Original Research

Investigating The Prognostic Value Of CT Angiography Criteria In Patients With Acute Pulmonary Thromboembolism

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Abstract

Background: Today, knowing the prognosis of PTE patients is of particular importance, because currently some of these patients can be treated on an outpatient basis, as well as determining the assignment of these patients in the emergency medicine service according to the prognosis of these patients helps a lot in survival. These patients will also reduce costs.

Methods: The present study is a longitudinal and retrospective study for all patients hospitalized in Qaem and Imam Reza emergency rooms between 2017 and 2020, who were over 18 years old and were candidates for CT angiography of the lung according to the standard protocol, and they had acute embolism. In CT angiography it was diagnosed by the radiologist, it was considered. Qualitative and quantitative imaging criteria were evaluated.

Results: No statistically significant relationship was found between survival status and gender, presence of DVT, history of smoking and history of retplase injection ($P>0.05$). There was a significant difference in the systolic and diastolic blood pressure of patients in the two groups, and in the improved group, blood pressure was lower, but no significant difference was observed in the breathing rate and heart rate ($P>0.05$). Adjusted for age, sex, systolic and diastolic blood pressure, having a higher ratio of the maximum longitudinal and transverse diameters of the right to left ventricle, protrusion (Bow) of the interventricular septum and having an embolism at the fourth level and age over 65 years with a higher chance of death was associated ($P<0.05$).

Conclusion: The results indicated that CT angiography criteria have predictive value in patients with acute pulmonary thromboembolism.

Keywords: CT Angiography, Pulmonary Thromboembolism, Prognosis.

Submitted: 29 Feb 2024, Revised: 21 March 2024 , Accepted: 29 Apr 2024

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Introduction

Pulmonary embolism is a common disease secondary to deep vein thrombosis of the lower limb. Approximately half of patients with pelvic vein thrombosis or proximal deep venous thrombosis of the leg develop pulmonary embolism, which is usually asymptomatic. In the United States, between one hundred thousand and three hundred thousand deaths related to venous thromboembolism occur annually, and in Europe, approximately 37 thousand deaths related to pulmonary embolism occur annually (1). Pulmonary thromboembolism is the third most common vascular disease after coronary artery disease and stroke, which 2-5% of patients experience in their lifetime. Pulmonary embolism is an important clinical issue in patients after major surgeries and is often diagnosed late due to non-specific clinical symptoms. The risk factors of this disease include: cigarette smoke, malignancies, obesity, age, heredity and long immobility, as well as history of surgery (2). Considering that the clinical symptoms of this disease, such as chest pain and shortness of breath, are non-specific and are seen in many diseases of the lung, pleura, chest, heart, and digestive system, imaging plays an important role in its diagnosis. The use of angiography is the gold standard in the diagnosis of this complication, but its use is limited due to its invasiveness and complications, high cost, and limited availability. Today, the most common method of diagnosing pulmonary embolism is using CT angiography (3). This method is used exclusively for the diagnosis of pulmonary embolism due to its availability, speed, as well as its high diagnostic sensitivity and accuracy (4). Venous thromboembolism is the formation of a blood clot in a vein. If a clot forms in a deep vein, it is called a deep vein thrombosis. If this clot is released and moves to the lungs, it is called a pulmonary embolism. Venous thromboembolism and pulmonary embolism are collectively known as VTE, which is a very dangerous and fatal condition. Only in the United States, 7 to 10 billion dollars are charged annually to the healthcare system due to venous thromboembolism (5). Venous thromboembolism, which clinically includes deep vein thrombosis and pulmonary embolism, is the third most common acute cardiovascular syndrome after myocardial infarction and stroke. The prevalence of venous thromboembolism in patients over 80 years old is almost eight times higher than in the fifth decade of life (5, 6). Also, longitudinal studies show an annual increase in the incidence of pulmonary thromboembolism over time. Pulmonary thromboembolism accounts for approximately 4% of in-hospital mortality in persons 65 years of age or older. However, the 30-day readmission rate is 15% and the six-month mortality rate increases to 20% in this population (7). Failure to diagnose and treat deep vein thrombosis and pulmonary thromboembolism causes complications and increases hospitalization and treatment costs. Prophylaxis reduces the risk of DVT and subsequent PTE in hospitalized patients. Pulmonary embolism is one of the important differential diagnoses, especially in patients who come to medical centers with cardiopulmonary symptoms, which is associated with an increase in mortality if not diagnosed and treated on time. Accurate and reliable diagnosis of acute pulmonary embolism makes it possible for patients to be properly managed and treated (8). Pulmonary thromboembolism is one of the problems of the country's medical and health system, and both its diagnosis and treatment have a heavy financial burden on this system. Considering the increase in life expectancy in the country and the increase in the quality of health care for the elderly, it is expected that we will see more occurrences of this disease. Therefore, determining the best evaluation method and criteria for patients' prognosis not only reduces

