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CORRELATION OF RVD AFTER ACUTE PULMONARY EMBOLISM AND THROMBOEMBOLIC EVENTS RECURRENCE: FOLLOW UP STUDY

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Abstract :

Background : Acute pulmonary embolism may lead to a serious consequence known as right ventricular dysfunction, which has a substantial influence on patient outcomes and requires meticulous treatment. An acute pulmonary embolism occurs when a blood clot becomes lodged in the pulmonary arteries, blocking blood flow to the lungs. This blockage may result in elevated pressure in the pulmonary circulation, putting stress on the right ventricle of the heart.
Aim: This study aims to investigate the relationship between persistent right ventricular dysfunction (RVD) after hospital discharge following acute pulmonary embolism (PE) and the occurrence of recurrent thromboembolic events during a one-year follow-up period.
Method: The study included a group of 79 persons who were admitted to Banha teaching hospital and Zhraa hospital, Faculty of Medicine for girls with acute pulmonary embolism from May 2021 to May 2022. Acute pulmonary embolism (PE) was confirmed using computed tomography (CT) pulmonary angiography. Exclusion criteria included patients having a proven medical history of recurrent pulmonary embolism, chronic obstructive lung disease, congestive heart failure, and evidence of right ventricular hypertrophy on echocardiography. Patients with a history of deep vein thrombosis (DVT) were included. A thorough evaluation, which including Duplex ultrasonography,

was conducted at the first hospitalization to differentiate between new deep vein thrombosis (DVT) and previous occurrences.
Results Age was found to be a factor influencing RVD persistence, with younger individuals showing higher rates. The study also compared concurrent illnesses and risk factors for venous thromboembolism. The results revealed the presence of statistically significant differences between study groups regarding recurrent thromboembolic event. The RVD Regression group had a higher incidence of both DVT and acute pulmonary embolism, while the Persistence group had a higher percentage of patients receiving thrombolysis. As nearly half of those with RVD persistence (48.15%) developed recurrent DVT, while recurrent DVT was observed in only 10.34% among those who had no RVD.
Conclusion: The results may provide valuable insights for developing risk stratification models, making therapy choices, and establishing long-term care plans for persons with persistent RVD. Acquiring this information has the capacity to enhance the quality of treatment and results for individuals who previously had acute pulmonary embolism.

Keywords: acute pulmonary embolism, right ventricular dysfunction, recurrent thromboembolic episodes.

Introduction

When the right ventricle faces reduced contractility and decreased pumping cardiac output, it signifies right ventricular dysfunction **[1]**. During a sudden pulmonary embolism (PE), the right ventricle undergoes stress due to increased pressure in the pulmonary circulation **[2]**. This stress can lead to RV dilation and both systolic and diastolic functional impairment **[3].**
In some cases, the right ventricular dysfunction persists beyond the initial phase of a pulmonary embolism **[4].** This prolonged impairment may be associated with factors like persistent pulmonary hypertension, chronic thromboembolic conditions, or other cardiovascular diseases **[5].**
To assess the continued impact on the right ventricle, medical professionals often turn to imaging techniques such as echocardiography or cardiac magnetic resonance imaging (MRI) **[6]**. Echocardiography, for instance, evaluates right ventricular functions through measurements like right ventricular dimension and tricuspid annular plane systolic excursion (TAPSE) **[7].**
Persistent right ventricular dysfunction can have serious consequences, including an increased risk of developing chronic heart failure **[8]** and limitations in physical activity **[9].** Patients experiencing prolonged dysfunction may require ongoing medical supervision and monitoring to address the underlying causes and manage symptoms effectively.
Treatment strategies for chronic right ventricular dysfunction may involve anticoagulation to prevent further chronic pulmonary embolism **[10],** and pharmacotherapy to reduce pulmonary artery pressure **[11]**. This research aimed to assess the prognostic significance of persistent right ventricular dysfunction (RVD) at the time of hospital discharge in predicting the chance of recurrent venous thromboembolism (VTE).

Method

Seventy-nine patients who were admitted to Banha teaching hospital and Zhraa Hospital, faculty of Medicine for girls, Egypt, started from May, 2021 till May, 2022. Patients who were diagnosed with acute pulmonary embolism (PE) using CT pulmonary angiography and successfully survived their hospital stay were included in the research. The exclusion criteria consisted of individuals with a confirmed medical background of congestive heart failure, repeated pulmonary embolism, or chronic obstructive pulmonary disease. Additionally, those with signs of right ventricular hypertrophy on echocardiography, indicating long-term dysfunction of the right ventricle, were also excluded. The investigation did not exclude patients with a history of deep vein thrombosis (DVT). During the patients' first hospitalization, we conducted a thorough evaluation using Duplex ultrasonography to differentiate between newly developed DVT and recurrent DVT, in order to track their progress during follow-up.

Lab tests were performed for all admitted patients. The lab tests included routine laboratory tests such as prothrombin time (PT), partial thromboplastin time (PTT), Complete blood count (CBC), D-dimer and NT-ProBNP.

During the echocardiographic test upon admission, significant results were seen that suggest right ventricular dysfunction after an acute pulmonary embolism. The right ventricle was noticeably larger than the left ventricle on the parasternal long axis image, showing significant dilatation. The right ventricle was enlarged compared to the left ventricle, with a basal ratio surpassing 1.0, and the McConnell sign may be seen in the four-chamber image. The parasternal short axis picture showed compression of the interventricular septum, resulting in aberrant septal wall motion and a D-shaped left ventricle. The subcostal view revealed a dilated inferior vena cava with less than 50% collapse during inspiration. Echocardiographic doppler evaluation showed a short pulmonary artery acceleration time (<60ms), a mid-systolic "notch," and a slightly raised peak pulmonary artery systolic pressure (<60mmHg) measured by the tricuspid regurgitation (TR) peak systolic velocity (60/60 sign).

