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ACUTE PULMONARY THROMBOEMBOLISM AND ITS CORRELATION WITH SPECIAL REFERENCE TO RIGHT VENTRICULAR FUNCTION

Cardiology

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ABSTRACT

Objective: Venous thromboembolism (VTE) is a disease spectrum that includes everything from deep venous thromboembolism (DVT) of the extremities to massive pulmonary thromboembolism (PE), both of which are associated with high morbidity and mortality if left untreated. We correlated patients having acute PE with right ventricular (RV) function. **Methods:** A prospective study was carried out on all the cases who were above 18 years of age and were having demonstrable thrombus in pulmonary artery. RV function (multiple parameters) was evaluated by means of Echocardiography which can help to prognosticate the disease as well. **Results:** Total 50 patients underwent Echocardiography. The mean age of the patients was 48.73 ±15.85 years, majority 37 (74%) below the age of 60 years. There were 30 (60%) males and 20 (40%) females with ratio of 1.5:1. 3 (6%) and 2 (4%) patients had diabetes and hypertension respectively. 13 were smokers, 5 had history of COVID, 4 had recent surgery, 3 had thrombosis, 2 each had RA, malignancy, hypothyroidism & DVT and 1 each hyperhomocysteinemia and sepsis. There was positive association of TAPSE with FAC (p=0.005) and ratio of RV E/A (p=0.049). TDI (Tissue Doppler Imaging) was found to be negatively associated with ratio of RV/LV (p=0.004) and RV E '(p<0.001). RVEDD was negatively associated with FAC (p=0.015) & RV S '(p=0.045) and positively associated with ratio of RV/LV (p<0.001). Ratio of RV E/A was positively associated with E '(p=0.006). **Conclusion:** Parameters of RV dysfunction other than TAPSE (Tricuspid Annular Plane Systolic Excursion) are statistically correlated and can help to point to a diagnosis of PE even if the gold standard test of CTPA is not available.

KEYWORDS

CT pulmonary Angiogram, Echocardiography, Pulmonary thromboembolism, Tricuspid Annular Plane Systolic Excursion, Venous thromboembolism

1. INTRODUCTION

PE occurs when a thrombus from lower or upper extremities blocks blood flow in the pulmonary artery or its branches. When a piece of the thrombus breaks off and enters the pulmonary circulation, PE occurs.[1,2] Despite its high mortality, acute PE is an underdiagnosed and under recognized condition. "The Great Masquerader" is how PE is known. Because the symptoms, signs, and investigations required to support the diagnosis are relatively nonspecific, diagnosis is difficult. Despite advancements in the diagnosis and treatment of this condition, there are disparities in rates and clinical outcomes around the world. The key to a successful outcome is early diagnosis and aggressive management. 10% of symptomatic PE patients die within the first hour, and hospital mortality from untreated PE can be reduced from 30% to nearly 8% if treated properly.[3]The landmark trials PIOPED I and II (Prospective Investigation of PE Diagnosis) looked at the clinical characteristics of patients with mild to severe PE.[4] Right ventricular (RV) function appears to be an important prognostic indicator in patients who are clinically stable. Transthoracic Echocardiography (TTE) can detect RV dysfunction in up to 30% of normotensive PE patients. When compared to normotensive patients without RV dysfunction, those who have RV dysfunction but no hemodynamic compromise have a two to tenfold higher risk of short-term death.[5-7] As the cycle of elevated afterload, RV dilation, tricuspid insufficiency, and RV hypokinesis unfolds, the onset of RV failure can be delayed by 12 to 48 hours. The goal of this study was to evaluate the clinical profile of patients with acute PE and to correlate and evaluate RV dysfunction in PTE patients using TTE.

2. METHODS

2.1 Study design and population

The present study was conducted in Department of Cardiology, Bharati Vidyapeeth (DTU) Medical College Hospital and Research Centre, Pune. It was a prospective observational study including cases with age over 18 years of either gender. Cases who demonstrated thrombus in pulmonary artery by CT pulmonary Angiogram (CTPA) from March 2020 to March 2022 were obtained from patients in the Cardiology OPD and Ward. RV function (multiple parameters) was evaluated by means of Echocardiography which helped to prognosticate the disease as well. Ethics committee approval was obtained from Institutional Ethics committee.