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the financial burden on the system, but is also effective in the success of patients' treatment. Today, knowing the prognosis of PTE patients is particularly important because with the advent of new treatments, some of these patients can be treated on an outpatient basis. Also, determining the correct assignment of these patients in the emergency medicine service and the emergency department, according to the prognosis of these patients, will help to determine the final outcome of the patients' survival, the duration of the patient's stay in the hospital, and prevent the wastage of financial resources. Considering the few studies in this field in Iran, it seems necessary to conduct this study. This research, if confirmed, can lead to a report on the prognostic value of CT angiography criteria in patients with acute pulmonary thromboembolism (PTE) and will increase the chance of success in treatment.

Methods

This study was conducted longitudinally and retrospectively. Patients who were over 18 years of age and with a possible diagnosis of PTE by an emergency medicine specialist (based on history, physical examination and D-Dimer test above 500 µg if performed) were candidates for CTA and suffering from acute pulmonary thromboembolism with CT angiography of the lung was confirmed by the radiology professor, they were checked. Sampling was done as available from patients eligible to enter the study. The sample size, considering the alpha error of 5% and the power of 80%, the sample size in each group was calculated to be equal to 53 patients, including 10% attrition, a total of 116 patients (at least 58 deceased patients and at least 58 living patients) was evaluated. Inclusion criteria include; All patients over 18 years of age with acute pulmonary thromboembolism were confirmed by CT angiography of the lungs by the radiology professor in the emergency rooms of Qaem and Imam Reza between 2017 and 2020. Exclusion criteria also include; Chronic pulmonary embolism and lack of access to CT angiography is a patient in the PEX system. In this study, measurable outcomes include mortality and ICU hospitalization outcomes, and independent variables include quantitative and qualitative imaging measures. Qualitative imaging criteria include: bulging of the interventricular septum (IVS), contrast reflux into the IVC (inferior vena cava), reflux into the azygos vein, contrast reflux into the hepatic veins and embolus level. Quantitative imaging measures include measurements of; the ratio of the maximum transverse diameter of the right ventricle to the left ventricle, the ratio of the maximum longitudinal diameter of the right ventricle to the left ventricle, the ratio of the transverse diameter of the main pulmonary artery to the aorta, the diameter of the main pulmonary artery and the diameter of the superior vena cava (SVC); is. The results of the study also include; Mortality, ICU admission and discharge and recovery. Other parameters that were measured as potential confounding or influencing factors include; age, sex; Simultaneous association with DVT (deep vein thrombosis), history of sepsis and history of smoking, which were extracted from the patient's file. Systolic and diastolic blood pressure, breathing rate, heart rate were also recorded at the time of initial triage and were extracted from the file. Data analysis was done using spss software version 21 and descriptive statistics (mean, standard deviation, percentage and number) and inferential statistical tests (Kolmogrov-Smirnov, Mann-Whitney, Fisher, chi-square). Logistic regression analysis was used to investigate factors influencing patient mortality. Odds ratios, along with 95% confidence intervals, are reported. It was done at the significance level of $P<0.05$.

Results

In the present study, 122 patients were examined, 60 of whom had died (group 1) and

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62 had recovered (group 2). In total, 67 patients (55%) were men and 55 patients (45%) were women. 60% of patients did not smoke. 78% of patients did not have deep vein thrombosis. 35% did not need to use ICU services. Based on Kolmogrov-Smirnov test, age, length and width of left ventricle and width of pulmonary artery had normal distribution and the rest of the continuous data were of non-parametric type (Table 1).

Table 2 classifies the survival results of patients based on demographic and clinical variables, a total of 62 patients recovered and 60 patients died. Among women, 29 patients (52.72%) and 31 patients (46.26%) died among men. Fisher's exact test showed that there is no statistically significant relationship between survival status and gender (P=0.505). A total of 27 patients had DVT, of which 15 (55.5%) died. Fisher's exact test showed that there is no statistically significant relationship between survival status and having DVT (p=0.516). Smoking (p=0.356), sepsis (p=0.482) and history of retplase injection (p=0.616) also had no significant relationship with mortality. 49.42% of patients hospitalized in ICU and 48.57% of patients hospitalized in the ward died, and there was no significant relationship between hospitalization in the ICU and mortality (p=0.999).

