index using CTPA which is based on the percentage of vascular obstruction of the pulmonary arterial tree developed secondary to PE. In brief, the Qanadli index determines the number of blocked segmental arterial branches and then to be adjusted by a factor of one for partial blockage or a factor of two for completely obstructive PE. The maximum attainable score in this system is 40 (pulmonary trunk completely obstructed by thrombus), which represents complete obstruction index (100%). In this study, we used the same scoring system based on the site and degree of occlusion of pulmonary arteries.

## Computed tomography signs of right heart dysfunction

CT findings considered for the functional cardiovascular measurements include the ratio of RV to LV diameter (RV/LV ratio), ratio of main PA diameter to ascending aorta (AO) diameter (PA/AO ratio), superior vena cava (SVC) and azygos vein diameter, bowing of interventricular septum, clot burden (Qanadli score [QS]). The other observations such as infarction, pulmonary effusion (right, left, and bilateral), pneumothorax and rib fracture, and pulmonary metastasis were also recorded. RV and LV dimensions were identified based on the maximal distance between the ventricular endocardium and the interventricular septum, perpendicular to the long axis. RV dysfunction was diagnosed if the RV to LV diameter ratio was  $>1.2$ .<sup>[14]</sup>

## Inferior vena cava reflux to determine signs of right ventricular dysfunction

Aviram *et al.*<sup>[19]</sup> classified reflux of contrast medium into inferior vena cava (IVC) or hepatic veins based on severity into six different categories such as (a) no reflux into IVC, (b) trace of reflux into IVC only, (c) reflux into IVC but not hepatic veins, (d) reflux into IVC with opacification of proximal hepatic veins, (e) reflux into IVC with opacification of hepatic veins down to the mid-portion of the liver, and (f) reflux into IVC with opacification of distal hepatic veins.

The Institutional Review Board (IRB# 15139/15) of the Hamad Medical Corporation has approved and granted exempt status for this retrospective study.

### Statistical analysis

Data were reported as percentage, mean ( $\pm$ standard deviation), median, and range, where applicable. Baseline characteristics, echocardiography, and right ventricular dysfunction (RVD) parameters were analyzed according to clot burden (QS  $\leq$ 18 vs. QS  $>$ 18) and outcome (survivors vs. nonsurvivors). Student's *t*-test was used to compare continuous variables, and Pearson's Chi-square test was used for categorical variables. Pearson's correlation coefficient (*r*) has been calculated between QS and cardiovascular measurements. Receiver operating characteristic (ROC) curve was constructed to establish the best cutoff for QS and RV dysfunction. To look for predictors of mortality, multivariate regression analysis was performed after adjustment for the significant variables on univariate analysis, and data were expressed as odd ratio and 95% confidence interval (CI). Two-tailed *P* < 0.05 was considered statistically significant. Data analysis was carried out using the Statistical Package for Social Sciences version 18 (SPSS Inc., Chicago, IL, USA).

### Results

A total of 45 consecutive patients with radiologically confirmed diagnosis of PE were eligible for enrollment in the present study. Table 1 shows the demographics, comorbidities, and outcome of PE patients. The mean age of the patients was 49  $\pm$  11.4 years, and 29 (64.4%) were males. Thirty (67%) patients developed PE during hospitalization whereas 15 (33%) patients presented to the emergency department with PE. Deep vein thrombosis (DVT) (60.0%), hypertension (37.8%), obesity (average BMI 32.8  $\pm$  8.6; 28.9%), diabetes mellitus (26.7%), and abnormal coagulation (24.4%) were the frequent preexisting comorbidities. Recurrent PE was observed in 6 (14.6%) patients. Overall mortality was 18% during the hospital course.

Table 2 shows the coagulation profile and echocardiography findings. Thirty-three patients (73.3%) underwent echocardiography, of which 13 (39.4%) cases had RV dysfunction in terms of RV dilatation and hypokinesia. Pulmonary arteries dilation was found in 8 (24.2%) patients. Protein S deficiency was found in one-third (30%) of the patients, and the median D-dimer value was 5.7 (1.2–72.2) mg/L FEU.

Parameters of the right heart dysfunction as identified by the CTPA are shown in Table 3. The mean clot burden (QS) was 19.5  $\pm$  11.3 points and 53% of patients had QS  $>$ 18 points. One-third (33.3%) of the patients had PA/AO ratio  $>$ 1.0. The number of patients with RV dysfunction (RV/LV ratio  $>$ 1.2) was 27 (60.0%). IVC reflux was found to be mild-to-moderate (Grades I–III) in 73.3% of patients and severe (Grades IV–VI) in 26.7% of patients. Interventricular septal abnormality was identified in 29 (64.4%) patients.