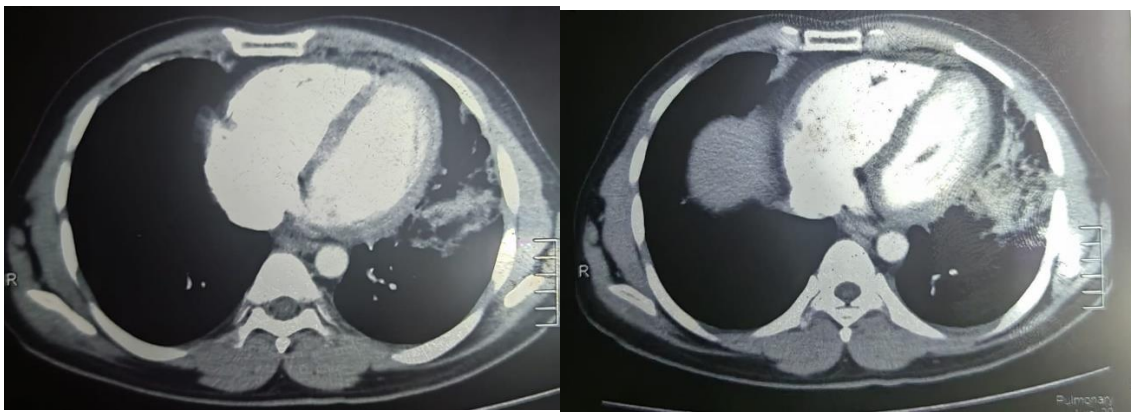
Movable thrombi were seen in the right atrium and/or right ventricle. Furthermore, there was impaired global systolic function of the right ventricle, indicated by a reduced 'tricuspid annular plane systolic excursion' (TAPSE) of less than 17 mm using M-Mode, along with a diminished peak systolic velocity at the lateral annulus of the tricuspid valve (RV-Sa) measuring less than 9.5 cm/s. The echocardiographic results emphasized the presence of right ventricular dysfunction and demonstrated the intricate cardiovascular complications that occur after an acute pulmonary embolism.

Echocardiographic Doppler exams were performed in two dimensions upon admission (within one hour of PE diagnosing) using Philips, Advanced Ultrasound System 795200 EPIQ ELITE System with X MATRIX PHILIPS probe (X5-1) PHILIPS and prior to hospital discharge, using recognized guidelines. The discharge echocardiography was conducted in a manner that did not include any awareness of the admission findings or the patient's clinical background. RVD was diagnosed by meeting one of the following criteria: right ventricle enlargement at the base (end-diastolic diameter >40 mm or right/left ventricular end-diastolic diameter ratio >1 in the apical 4-chamber view), abnormal septal wall motion, or elevated pulmonary artery pressure (Doppler pulmonary artery acceleration time <60 milliseconds or right ventricular systolic pressure >36 mmHg and < 60 mmHg). Patients showing signs of right ventricular hypertrophy of the right ventricular free wall, with an end-diastolic thickness more than 7 mm, were not included in the research. Patients were classified into three groups based on echocardiographic findings at admission and discharge: (1) those without right ventricular dysfunction (RVD) at admission (No RVD), (2) those with improved RVD at discharge (RVD regression), and (3) those with persistent RVD at discharge (RVD persistence).

Upon admission, echocardiography detected evidence of RVD, suggesting possible problems related to venous thromboembolism. After commencing treatment, which included thrombolytic therapy and anticoagulation, or just anticoagulation, a subsequent echocardiogram at the time of discharge revealed a significant enhancement in RV function. Nevertheless, it is important to mention that the RV function did not fully normalize during the first stage of therapy. Follow-up echocardiographic evaluations performed after three months of uninterrupted treatment intervention demonstrated a significant restoration of RV function in most patients. As a result of this favorable development, the use of therapeutic anticoagulation was stopped in these patients. Notably, when anticoagulant medication was stopped successfully, subsequent echocardiograms showed consistently normal right ventricular functioning. This series of echocardiographic assessments highlights the adaptable and reactive characteristics of RV performance in response to suitable medical treatments, offering vital understanding into the development and resolution of venous thromboembolic events.

All patients undergone CT pulmonary angiography to effectively diagnose pulmonary embolism. CT data capture and reconstructions were conducted using Toshiba 160 multidetector CT with a section thickness of 0.5- or 1-mm. The scan was completed utilizing a single breath-hold contrast-enhanced CT pulmonary angiography. The duration of rotation was 0.4 seconds, the pitch factor was