In terms of clinical factors, 52.30% of patients with bulging interventricular septum (indicating the severity of PTE) died. There was no significant relationship between this finding and mortality (P=0.474). Contrast reflux to the inferior vena cava, contrast reflux to the azygos and contrast reflux to the hepatic vein and embolus level had no significant relationship with mortality (P>0.05) (Table 3).

The average systolic blood pressure of all studied patients was 114.5±19 mmHg and the average diastolic blood pressure was 69.6±12.55 mmHg. The average level of breathing per minute was 24.3±5.44. The average heart rate per minute was 100.5±17.5. The results of the Mann-Whitney test show that there was a significant difference in the systolic and diastolic blood pressure of patients in the two groups, and in the improved group, blood pressure was lower, but no significant difference was observed in the breathing rate and heart rate (P>0.05) (Table 4).

In all studied patients, the average ratio of the maximum transverse diameter of the right to left ventricle in the studied patients was 1.19±0.4 mm, the average ratio of the maximum longitudinal diameter of the right to left ventricle was 0.98±0.17 mm, the average ratio The transverse diameter of the pulmonary artery trunk to the aorta is 0.9±0.18, the average pulmonary trunk diameter is 31.28±4.54 mm and the average SVC diameter in the studied patients is 20.63±4 mm (Table 4).

The results of the Mann-Whitney test showed that in the examination of the ratio of the maximum transverse diameter of the right ventricle to the left, the ratio of the maximum longitudinal diameter of the right ventricle to the left, the ratio of the transverse diameter of the trunk of the pulmonary artery to the aorta, the diameter of the pulmonary trunk and the diameter of the superior vena cava, there is a significant difference between deceased patients and there was no improvement (P>0.05)

In order to investigate the effect of quantitative imaging criteria on the survival rate (dependent variable), the variables of the ratio of the maximum transverse diameter of the right ventricle to the left, the ratio of the maximum longitudinal diameter of the right ventricle to the left, the ratio of the transverse diameter of the trunk of the pulmonary artery to the aorta, the diameter of the pulmonary trunk and the diameter of the SVC as independent variables. Entered into the logistic regression model, adjustments were made based on initial systolic and diastolic blood pressure and other demographic variables. After adjusting for other variables included in the model, sepsis,

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hospitalization in ICU and respiratory rate significantly predicted higher mortality (P<0.05). The interventricular septum protrusion variable has statistical significance (p=0.022), which indicates its relationship with mortality. An odds ratio of 2.609 indicates that having this imaging finding is associated with a 2.609-fold increase in the odds of death. The variable of age over 65 years has statistical significance (p=0.035), which indicates its relationship with mortality. It means that age over 65 years is associated with an increase of 1.87 times in the chance of death. Having a higher ratio of the maximum longitudinal and transverse diameters of the right to left ventricle, Bow of the interventricular septum, and having an embolism at the fourth level were associated with a higher chance of death (P<0.05).

None of the imaging variables in adjusted regression analysis had a significant relationship with hospitalization in ICU (P>0.05).

Discussion

The positive predictive value of CTPA is higher in cases where clinical suspicion is strongly weak for PE than in cases where clinical suspicion is intermediate and moderate. The results of the study by Etesamifard et al. (2013) showed that in patients with acute pulmonary embolism without underlying disease, neither the ratio of the right to left ventricular axis nor the pulmonary artery obstruction severity score can independently predict mortality in pulmonary embolism. Which is consistent with the results of the present study, no significant difference was observed in the diameter of the pulmonary trunk between the two groups in the present study (Table 3). At the same time, this study examined only two criteria, the right-to-left ventricular axis and the severity of pulmonary artery obstruction, and the sample size was relatively small (9). The results of the study by Zantonelli et al. (2022) showed that computed tomography angiography of the lung (CTPA) is considered the gold standard diagnostic method in patients suspected of acute pulmonary embolism in emergency departments. CTPA is a first-line tool for the diagnosis of APE, which is also able to measure the severity of PE with high accuracy, wide availability and fast response time. By using the minimum amount of contrast material (20 ml) it is still possible to maintain the quality of the image necessary to remove or detect PE, which can be considered in future studies. In this study, the transverse diameter of right to left ventricle was introduced as a predictor of mortality in pulmonary embolism patients, the present study also indicated the same finding (10). The results of the study by Bach et al. (2015) showed that reflux contrast measurement is an important risk factor in determining the mortality of patients with acute PTE, and the morphological measurements of the right ventricle did not perform well in determining the risk of these patients, which is not consistent with the results of the present study; In the present study, the criteria for measuring heart ventricles had an effect on the prognosis of patients (11). The results of Meinel et al.'s (2015) study, similar to our study, showed that the ratio of RV/LV diameter in CT cross-sections had the highest predictive value for negative outcomes in PTE patients