Table 4 demonstrates univariate association between cardiovascular measurements and mortality. The RV/LV ratio, PA/AO ratio, bowing of interventricular septum, IVC reflux, SVC, and azygos vein diameters were comparable in survivor and nonsurvivor groups. In our study, cancer patients were more likely to die due to paraneoplastic embolism than those without malignancy (71.4% vs. 16.7%; *P* = 0.002).

**Table 1: Demographics, clinical presentation, comorbidities, and outcome of patients with pulmonary embolism (n=45)**

Variable	Value
Age (mean $\pm$ SD)	49 $\pm$ 11.4
Males (%)	29 (64.4)
Qatari (Arabs) (%)	6 (13.3)
Body mass index	32.8 $\pm$ 8.6
Locations of diagnosis (%)	
ICU/in-hospital wards	30 (67)
Outpatient presented at ED	15 (33)
Comorbidities/risk factors (%)	
DVT	27 (60.0)
Hypertension	17 (37.8)
Obesity	13 (28.9)
Diabetes mellitus	12 (26.7)
Abnormal coagulation	11 (24.4)
Cancer	11 (24.4)
History of DVT	9 (21.4)
History of pulmonary embolism	6 (14.6)
History of surgery (>24 h)	6 (14.6)
Polytrauma	4 (8.9)
History of travel	4 (8.9)
Mortality	8 (18)

DVT = Deep vein thrombosis, ED = Emergency department, SD = Standard deviation, ICU = Intensive Care Unit

**Table 2: Echocardiography and coagulation profile**

Variable	Value
Right ventricular wall hypokinesia (%)	13 (39.4)
Pulmonary arteries dilation (%)	8 (24.2)
Abnormal coagulation	
Protein S deficiency	10 (29.4)
Protein C deficiency	5 (14.7)
Hyperhomocysteine	4 (15.4)
Antithrombin III deficiency	4 (13.3)
Antiphospholipid syndrome	2 (5.6)
D-dimer (mg/L FEU) median, range (n=35)*	5.7 (1.2-72.2)

\*Positive in all cases

Clinicoradiological characteristics of PE patients according to clot burden (QS  $\leq$ 18 vs.  $>$ 18) are shown in Table 5. The two groups were comparable for age, gender, and preexisting comorbidities/risk factors and echocardiography findings. However, obesity (52.4% vs. 12.5%; *P* = 0.01), hypertension (54.4% vs. 23.8%; *P* = 0.03), and median D-dimer levels (7.8 vs. 3.4; *P* = 0.03) were significantly higher in patients with QS  $>$ 18. Among RV dysfunction parameters, only RV/LV ratio (1.61  $\pm$  0.48 vs. 1.04  $\pm$  0.29; *P* = 0.001) and bowing of interventricular septum (91.7% vs. 33.3%; *P* = 0.001) were associated with higher QS. The mortality rate was comparable in patients with higher clot scores (QS  $>$ 18) (16.7% vs. 19.0%; *P* = 0.83) as compared to low scores (QS  $\leq$ 18). A significant positive correlation was found between RV short axis (*r* = 0.499, *P* = 0.001), RV/LV ratio (*r* = 0.592, *P* = 0.001), and PA diameter (*r* = 0.301, *P* = 0.04) with the PA clot burden. Moreover, LV short axis showed a significant negative correlation with clot burden (*r* = -0.515, *P* = 0.001) [Table 6]. Figures 1 and 2 demonstrate CTPA findings of two of our PE patients.



**Table 3: Computed tomography pulmonary angiography findings of right ventricular dysfunction**

Variable	Value
RV/LV ratio	1.3±0.49
>1.2 (%)	27 (60.0)
≤1.2 (%)	18 (40.0)
Bowing of interventricular septum (%)	29 (64.4)
PA diameter	2.9±0.42
AO diameter	3.1±0.38
PA/AO ratio	0.95±0.17
>1.0 (%)	15 (33.3)
≤1.0 (%)	30 (66.7)
SVC diameter	2.1±0.3
Azygos vein diameter	0.88±0.16
Inferior vena cava reflux	
Mild-moderate (Grades I-III) (%)	33 (73.3)
Severe (Grades IV-VI) (%)	12 (26.7)
Clot burden (QS)	19.5±11.3
QS >18 points (%)	24 (53.3)
QS ≤18 points (%)	21 (46.7)
Clot burden (%)	48.7±28.4
Infarction (%)	10 (22.2)