2.2 Definitions

Fractional area change (FAC)(Figure 1A) - Its measured by tracing the RV endocardial border manually from the lateral tricuspid annulus to the apex, then back along the interventricular septum to the medial tricuspid valve annulus in end-diastole and systole.[8]

FAC=(RV Area diastole−RV Area systole)/RV Area diastole×100. RV FAC ≥30% in males, or ≥35% in females, is considered normal

Tricuspid annular plane systolic excursion (TAPSE) (Figure 1B) - Measured after placing M-mode on lateral leaflet of tricuspid valve. Using the leading-edge to leading-edge technique, the measurement should be a vertical line. A measure of RV systolic function over time, TAPSE 1.7 cm is strongly associated with RV systolic dysfunction.[9]

RV/LV basal diameter ratio -
At the end of diastole, the measurement is taken. RV dilatation is indicated by a ratio greater than one at end-diastole (Figure 1D).

RV S′ (Figure 1C)
S wave velocity ≥9 cm/s indicates normal RV long axis systolic function.[10]

RV E′ and A′ (Figure 1C)
E′ <8 cm/s and A′ <7 cm/s are abnormal. An E/e′ >6 suggests elevated RA pressure.[9]

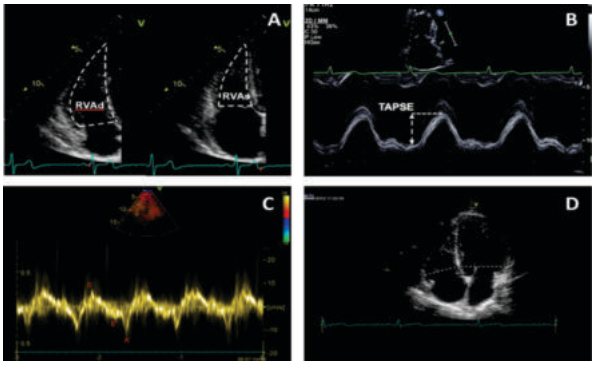

Figure 1: A. RVAd- RV area (in end diastole), RVAs- RV area (in end systole) ; B. Dotted vertical line adjacent to slope measured after placing M-mode in direction of lateral tricuspid valve ; C. Measurement of RV S', E', A' after placing tissue doppler and pulse wave over tricuspid valve; D. view depicting RV and LV base diameter in end diastole

2.3 Statistical Analysis

The collected data was coded and entered in Microsoft Excel sheet. The data was analysed using SPSS (Statistical Package for Social Sciences) version 25.0 software. The results were presented in tabular and graphical format. For Qualitative data various frequencies and percentages were calculated. Chi-square test / Fisher's exact test was used to find the association between 2 or more attributes for qualitative data variables. For Quantitative data Mean ± SD was calculated. Unpaired t-test was used to compare the 2 independent group for Quantitative data variables. ANOVA test was used to compare the 2 or More independent group for Quantitative data variables. P-value < 0.05 considered as significant.

RESULTS

The present study was carried out to study the clinical profile in patients who present with acute pulmonary thromboembolism with special reference to right ventricular dysfunction. Total 50 patients who demonstrated thrombus in pulmonary artery by CT pulmonary Angiogram (CTPA) or 2D Echo were included. The mean age of the patients was 48.73 ± 15.85 years, with majority i.e. 37 (74%) below the age of 60 years. There were 30 (60%) males and 20 (40%) females with male:female ratio of 1.5:1. Among all the patients 3 (6%) and 2 (4%) patients had diabetes and hypertension respectively. The results are depicted in table 1.