1.4, the tube current ranged from 250 to 300 mA, and the tube voltage was 100 kV. Density of acute thrombus have been measured using CT and the results were recorded for the three groups.
Following the chest scan, a retrospectively ECG-synchronized CT scan was obtained, encompassing the entirety of the heart from the aortic root to the diaphragm level, with a single breath-hold. Prior to commencing the acquisition, a predetermined wait of 15 seconds was implemented to restrict the radiation dose. This delay allowed for enough contrast enhancement, enabling the delineation of endocardial contour borders.
Consequently, functional analysis could be conducted by drawing endocardial contours. During the function scan, a flow rate of 2.5–3.0 mL/s was used to inject 35–50 mL of contrast agent (either 40–50 mL of iobitridol 300 or 35–40 mL of iomeprol 400). This was followed by a saline bolus chaser of 30 mL at a flow rate of 3.0 mL/s. Transverse non-ECG-synchronized CT scans were utilized to evaluate the ratio between the diameter of the right ventricle (RV) and left ventricle (LV). This step help in diagnosing RVD **[12].**
Structural problems inside the heart can be identified by the presence of an aberrant location of the interventricular septum, flattening of the interventricular septum, and paradoxical interventricular septal bowing, especially towards the left ventricle. These irregularities may indicate the presence of underlying cardiovascular disorders, such as right ventricular enlargement, which is defined by the right ventricle seeming larger than the left ventricle, or pulmonary trunk enlargement, which is characterized by the pulmonary trunk being larger than the aorta. These alterations in structure can result in characteristics of right heart failure, which indicate impaired cardiac function.
Furthermore, the presence of inferior vena caval contrast reflux and a dilated azygos venous system may indicate disturbances in venous return and circulation. The presence of contrast reflux in the inferior vena cava indicates the occurrence of retrograde flow, which is attributed to elevated pressure within the venous system. Venous congestion and altered hemodynamics are further supported by the dilatation of the azygos venous system.



Figurer1: Axial CT chest mediastinal window showing RT ventricular enlargement with flatting of interventricular system

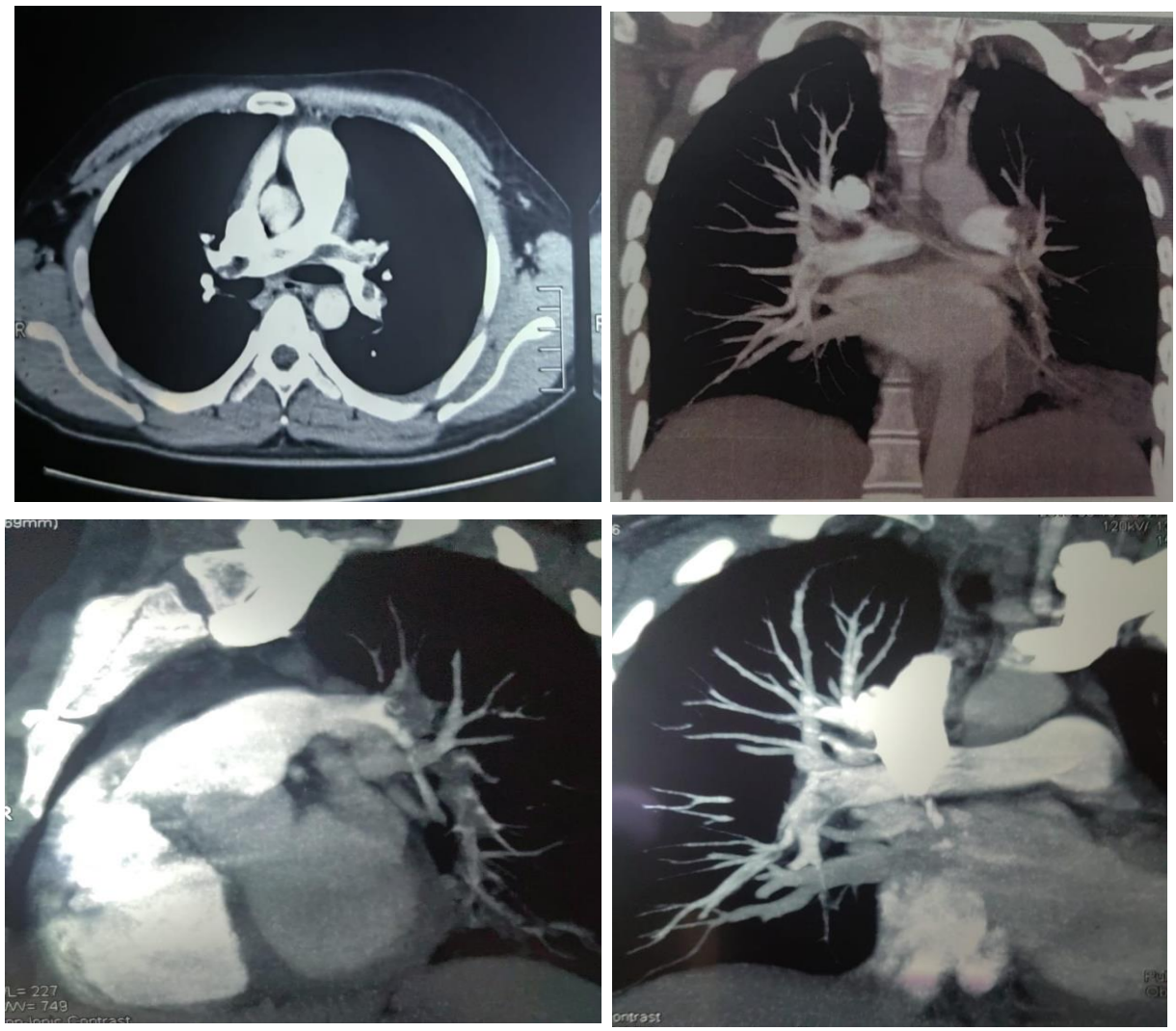


Figure 1: CT pulmonary angiography showing bilateral main pulmonary arteries saddle intramural thrombus (2nd order) extends to 3rd order branches