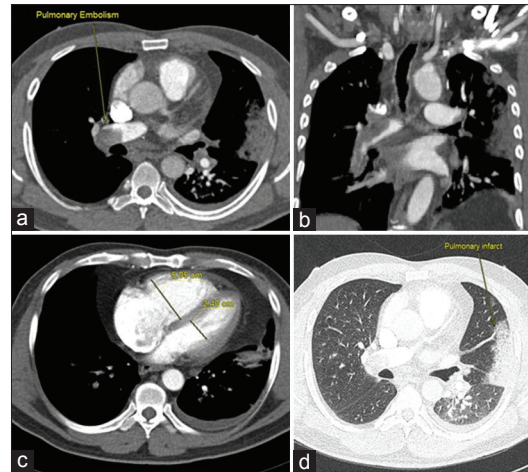
QS = Qanadli score, AO = Aorta, PA = Pulmonary artery, RV = Right ventricle, SVC = Superior vena cava, LV = Left ventricle

**Table 4: Univariate association between cardiovascular measurements and mortality**

	Survivors	Nonsurvivors	P
Age (mean±SD)	47.1±10.4	60±10.3	0.003
Deep vein thrombosis	62.2	50.0	0.52
Cancer (%)	16.7	71.4	0.002
Abnormal coagulation	29.7	0.0	0.12
Cardiovascular measurements			
RV/LV ratio	1.33±0.45	1.42±0.67	0.87
>1.2	59.5	62.5	0.87 for all
≤1.2	40.5	37.5	
Bowing of interventricular septum	64.9	62.5	0.89
PA diameter	2.93±0.44	2.91±0.32	0.88
AO diameter	3.07±0.36	3.18±0.49	0.47
PA/AO ratio	0.96±0.18	0.93±0.16	0.63
>1.0	32.4	37.5	0.78 for all
≤1.0	67.6	62.5	
SVC diameter	2.13±0.30	2.05±0.27	0.46
Azygos vein diameter	0.90±0.16	0.82±0.11	0.23
Clot burden (QS)	20.1±11.7	16.9±9.4	0.47
QS >18 points	54.1	50.0	0.83 for all
QS ≤18 points	45.9	50.0	
Clot burden (%)	50.1±29.4	42.2±23.6	0.47
Infarction	21.6	25.0	0.83
Inferior vena cava reflux			
Grades 1-3	75.7	62.5	0.44 for all
Grades 4-6	24.3	37.5	

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

ROC curve showed an area under the curve (AUC) for the prediction of RV dysfunction based on PA clot burden to be



**Figure 1:** Computed tomography pulmonary angiography axial (a, c, and d) and coronal (b) images reveal pulmonary embolism involving bilateral main pulmonary arteries with infarct in the left lung. (d) Right ventricular/left ventricular ratio = 2.1

0.822 (95% CI: 0.698–0.947,  $P = 0.001$ ). In our study, the optimal cutoff value of QS for the identification of RV dysfunction was considered based on highest pair of sensitivity (77.8%) and specificity (72.2%). In addition, the AUC was 0.822; 95% CI: 0.698–0.947,  $P = 0.001$ , which is considered a good diagnostic value. Hence, the clot burden cutoff level of 17.5 points was found to predict RV dysfunction which is also consistent with Qanadli *et al.*<sup>[13]</sup> scoring system.

Multivariate regression analysis showed that after adjustment for age and cancer, neither RV/LV ratio (odds ratio [OR] 1.6; 95% CI: 0.13–20.15,  $P = 0.71$ ) nor clot scores (OR 0.99; 95% CI: 0.87–1.14,  $P = 0.92$ ) were independent predictor for mortality.

## Discussion

PE is a serious medical condition that could ultimately lead to death within few hours due to RV failure and circulatory collapse. Therefore, RV burden should be detected rapidly to identify patients who could benefit from early aggressive therapy. The noninvasive CTPA can safely and quickly identify the presence and extent of PE.