The results of the study by Costantino et al. (2008) showed the non-optimal use of CTA before the subjective estimation of the Wells criteria and the probability of PE. Although an acceptable definitive positive rate of PE for CTA has not been established, a yield of 10% suggests an overuse of CTA as a screening rather than a diagnostic examination, which is consistent with the results of the present study. Risk factors and clinical symptoms alone cannot play a decisive role in the management of patients suspected of pulmonary embolism, and examining these factors together is important (13). Among the advantages of

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pulmonary CT angiography, CTPA compared to traditional methods in the diagnosis of pulmonary embolism, we can mention its wide availability, non-invasiveness, high sensitivity and specificity. Through the accurate and effective triage of patients, the costs of care, follow-up and management of patients, as well as the amount of radiation and medical risks can be significantly reduced. The results of the present study can pave the way for further studies on the research topic. CT angiography criteria in patients with acute pulmonary thromboembolism alone do not have predictive value, and therefore knowing the prognosis of PTE patients is important. Because some of these patients can be treated on an outpatient basis. Therefore, clinical examinations and more factors should be considered in this regard. Determining the duties of these patients in the emergency medicine service according to the prognosis of these patients will help to improve their survival and also reduce costs. One of the strengths of the present study is that the idea and working method of this study are almost novel and there are very few similar studies in this field. Among the limitations of this study, it can be mentioned that the mortality of patients was not examined in the long term.

Conclusion

CT angiography criteria in patients with acute pulmonary embolism in our study provided a predictive value in predicting mortality. Variables of interventricular septal bulge and maximum right-to-left ventricular longitudinal and transverse diameter, considered as qualitative indicators of PTE severity, were associated with mortality. Therefore, the use of CT angiography will be helpful in determining the assignment of pulmonary embolism patients in the emergency medicine service.

Acknowledgment:

None

Funding:

Mashhad University of Medical Sciences

Authors Contributions:

ZA, MF, RA, and BA conceptualized the study objectives and design. RA, MF are infectious disease specialists who contributed to data collection from patients along with ZA. FM, MM and MF drafted the study design protocols to be submitted to research centers. Data were was analyzed by MM and RA. Manuscript was drafted by ZA, MF, and FM. All authors contributed in revisions.

Ethical Consideration:

IR.MUMS.MEDICAL.REC.1400.082

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Tables:

Table 1: Demographic information of patients participating in the study

P-Value	All patients	Variable
0.2	122	Age
<0.0001	122	Systolic blood pressure (SBP)
<0.0001	122	Diastolic blood pressure (DBP)
<0.0001	122	Breathing rate
<0.0001	122	heart beat (HR)
0.001	122	RV Length
0.032	122	RV Width
0.2	122	LV Length
0.2	122	LV Width
0.071	122	PA Width
<0.0001	122	Ascending Aorta Width
0.002	122	SVC Diameter (Superior Vena Cava)

Table 2: Relative distribution of qualitative variables of the examined patients

P-Value	Improved		Died		All patients		Group	
	Percent/SD	n/Mean	Percent/SD	n/Mean	Percent/SD	n/Mean	Variable	
**0.85	14.56	69.03	14.38	68.56	14.41	68.80	age, year	
**0.50	58	36	51.7	31	55	67	Male	Sex
	42	26	48.3	29	45	55	Female	
**0.51	19.4	12	25	15	22	27	Yes	DVT
	80.6	50	75	45	78	96	No	
**0.35	5.35	22	45	27	40	49	Yes	history of smoking
	64.5	40	55	33	60	73	No	
**0.48	21	13	15	9	18	22	Yes	Sepsis
	79	49	85	51	82	100	No	
**0.61	1.6	1	3.3	2	2.5	3	Yes	Reteplase
	4.98	61	96.7	58	97.5	119	No	
**0.99	71	44	71.7	43	71	87	Yes	Hospitalization in ICU
	29	18	28.3	17	29	35	No	