Patients' management

Patients who were confirmed to have pulmonary embolism (PE) were quickly treated with intravenous unfractionated heparin according to hospital protocol (17-20 u/kg/h) and dose of intravenous unfractionated heparin was adjusted according to activated partial thrombo-plastine test to be 1.5 to 2 times control value or LMWH in the form of enoxaparin with dose 1 mg /kg every 12 hours for at least one week. Tissue-type plasminogen activator (t-TPA) was given intravenously at a dose of 100 mg over a two-hour period. This thrombolytic therapy method was used in three different clinical situations with individuals who had been diagnosed with PE. If systolic arterial pressure consistently stayed below 100 mm Hg, indicating shock, treatment was started. Patients were then monitored for signs of organ hypoperfusion such as confusion, reduced urine output, cold and clammy skin, and possible lactic acidosis detected through arterial blood gas analysis. Therapy should be administered in cases that progress to shock or require catecholamine infusion, except when dopamine exceeds a rate of ≤5 μg/kg per minute, and when there are signs of right ventricular dysfunction (RVD) upon admission followed by delayed hemodynamic instability. Oral anticoagulants in the form of vitamin K antagonist (warfarin) or Direct new oral anticoagulants (DOAC) medication in the form of rivaroxiban 20 mg OD or apixiban 5 mg BID was started after the first intense period and continued for three months. Dosage modifications in patients taking warfarin were made to keep the international normalized ratio (INR) within the therapeutic range of two to three.

The duration of oral anticoagulation medication, which was set by the presence of documented risk factors for recurrent VTE, was not affected by the presence of residual RVD after the patient was discharged from the hospital. It was also shown that the length of therapy was comparable across patients who had RVD and those who did not have RVD. Patients were instructed to plan follow-up visit after 3 months after being discharged from the hospital. These appointments were to be scheduled after the patients were discharged. A full evaluation of the patient's medical history, a comprehensive physical examination, and echocardiography were all components of the visit. Patients were provided with information on the key symptoms and signs of recurrent VTE, and they were asked to rapidly report any findings of this kind to the study facility.

Primary and secondary outcomes

The research aimed to identify recurring venous thromboembolism in individuals by using symptomatic and objectively validated criteria. Independent specialists conducted diagnostic evaluations using established techniques, without considering patients' clinical situations or prior echocardiographic results. The diagnostic criteria for PE include detecting a new blockage in the pulmonary arteries by pulmonary angiography or spiral computed tomography pulmonary angiography. For the recurrence of VTE in the form of DVT, the criteria include identifying a non-compressible proximal vein with ultrasonography or detecting an intraluminal filling defect using venography. Recurrent DVT in patients with a history of DVT is identified by abnormal findings on compression ultrasonography or MSCT venography in the proximal veins of the other leg, an enlargement of a blood clot on MSCT venography, the appearance of a new non-compressible segment of the vein, or a 4-mm or greater growth in thrombus diameter on ultrasonography in the same leg. A fatal PE is described as a deadly event occurring within hours following a recurring PE, which has been objectively diagnosed.

Statistical analysis

The study used unpaired t tests and Fisher exact tests to compare data from a normal distribution and non-continuous variables. It used Cox proportional hazards regression models to generate relative risks for continuous variables and hazard ratios for non-continuous variables. A stepwise forward regression model was used for multivariate analyses, focusing on variables with a significance level of P<.05 or below. Survival curves were generated using the Kaplan-Meier technique. P values were calculated for both sides of the distribution, with a P value less than 0.05 considered statistically significant. The calculations were conducted using SPSS statistical software.

Results

The study included 79 confirmed PE patients who were distributed into three groups as follows: Group 1 n=23, group 2 n=27 and group 3 n=29, total cases n=79. Demographic data as shown in Table 1.

Table (1): Comparison between the three studied groups according to demographic data

		RVD Regression (n = 23)		**RVD Persistence (n = 27)**		**No RVD (n = 29)**		**F**	**p**
		No.	**%**	**No.**	**%**	**No.**	**%**		
Sex	**Male**	**11**	**47.8**	**11**	**40.7**	**10**	**34.3**		
	Female	**12**	**52.3**	**16**	**59.3**	**19**	**65.7**		
Age	**Min. – Max.**	**60.0 – 79.0**		**65.0 – 72.0**		**67.0 – 75.0**		**-**	**-**
	Mean ± SD.	**72.40 ± 4.65**		**68.03± 2.65**		**71.2. ± 2.63**			
	Median (IQR)	**69 (71 - 69)**		**70 (70 – 68)**		**71 (72– 69)**			

IQR: Inter quartile range, SD: Standard deviation, F: F for One-way ANOVA test, p: p-value for comparing between the three studied groups

Researchers examined demographic data on the continued presence of right ventricular dysfunction after an acute pulmonary embolism. The patients were classified into three groups: RVD Regression, RVD Persistence and No RVD. The data exhibited different sex distributions, with both men and females in the RVD Regression group and in the Persistence group. Age was identified as a factor influencing the persistence of RVD, with younger persons showing greater rates of persistence.