The present study highlights the diagnostic implications of CTPA parameters and assesses the correlation between clinico-radiological characteristics of 45 patients with PE. In our series, echocardiographic evaluation revealed RV wall hypokinesia and PA dilation in 39.4% and 24.2% of cases, respectively. Earlier studies have suggested that echocardiography might be effective in predicting RV dysfunction and clinical outcome.<sup>[20]</sup> However, due to its lower sensitivity to diagnose PE, echocardiography is recommended mainly for hemodynamically unstable patients.<sup>[15]</sup> At present, CTPA is considered as the modality of choice for accurate diagnosis of PE.<sup>[6]</sup> In comparison to echocardiography, CTPA enables a thorough assessment of embolization in the pulmonary arteries and detects associated underlying pulmonary disorders and other causes of acute chest pain.<sup>[21]</sup> Moreover, it facilitates risk stratification of patients based on the degree of vascular obstruction (i.e., clot burden) which could be used as a marker for appropriate selection of treatment.<sup>[22]</sup> Apart from the size of

**Table 5: Clinicoradiological characteristics of pulmonary embolism patients according to clot burden (Qanadli score)**

	QS ≤18 (n=21)	QS >18 (n=24)	P
Males (%)	71.4	58.3	0.36
Age (mean±SD)	47.5±12.8	51±10.1	0.32
Obesity (%)	12.5	52.4	0.01
Diabetes mellitus (%)	23.8	31.8	0.55
Deep vein thrombosis (%)	57.1	62.5	0.71
Abnormal coagulation (%)	14.3	36.4	0.09
Cancer (%)	38.1	13.6	0.06
Pregnancy (%)	5.0	25.0	0.07
History of pulmonary embolism (%)	19.0	10.0	0.41
History of surgery (>24 h) (%)	15.8	14.3	0.89
History of DVT	28.6	14.3	0.25
Hypertension (%)	23.8	54.4	0.03
D-dimer (median, range)	3.37 (1.2-72.2)	7.8 (2.01-35.2)	0.03
RV wall hypokinesis (%)	20.0	40.9	0.14
Pulmonary arteries dilation (%)	15.4	35.3	0.22
RV dysfunction parameters			
RV/LV ratio	1.04±0.29	1.61±0.48	0.001
>1.2	33.3	83.3	0.001 for all
≤1.2	66.7	16.7	
Bowing of interventricular septum (%)	33.3	91.7	0.001
PA diameter	2.81±0.47	3.03±0.35	0.08
AO diameter	3.0±0.44	3.1±0.34	0.57
PA/AO ratio	0.93±0.21	0.97±0.14	0.16
>1.0	23.8	41.7	0.20 for all
≤1.0	76.2	58.3	
SVC diameter	2.05±0.36	2.17±0.22	0.17
Azygos vein diameter	0.85±0.18	0.91±0.13	0.25
Infarction (%)	14.3	29.2	0.23
Inferior vena cava reflux			
Grades 1-3	81.0	66.7	0.28 for all
Grades 4-6	19.0	33.3	
Mortality (%)	4 (19.0)	4 (16.7)	0.83

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

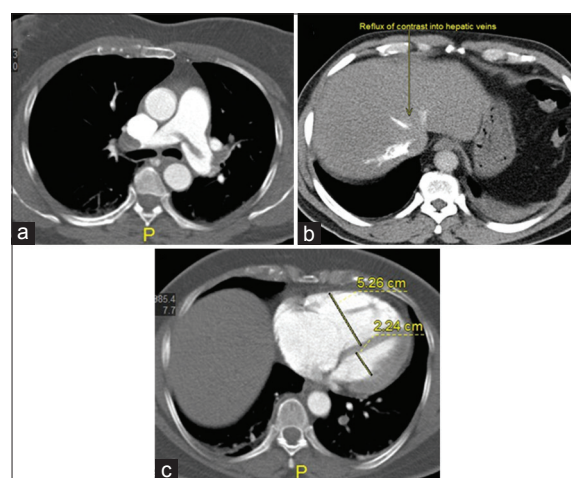
**Table 6: Correlation between Qanadli score and cardiovascular measurements**

Measurement	Correlation coefficient (r)	P
RV short axis	0.499	0.001
LV short axis	-0.515	0.001
RV/LV ratio	0.592	0.001
PA diameter	0.301	0.04
AO diameter	0.045	0.76
PA/AO ratio	0.175	0.25
SVC diameter	0.247	0.10
Azygos vein diameter	0.225	0.14

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

embolus, the clinical outcome of patients with PE also depends on various cardiopulmonary measurements (RV, LV, RV/LV ratio, PA, AO diameter, and PA/AO ratio) identified by CTPA.