Table 1: Baseline characteristics

		N	%
Mean age (in Years)	48.73 ± 15.85		
Age	<60	37	74
	≥60	13	26
Gender	Male	30	60
	Female	20	40
Comorbidities	Diabetes	3	6
	Hypertension	2	4

Out of 50 patients 13 were smokers, 5 had history of COVID, 4 had recent surgery, 3 had thrombosis, 2 each had RA, malignancy, hypothyroidism & DVT and 1 each had hyperhomocysteinemia and sepsis (Figure 2B). The parameters for prediction of RV dysfunction including tricuspid annular plane systolic excursion (TAPSE), RV E to E prime (E/E') ratio by TDI, right-ventricular end-diastolic diameter (RVEDD), left-ventricular end-diastolic diameter (LVEDD), ratio of RVEDD/LVEDD, fractional area change (FAC) etc. were measured and their mean ± SD values are reported in table 2.

Table 2: Descriptive statistics of parameters for evaluation of RV dysfunction

	Mean	SD
TAPSE (mm)	14.36	4.30
TDI (E/E')	7.63	2.34
RVEDD	42.40	4.28
LVEDD	38.78	4.58
PASP (mmHg)	52.98	18.53
FAC (%)	18.45	9.45
RV/LV	1.09	0.17
E' (m/s)	0.08	0.03
S' (cm/s)	8.74	2.17
E/A	0.87	0.47
PAT (ms)	69.06	22.65

The patients were distributed as per the cut off points of the parameters for prediction of RV dysfunction, almost all the patients 49 (98%) had abnormal FAC (cut off value of <35%), followed by 46 (92%) with abnormal RVEDD values (cut off value of >39), 44 (88%) with abnormal TAPSE (cut off value of <17 mm), 42 (84%) with abnormal ratio of RV E/E' (cut off value of >6), 40 (80%) had abnormal ratio of RV/LV (cut off value of >1), E/A was abnormally distributed among 37 (74%) patients, while troponin I with cut off value of 0.04 was abnormally high in 30 (60%) patients. The distribution of patients according to presence of parameters for RV dysfunction is shown in Figure 2A. Among the 9 parameters evaluated for prediction of RV dysfunction, all were positive among 5 (10%) patients, while majority i.e. 16 (32%) of patients had 8 parameters out of cut off values, followed by 10 (20%) patients with 7 parameters, 9 (18%) with 6, 8 (16%) with 5 and only 2 (4%) with 4 parameters positive. The distribution of patients as per the number of parameters positive for prediction of RV dysfunction is indicated in Figure 2C. The association between the predictive parameters for RV dysfunction among the patients with pulmonary thromboembolism was studied by means of Pearson's correlation coefficient. The evaluation revealed positive association of TAPSE with FAC (p=0.005) and ratio of RV E/A (p=0.049). TDI was found to be negatively associated with ratio of RV/LV (p=0.004) and RV E' (p<0.001). RVEDD was negatively associated with FAC (p=0.015) & RV S' (p=0.045) and positively associated with ratio of RV/LV (p<0.001). Ratio of RV E/A is positively associated with E' (p=0.006). The association between the prediction parameters is shown in table no.3, with respective 'r' and 'p'values.

Table 3: Association among the prediction parameters of RV dysfunction

		r	p value
TAPSE	FAC	0.391	0.005
	E/A	0.280	0.049
TDI	RV/LV	-0.400	0.004
	E'	-0.493	<0.001
RVEDD	FAC	-0.341	0.015
	RV/LV	0.525	<0.001
	S'	-0.285	0.045
E/A	E'	0.384	0.006

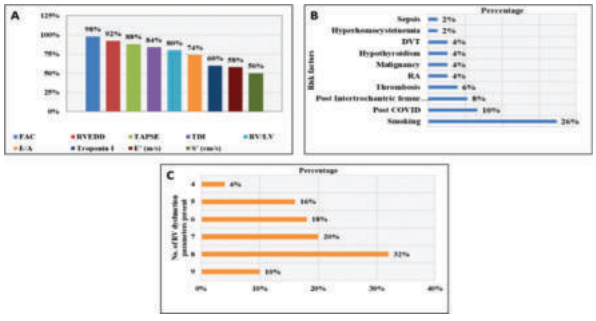

Figure 2. A. Distribution of parameters for evaluation of RV dysfunction; B. Risk factors; C. Distribution of patients with number of risk factors present