Table 2: Comparison between the three studied groups according to concomitant disease

Characteristics of study patients based on the in-hospital course of RVD*					
Characteristics	**RVD Regression**	**RVD Persistence**	**No RVD**	**f**	**P**
	(n = 23)	**(n = 27)**	**(n = 29)**		
Previous or concurrent disease					
Diabetes	**10**	**12**	**9**		
CVD	**10**	**9**	**9**	**0.045**	**0.98**
Cancer	**5**	**5**	**4**		
Risk factors for VTE					
Permanent	**9**	**9**	**9**		
Transient	**6**	**10**	**8**	**0.14**	**0.87**
Idiopathic	**8**	**6**	**7**		

F: F for One-way ANOVA test, p: p-value for comparing between the three studied groups

Table 2 contrasts three groups according to concurrent illnesses and risk factors for venous thromboembolism (VTE). There are three groups: RVD Regression, RVD Persistence, and No RVD. There are small variations in the distribution of people with diabetes, cardiovascular disease, and cancer across the categories. Table 2 displays the distribution of patients with permanent, transitory, and idiopathic risk factors for VTE. No significant differences were seen in temporary and cardiovascular disease risk factors. The findings show that while there are differences in the frequency of associated diseases and risk variables, these differences are not statistically significant.

Table 3: Comparison between the three studied groups according to Concomitant DVT and PE during admission, Thrombolytic therapy, past history of Vena cava filter use

Concomitant DVT, Thrombolysis, Vena cava filter course of RVD*					
Characteristics	**RVD Regression**	**RVD Persistence**	**No RVD**	**Chi-square**	**p**
	(n = 23))	**(n = 27))**	**(n = 29)**		
Concomitant DVT and PE during admission	**3**	**9**	**1**		
Thrombolytic therapy	**2**	**3**	**0**	16.1	0.02
DVT with Past history of Vena cava filter	**1**	**4**	**0**		

F: F for One-way ANOVA test, p: p-value for comparing between the three studied groups

Table 3 compares three groups depending on the presence of deep vein thrombosis (DVT) and PE upon admission, the use of thrombolytic therapy, and DVT with past history of vena cava filters. The RVD Regression group exhibited a higher incidence of individuals with both DVT and acute pulmonary embolism compared to the RVD Persistence group. Statistical analysis revealed a significant disparity in the use of thrombolytic therapy across the groups. The RVD Persistence group had a greater percentage of patients receiving thrombolytic therapy. Nevertheless, the variations in DVT with past history of vena cava filter use did not achieve statistical significance.

Table 4: Comparison between the studied group according to the CT findings.

Thrombus density, sensitivity and specificity, RV/LV measurements					
Characteristics	**RVD Regression (n = 23))**	**RVD Persistence (n = 27))**	**No RVD (n = 29)**	**f**	**P**
Thrombus density (Hu)	85±5	90±6	88±4	**6.1333**	**0.0034**
Qanadli Index (%)	37±22	36±25	35±23.5	**0.0462**	**0.9548**
RV EDV (mL)	150±23	145±20	153±15	**1.216**	**0.3021**
RV ESV (mL)	173±23	165±20	168±15	**1.0773**	**0.3457**
RV EF (%)	40±5%	40.7±3%	40.0%±7%	**0.1535**	**0.858**
LV EDV (mL)	130 ± 20	125 ± 20	133 ± 15	**1.3514**	**0.265**
LV ESV (mL)	70 ±12	65±11	75±10	**5.8319**	**0.0044**
LV EF (%)	46.15 ±5	48±7	43.61±10	**2.2385**	**0.1136**

This table shows a statistically significant (p= 0.003) increased thrombus density in RVD persistent group (90±6) when compared with that of RVD regression group (85±5) and that of no RVD group (88±4). A statistically significant (p= 0.004) decreased LV ESV in RVD persistent group (65±11) when compared with that of RVD regression group (70±12) and that of no RVD group (75±10). No statistically significant (P> 0.05) differences between the studied groups as regard other CT findings.

Table5: Comparison between the three studied groups according to Hospital stay, (day)

Characteristics of study patients based on the in-hospital course of RVD*					
Characteristics	**RVD Regression**	**RVD Persistence**	**No RVD**	**f**	**p**
	(n = 23))	**(n = 27))**	**(n = 29)**		
Min. – Max.	**10-14**	**12-16**	**7-15**		
mean ± SD, day	**13.5±1.89**	**13.4±1.89**	**13.2±1.9**	3.2	0.04
Median (IQR)	**1.5(14.25-12.75)**	**51.5(14.25-12.75)**	**1.5(14.25-12.75)**		

IQR: Inter quartile range, SD: Standard deviation, F: F for One-way ANOVA test, p: p-value for comparing between the three studied groups.

Table 5 compares three groups based on hospital stay lengths: RVD Regression, RVD Persistence, and No RVD. The average length of hospitalization varies significantly among the three groups, with the RVD Regression group having an average stay of 13.5 days, the RVD Persistence group having an average stay of 13.4 days, and the No RVD group having an average stay of 13.2 days. The results suggest that while there are no significant differences in the shortest and longest hospital stays, the average length of hospital stay significantly varies.

***Table 6: recurrence of DVT,* compare between all groups regarding thromboembolic events after hospital discharge whether patients had past history of DVT or DVT during admission (Chi test)**

	RVD Regression (n = 23)	***RVD Persistence (n = 27)***	***No RVD (n = 29)***	***X^2***	***P Value***
Recurrence of DVT	***5 21.74%***	***13 48.15%***	***3 10.34%***	***10.62***	***0.004***

X^2: Chi-square test

This Table shows that: there was statistically significant difference between the studied groups as regard recurrence of DVT. As nearly half of those with RVD persistence (48.15%) developed recurrent DVT, while recurrent DVT was observed in only 10.34% among those who had no RVD.