In our study, patients with PE presented at a young age, more likely to be males, and two-thirds of them were identified during hospitalization. Our findings are consistent with an earlier study from Saudi Arabia with a similar



**Figure 2:** (a-c) Computed tomography pulmonary angiography axial images reveal saddle thrombus extending to bilateral pulmonary arteries with reflux of contrast into inferior vena cava and hepatic veins. (b) Right ventricular/left ventricular ratio = 2.4

age at presentation, male predominance, and in-hospital diagnosis of PE.<sup>[15]</sup> Prior hospitalization could not represent

a real limit in our study as only one patient had prolonged immobilization (bedridden) which could associate with venous thromboembolism (VTE). We do not believe that our findings are influenced by other acute diseases as we anticipated all major risk factors in our study. A previous study from our center reported mean age of 50 years in patients with confirmed diagnosis of thromboembolism.<sup>[23]</sup> In that study, the proportion of PE was 12.2% among 662 thromboembolism cases who were screened over 5 years. However, other investigators reported the diagnosis of PE with an advanced mean age of 63 years.<sup>[24]</sup>

We observed a higher rate of protein S deficiency (30%) in patients who developed PE at relatively younger age. Similarly, an earlier study showed that low free protein S carried a high risk of developing or recurring of VTE in young patients with a mean age 39 years.<sup>[25]</sup> In addition, preexisting comorbidities were frequent in our study cohort. Al Otair *et al.*<sup>[15]</sup> reported recent surgery, obesity, immobilization, and recurrent DVT to be the frequent risk factors associated with PE.

PA obstructive index is important as it facilitates direct visualization of the clot and allows accurate diagnosis of PE.<sup>[26]</sup> There are several scoring systems reported to evaluate the pulmonary vascular tree and assessment of clot burden score.<sup>[16]</sup> The present study quantified clot burden scoring according to QS as it is more objective, easy to calculate, distinguish between partial and complete obstruction, and has less interobserver variability.<sup>[13,19]</sup> Serial imaging studies could be used to assess the degree of vascular obstruction which helps a clinician determine real-time risk stratification and monitoring of treatment in an objective way. Previous studies have identified the clot burden score to be a predictor of RV dysfunction and poor outcomes. Qanadli *et al.*<sup>[13]</sup> found that an obstruction score >40% correlates well with RV dilatation. It has been observed that PE patients with 40% or higher obstruction index had 11-fold increased risk of mortality.<sup>[11]</sup> Another study reported significant correlation between RV/LV ratio, IVC reflux, QS, and the short-term PE-related mortality.<sup>[14]</sup> Bazeed *et al.*<sup>[26]</sup> observed a significant difference in clot burden scoring among PE patients who died than those who survived. On the other hand, other investigators reported no significant association of obstruction score with PE-related mortality.<sup>[14]</sup> Consistent with these reports, our findings revealed no correlation of clot burden with in-hospital mortality. This variability could be explained by the fact that pulmonary obstruction could be related to other factors such as mechanical obstruction, vasoactive agents, reflex vasoconstriction, and systemic hypoxemia occurred during PE.<sup>[14]</sup> However, obstructive index can be accurately used as an indicator of the severity of PE and for treatment response.<sup>[27]</sup>

The assessment of cardiorespiratory status secondary to an acute PE should not only rely on the degree of pulmonary obstruction but also consider the signs of RV strain (RV/LV diameter ratio >1) as a potential indicator for the RV dysfunctions, which occurs due to sudden increase in the afterload caused by mechanical obstruction and vasoconstriction.<sup>[28]</sup> It has been suggested that the severity of PE could be assessed more accurately by RV failure rather than the degree of obstruction.<sup>[29]</sup> Earlier studies have suggested threshold values for RV/LV ratio ranged from 1 to 1.5 as

indicative of RV strain<sup>[12,30]</sup> and can be used as a predictor of PE mortality.<sup>[14]</sup> In our series, we used a threshold of RV/LV ratio of 1.2 for the diagnosis of RV dysfunction. However, we did not observe a significant correlation between RV dysfunction and PE-related mortality. Our findings are in accordance with previous studies which suggest that RV/LV ratio and clot burden are not associated with PE-related mortality.<sup>[31,32]</sup> The reason for these controversies could be partially explained by the variability in measurements of RV/LV ratio.