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Table 3: Distribution of qualitative findings of CTA imaging in patients

P-Value	Improved		Died		All patients		Group	
	%	n	%	n	%	n	Variable	
0.47*	50	31	43.3	26	47	57	No	Bow of the interventricular septum
	50	31	56.7	34	53	65	Yes	
*0.8	61.3	38	63.3	38	62	76	No	Contrast reflux into the inferior vena cava
	38.7	24	36.7	22	38	46	Yes	
*0.92	79	49	78.3	47	79	96	No	Contrast reflux to azygos
	21	13	21.7	13	21	26	Yes	
*0.06	85.5	53	71.7	43	79	96	No	Contrast reflux into the hepatic vein
	14.5	9	28.3	17	21	26	Yes	
**0.1	8	5	5	3	6.6	8	1	Embolic level
	45.3	28	35	21	40	49	2	
	23.3	20	38.3	23	35	43	3	
	14.5	9	21.7	13	18	22	4	

Table 4: Quantitative variables of the vital signs of the examined patients upon entering the emergency room

PR mean±sd	RR mean±sd	DBP mean±sd	SBP mean±sd	Group
100.5±17.5	24.3±5.44	69.6±12.55	114.5±19	All patients
100.5±21.5	24.15±5.48	77.2±3.14	119.5±20	Died
100.5±12.3	24.15±5.06	66±9.8	109.5±16	Improved
0.48*	0.47*	0.02*	0.007*	P-Value

*Mann-Whitney Test

Table 5: Comparison of average quantitative imaging criteria of examined patients in two groups, deceased and recovered

P-value	Improved n = 62	Died N= 62	All patients	Variable
	mean±sd	mean±sd	mean±sd	

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0.34	1.13±1.08	1.25±0.46	1.19±0.4	The ratio of the maximum transverse diameter of the right and left ventricles
0.7	0.97±0.18	0.99±0.15	0.98±0.17	The ratio of the maximum longitudinal diameter of the right and left ventricles
0.8	0.91±0.14	0.89±0.23	0.90±0.18	The ratio of the transverse diameter of the trunk of the pulmonary artery to the aorta
0.3	31.5±4.7	31.05±4.38	31.28±4.54	Pulmonary trunk (PT) diameter

Table 6: Predictive role of imaging variables in predicting mortality due to PTE

p	95% CI higher	95% CI lower	OR	Variable
0.003	2.587	1.074	1.356	sepsis
0.035	2.475	1.031	1.870	Age>65
0.003	3.972	1.287	1.453	Performance of the 4-Level Pulmonary Embolism
0.0001	3.941	1.129	1.471	Hospitalization in ICU
0.022	3.206	1.146	2.609	Bow of the interventricular septum
0.048	1.579	1.003	1.173	breaths per minute
0.038	4.71	1.544	3.24	The ratio of the maximum longitudinal diameter of the right and left ventricles
0.047	1.89	1.013	1.57	The ratio of the maximum transverse diameter of the right and left ventricles
0.803	0.869	0.29	2.605	The ratio of the transverse diameter of the trunk of the pulmonary artery to the aorta
0.44	0.44	0.944	1.038	Pulmonary trunk diameter
0.588	0.588	0.928	1.029	Superior vena cava (SVC) diameter

Table 7: Predictive role of imaging variables in predicting ICU admission due to PTE

p	95% CI higher	95% CI lower	OR	Variable
0.67	1.024	0.919	1.141	Contrast reflux into the inferior vena cava
0.542	0.728	0.263	2.019	Contrast reflux to azygos
0.57	1.493	0.374	5.959	Contrast reflux into the hepatic vein

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0.683	1.255	0.422	3.732	Embolic level
0.328	0.328	0.028	0.305	The ratio of the maximum transverse diameter of the right and left ventricles
0.188	0.188	0.168	0.488	The ratio of the maximum longitudinal diameter of the right and left ventricles
0.519	0.519	0.066	0.511	The ratio of the transverse diameter of the trunk of the pulmonary artery to the aorta
0.875	0.99	0.877	1.119	Pulmonary trunk diameter
0.977	1.028	0.155	6.805	Superior vena cava (SVC) diameter

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