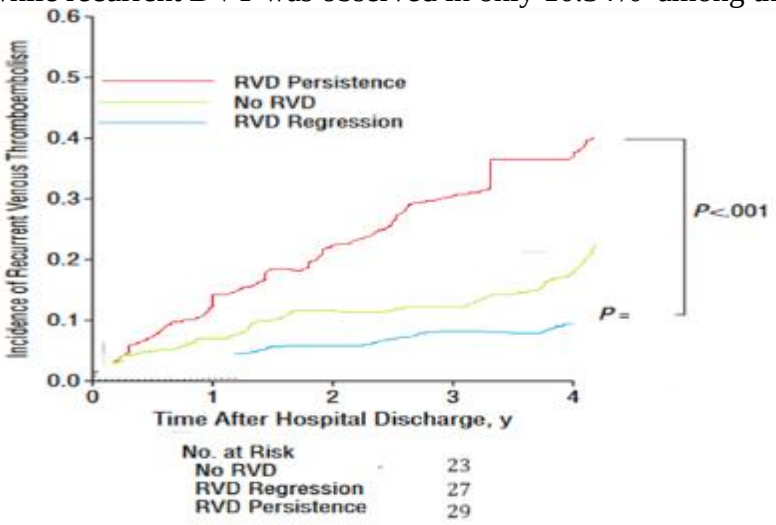


Figure 3: Cumulative incidence of recurrent venous thromboembolism.

Table 7: laboratory data of all studied groups.

	RVD Regression	RVD Persistence	No RVD	P Value
	(n = 23)	(n = 27)	(n = 29)	
NT-proBNP (pg/L)	154±7.7	562±13	94±2.2	<0.001
D. Dimer (ng/ml)	707±38.5	1007±46.9	462±11.8	<0.001
PT	23±3.5	29±2.9	12±0.8	<0.001
PTT	47±3.9	53±2	32±1.4	<0.001
WBCs (kμ/l)	7±1.1	7±1.6	6±0.9	0.06
RBCs (mμ/l)	4±0.6	5±0.7	4±0.7	<0.001
Hb (g/dl)	13.7±1	13.3±1.3	13.4±1.5	0.39
Ht %	47±2.4	53±2.8	43±4.3	<0.001
MCV (fL)	83±7.8	83±7.8	85±7.1	0.44
MCH (pg)	28±1.9	28±2.3	28±2.4	0.79
MCHC (g/dl)	32±1.9	32±1.6	31±1.7	0.57
RDW-CV%	12.2±0.5	12.3±0.9	12.6±0.9	0.3
PLT (kμ/l)	272±70.1	290±72	230±65.7	0.005

This Table shows comparison of all studied groups as regard laboratory data. As regard NT-ProBNP, there was high statistically significant (P<0.001) increase in patients with persistent RVD group (562±13) pg/L when compared with that of patients with regressed RVD (154±7.7) pg/L and that of patients with no RVD (94±2.2) pg/L.

As regard D. dimer, there was high statistically significant (P<0.001) increase in patients with persistent RVD group (1007±46.9) ng/ml when compared with that of patients with regressed RVD (707±38.5) ng/ml and that of patients with no RVD (462±11.8) ng/ml.

As regard PT, there was high statistically significant (P<0.001) increase in patients with persistent RVD group (29±2.9) when compared with that of patients with regressed RVD (*23±3.5*) and that of patients with no RVD (12±0.8).

As regard PTT, there was high statistically significant (P<0.001) increase in patients with persistent RVD group (53±2) when compared with that of patients with regressed RVD (*47±3.9*) and that of patients with no RVD (*32±1.4*).

As regard WBCs, there was no statistically significant (P= 0.06) difference between all studied groups.
As regard RBCs, there was high statistically significant (P<0.001) increase in patients with persistent RVD group (*5±0.7*) when compared with that of patients with regressed RVD (*4±0.6*) and that of patients with no RVD (*4±0.7*).
As regard Hb, there was no statistically significant (P= 0.39) difference between all studied groups.
As regard Hct, there was high statistically significant (P<0.001) increase in patients with persistent RVD group (*53±2.8*) when compared with that of patients with regressed RVD (*47±2.4*) and that of patients with no RVD (*43±4.3*).
As regard MCV, MCH, MCHC and RDW-CV, there were no statistically significant (P> 0.05) differences between all studied groups.
As regard PLT, there was a statistically significant (P= 0.005) increase in patients with persistent RVD group (*290±72*) when compared with that of patients with regressed RVD (*272±70.*) and that of patients with no RVD (*230±65.7*).