In our study, obesity, hypertension, and D-dimer were significantly associated with severity of obstruction (QS >18). Similar to our findings, Attia *et al.*<sup>[16]</sup> reported a significant association between obesity and higher mean obstructive index in patients with acute PE. In our study, patients with right heart dilatation (RV/LV ratio >1.2) were more likely to have larger clot volume as compared to those without RV dilatation. Similarly, the larger clot volume (QS >18) was observed in patients with interventricular septal defect in comparison to patients with normal interventricular septal morphology. The higher clot volume is likely to obstruct the pulmonary circulation, causing RV pressure overload and dilatation. Therefore, estimation of the degree of vascular obstruction (clot burden) would help in the PE risk stratification in clinical practice and also enable treatment monitoring. Moreover, we observed a significant positive correlation between RV/LV ratio and PA diameter with clot burden (QS). Our findings coincide with earlier studies which also observed a good correlation between RV dysfunction parameters (RV/LV ratio and PA diameter) and the severity of obstruction.<sup>[16,22]</sup>

In the present study, ROC curve analysis determined the cutoff point for the obstructive index (QS) to be 17.5 points (clot burden of 43.7%) which could predict RV dysfunction with reasonable sensitivity (77.8%) and specificity (72.2%). In line with findings of our study, other investigators observed the best cutoff point for clot burden which ranges between 40% and 49% with high sensitivity and specificity, and values  $\geq 40\%$  could potentially identify more than 90% of patients with RV dysfunction.<sup>[16]</sup> On the other hand, PE patients with a CT burden of <40% are unlikely to develop acute RV dysfunction.<sup>[13,22,33]</sup> Therefore, the findings of the present study highlighted the clinicoradiological implications of CTPA for the accurate diagnosis and risk stratification of patients with PE.

We observed no significant difference between mortality and clot burden which is consistent with an earlier study by Rodrigues *et al.*<sup>[22]</sup> Another important factor was reflux of the dye in the IVC which is an indirect sign of tricuspid valve insufficiency.<sup>[29]</sup> Kang *et al.*<sup>[34]</sup> found that contrast reflux is a bad prognostic factor. Our study did not observe any prognostic role of IVC reflux, and similar results were shown by Collomb *et al.*<sup>[35]</sup>

The interventricular septum may shift toward the LV due to increased right heart pressure with severe pulmonary obstruction.<sup>[36]</sup> The prognostic significance of interventricular septum abnormality is debatable. Araoz *et al.*<sup>[31]</sup> reported that patients with ventricular septal defects are more likely to be admitted to the ICU. On the other hand,



Van der Meer *et al.*<sup>[11]</sup> did not find any relation to mortality from acute PE. It has been revealed that the mean diameter of the azygos vein and SVC was higher in nonsurvivors.<sup>[21]</sup> A recent study by Furlan *et al.*<sup>[17]</sup> showed no significant association between the diameters of the SVC, the azygos vein diameters, and short-term mortality which corroborates our findings. Recently, Meinel *et al.*<sup>[37]</sup> concluded in a meta-analysis that increased RV/LV diameter ratio measured on transverse CT images was the strongest risk with a 2.5-fold higher risk for all-cause mortality and 5-fold higher risk for PE-related mortality. Furthermore, the degree of thrombus load and central thrombus location were not predictive for all-cause mortality although both were associated with adverse clinical outcome. In the present study, cancer patients were more likely to die due to paraneoplastic embolism than those without malignancy. Consistent with our findings, a large prospective study based on RIETE registry revealed a higher 3-month mortality rate in the patients with cancer-related VTE as compared to those without cancer (4%).<sup>[38]</sup> After adjustment for age and history of cancer, the present study showed that RV/LV ratio and clot scores were not independent predictors for mortality.

One of the limitations of our study is the retrospective design and underpowered due to small number of cases which needs further validation based on larger sample size. We did not consider the preexisting structural heart defects or pulmonary disease which could affect the cardiopulmonary measurements on CT angiography. Finally, the clot burden score does not consider clots situated within the small pulmonary arteries at the periphery as well as unresolved previous episodes of PE in cases of recurrence. Although multivariate logistic regression analysis could not identify the independent predictors of outcomes, this could be limited by the sample size which is insufficient to draw findings of statistical significance to be used for the risk stratification. The total number of PE cases in this study underestimates and does not reflect the real number in our institution as we retrospectively analyzed only cases with detailed CTPA data.

## Conclusion

Clot burden >18 is associated with RV dysfunction in patients with acute PE. Echocardiography and RVD parameters showed no correlation with in-hospital deaths. CTPA has clinicoradiological implications for risk stratification in PE patients. As the sample size is small, our findings warrant further larger prospective studies.

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## Conflicts of interest

There are no conflicts of interest.

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