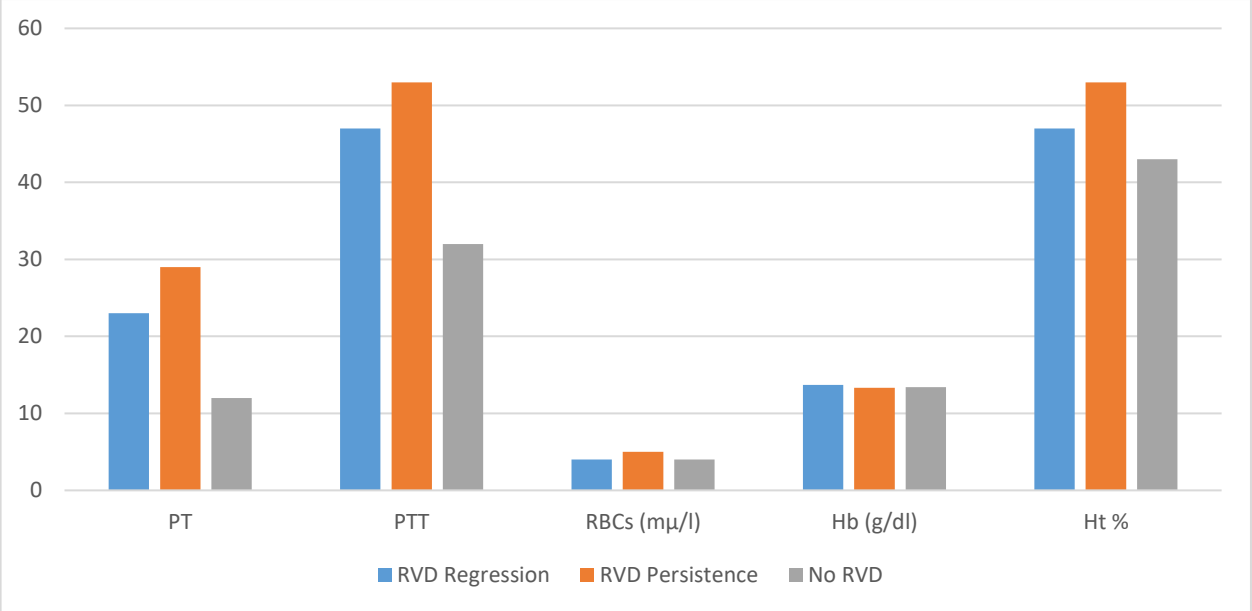


Figure 4 : **Comparison between the studied groups according to PT, PTT, RBCs, HB and Ht.**

Discussion

Venous thromboembolism, which includes DVT and PE, affects around 5% of persons over their lifetime, making it the third most common cardiovascular illness. [**13]**. The probability of VTE reoccurring after stopping anticoagulant treatment, without any specific triggers like major injury or surgery, may be as high as 36% during a 10-year period, with 3 to 4% of these cases leading to death **[14, 15].**
If a patient has VTE after stopping anticoagulant treatment, the typical course of action is to resume anticoagulation medication **[16].** Given its frequent and indefinite reinstatement, an inaccurate diagnosis puts the patient at avoidable risk of experiencing bleeding problems **[17].** Managing suspected recurrent VTE is difficult due to the absence of diagnostic criteria **[18].** Furthermore, the accuracy of pretest probability and imaging modalities used for diagnosing DVT is diminished when it comes to potential recurrence **[19].** This research aimed to assess the prognostic significance of persistent RVD at the time of hospital discharge in predicting the chance of recurrent VTE. The recurrence may be attributed to several factors, such as an underlying pro-thrombotic condition, changes in blood flow dynamics, and excessive strain on the right ventricle **[20].**
Results found that age was identified as a factor influencing the persistence of RVD, with younger persons showing greater rates of persistence. Age may be associated with the continuation of RVD caused by many physiological and pathological causes. One important factor to note is that as

people become older, there is a natural decrease in cardiovascular performance and reserve **[21].** This deterioration might present as decreased myocardial compliance, poorer contractility, and lower capacity of the heart to respond to sudden stresses such PE **[22].**

Right ventricular overload may occur due to several cardiac conditions, such as pulmonary hypertension or chronic lung diseases, leading to increased pressure inside the pulmonary circulation **[23].** Right ventricular overload may result in changes to blood flow, which might increase the chances of recurrence **[24].** This may include alterations in the blood vessels, increased stress on the heart, and resulting complications such as blood clot formation **[25].**

No substantial disparities were seen in transitory and CVD risk variables. The results indicate that while there are variations in the prevalence of accompanying illnesses and risk factors, these variations are not statistically significant. Comorbidities have a considerable negative impact on the prognosis of CVD patients. However, there are few studies that have examined the collective influence of several comorbidities **[26].**

The RVD Persistence group had a greater percentage of patients receiving thrombolysis. These results contradicted the finding by **Wang D, et al. [27]** who discovered that patients who received thrombolysis showed negative correlation with persistence RVD.

During PE, the right ventricle has greater workload as it pumps blood against heightened resistance in the pulmonary arteries **[28].** This sudden strain might result in transient malfunction **[29].**

Often, the right ventricular dysfunction may be resolved when the body spontaneously degrades the clot and the pulmonary circulation reverts to its normal state **[30].** Nevertheless, in some instances, especially with bigger or more severe pulmonary embolisms, the dysfunction may last **[31].**

Chronic thromboembolic pulmonary hypertension may be linked to long-lasting impairment of the right ventricle **[32].** This phenomenon arises when blood coagulates inside the pulmonary arteries without fully dissolving, resulting in heightened pressure within the pulmonary circulation **[33].** The PE-induced inflammatory response may exacerbate persistent harm and impairment in the pulmonary vasculature **[34].** Sustained impairment of the RV may result in manifestations such as dyspnea, lethargy, and reduced capacity for physical activity **[35].**

According to 2019 ESC Guidelines for Acute PE, modified risk-adjusted care protocol for patients with pulmonary embolism, considering the severity of the condition, RVD, and coexisting medical conditions. Hemodynamic instability is now characterized as cardiac arrest requiring resuscitation, obstructive shock, or persistent hypotension not due to other underlying conditions. Intravenous thrombolysis is now classified as a Class I suggestion, and interventional therapies are classified as Class IIa. Direct oral anticoagulants (DOACs) are preferred as primary anticoagulants, even for those qualified to take warfarin. After the first six months of therapy, a lower dosage of apixaban or rivaroxaban is recommended for prolonged anticoagulation. Edoxaban or Rivaroxaban should be used instead of low molecular weight heparin in cancer patients. Regular check-ups using a combined inpatient-outpatient care approach are recommended **[36].**

The comprehensive analysis of the Baseline echocardiographic parameters of the studied groups reveals that persons with persistent RVD often have increased dimensions, reduced ejection percentage **[37]** and altered tricuspids' velocities compared to those with regression of RVD or no RVD **[38**]. The discovered differences are statistically significant, indicating potential consequences for the cardiovascular function in people with persistent RVD.

Pulmonary emboli lead to an increase in RV afterload **[39].** In individuals lacking pre-existing cardiopulmonary disease, it is necessary to occlude around 25-30% of the pulmonary vasculature in order to induce an increase in pulmonary artery pressure, hence augmenting the pulmonary venous afterload **[40]**. The RV compensates for the obstruction of more than 50-75% of the pulmonary vasculature caused by emboli, when the pressure in the pulmonary artery increases over 40 mmHg **[41].** The emboli cause hypoxia, which worsens the afterload by stimulating localized vasoconstriction through the release of vasoactive mediators such as serotonin, thromboxane, and histamine **[42].** Once the afterload reaches the critical threshold, the right ventricle expands, the left ventricle becomes less filled, and the blood flow to the coronary arteries diminishes **[43].** The decrease in output to the coronary arteries and the increase in intramuscular pressure hinder the

passage of blood to the right ventricle, resulting in right ventricular ischemia **[41].**

As the ischemic condition of the right ventricle progresses, its contractility is further compromised, leading to a further reduction in right ventricular output. This, in turn, causes an increase in right ventricular dilatation and a decrease in left ventricular output. Consequently, a downward hemodynamic spiral ensues, which subsequently intensifies and ultimately culminates in cardiogenic shock **[41].** It is important to acknowledge that the administration of medications like propofol, which are utilized for the initiation and sustenance of general anesthesia, leads to a reduction in venous return to the right heart, also known as preload. This decrease is primarily caused by peripheral venous dilatation, which further impairs the right ventricle's output and its capacity to function effectively under increased afterload **[41, 44].**

Several researches primarily investigate the immediate treatment of pulmonary embolism, however, there may be a lack of comprehension of the long-term consequences linked to chronic RVD. This research aims to provide insights into the long-term prognostic consequences of persistent RVD beyond the immediate period after PE.

Current risk prediction models for recurrent thromboembolic events may not sufficiently include the influence of chronic RVD. This work has the potential to enhance the advancement of risk stratification models by including persistent RVD as a prognostic feature.

The study showed statistically significant differences between groups regarding recurrent DVT (P=0.004). There is a relationship between recurrent DVT and RVD following PE that stems from the fact that both conditions have a common underlying condition known as venous thromboembolism **[45].** People who have experienced many episodes of DVT are at a greater risk of experiencing pulmonary embolism in the future, which can lead to malfunction in the right ventricle of the heart **[46].** On the other hand, individuals who develop DVT after having a PE may be at risk for persistent venous thrombosis, which raises the probability that they may encounter repeated DVT. As an additional point of interest, the development of recurrent DVT and RVD after a PE is associated with increased rates of illness and mortality. This highlights the need of identifying venous thromboembolic events in a timely manner and treating them in the appropriate manner during emergencies.

Mortality and long-term morbidity are linked to recurrent venous thromboembolism (VTE), also known DVT and PE [**47].** On the other hand, anticoagulation increases the danger of potentially fatal bleeding **[48**]. To target awareness and prevention initiatives to the appropriate patients, it is critical to identify which patients are most at risk of developing a VTE recurrence. The conditions surrounding a VTE occurrence are crucially important: were risk factors present, and if so, what kind of risks were they and were they persistent? These risk variables are crucial when deciding how long to take anticoagulation.

A recent systematic review found that the rates of VTE recurrence at 24 months were 3.3% (95% CI, 2.8–3.9), 0.7% (95% CI, 0-1.5), 4.2% (95% CI, 2.8–5.6), and 7.4% (95% CI, 6.5-8.2) per patient year for people with a transient risk factor, a surgical risk factor, a nonsurgical risk factor, and VTE that wasn't caused by surgery, in that order **[49].** The European Society of Cardiology (ESC) **[50]** and the International Society on Thrombosis and Haemostasis (ISTH)1 have made guidelines that help group VTE risk factors into groups. VTE is a condition that can be caused by various short-term and long-lasting risk factors. Major transient or reversible RF events have a higher chance of the first VTE event, with a low chance of recurrence (<3%/year). Short-term or reversible factors, such as minor surgery, serious sickness, estrogen therapy, pregnancy, or leg injury, have a 10-fold higher chance of VTE (intermediate chance of recurrence (3-8%/year). Long-lasting risk factors include active cancer, at least one previous VTE episode without a major short-term or reversible factor, antiphospholipid antibody syndrome, and ongoing nonmalignant conditions. These factors have a high chance of recurrence (>8%/year). This classification helps divide VTE patients into groups based on their chance of recurrence, ensuring they receive the best care and management **[51].**

The research aims to resolve issues around the most effective anticoagulant methods for persons with chronic RVD. There is uncertainty about whether particular modifications to anticoagulation regimes or duration are necessary to reduce the risk of recurrent thromboembolic events in this group. This work has the potential to address the lack of understanding of the fundamental processes that cause recurrent RVD. It might investigate causes such as inflammation, endothelial dysfunction, or other pathophysiological mechanisms that lead to the continued deterioration of the right ventricle. The research intends to fill up the gaps in knowledge by providing vital information that may improve the understanding and treatment of patients who have persistent RVD after experiencing acute pulmonary embolism. This information may have ramifications for risk assessment, treatment options, and patient outcomes.

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