DISCUSSION

Despite modern diagnostic and treatment methods, PE still has a high three-month mortality rate. Seventy-five percent of the deaths occurred during the first hospitalization for PE. These deaths are almost certainly the result of recurrent PE, which could be reduced if more intensive anticoagulation was used.[11] A total of 50 patients were included in the study if CT pulmonary Angiogram (CTPA) revealed thrombus in the pulmonary artery. Indians appear to have a higher risk of developing PE at a younger age, especially massive PE, and have a higher mortality rate. In this study, we found that the mean age of the patients with pulmonary thromboembolism was 48.73 ±15.85 years as opposed to above 65 years as seen in the Western population.[12,13] Our findings are consistent with those found in the Arrive registry, which is one of the largest VTE studies in India.[14] The average age of presentation was 52 years in a recent trial in South India.[15] Miniati M et al.[16] found a significantly higher incidence of acute PE cases in patients over the age of 65 in another study. In contrast to our study, a similar study conducted in India found that the average age (39 12.1 years) was lower.[3]

There were 30 (60%) males and 20 (40%) females with male:female ratio of 1.5:1. Among all the patients 3 (6%) and 2 (4%) patients had diabetes and hypertension respectively. The majority of patients had at least one PE risk factor, highlighting the importance of looking for a risk factor in every patient with acute PE. It was discovered that each study had a unique risk factor for acute PE.[17,18] In present study smoking was the major risk factor for acute PE and was found in 13 (26%) of the patients. 5 (10%) had history of COVID, 4 (8%) had recent surgery, 3 (6%) had thrombosis, 2 (4%) each had RA, malignancy, hypothyroidism & DVT and 1 (2%) each had hyperhomocysteinemia and sepsis. In a study by Klok et al, 61% of the study cohort confirmed a smoking history (current or previous) at the time of PE diagnosis.[19] Cheng YJ et al [20] discovered in another meta-analysis that ever smokers had a 17 percent higher risk of developing PE. This could be due to the fact that smoking increases the risk of DVT, but DVT was only diagnosed as the primary cause of PE in 4% of patients. Any patient with unexplained or new-onset dyspnea, chest pain, palpitations,

syncope, or unexplained hypotension should be suspected of PE.[21] The RV dysfunction was assessed in this study using echocardiography to measure the right ventricular end-diastolic dimension (RVEDD) and tricuspid annular plane systolic excursion (TAPSE). TAPSE is an echocardiographic measure of global RV function that has been shown to have prognostic value in patients with myocardial infarction and pulmonary hypertension.[22,23] Forfia PR et al [24] previously demonstrated the value of TAPSE as a highly sensitive and specific parameter reflecting RV global function in non-surgical patients with chronic pulmonary hypertension. TAPSE had a mean value of 14.36 mm in our study (1.43 cm). Our findings are similar to those of Vitarelli A et al. [25], who found that TAPSE in patients with PTE was 1.5 cm. Gromadziński L et al [26], on the other hand, discovered a lower TAPSE value of 1.45 cm in patients with pulmonary thromboembolism, but no significant difference when compared to patients without pulmonary thromboembolism (1.63 cm). The patients were distributed as per the cut off points of the parameters for prediction of RV dysfunction, almost all the patients 49 (98%) had abnormal FAC (cut off value of <35%), followed by 46 (92%) with abnormal RVEDD values (cut off value of >39), 44 (88%) with abnormal TAPSE (cut off value of <17 mm), 42 (84%) with abnormal ratio of E/E'(cut off value of >6), 40 (80%) had abnormal ratio of RV/LV (cut off value of >1), E/A was abnormally distributed among 37 (74%) patients, while troponin I with cut off value of 0.04 was abnormally high in 30 (60%) patients. Majority 16 (32%) of patients had presence of 8 parameters abnormal, followed by 10 (20%) patients with 7 parameters out of nine parameters evaluated, while all 9 were positive among 5 (10%) patients, while minimum 4 were positive among only 2 (4%) patients. After a 19-month follow-up period, Forfia PR et al [24] found that a TAPSE of less than 18 mm was associated with a nearly fourfold increased risk of death in medical patients with pulmonary hypertension (TAPSE mean =11.7 mm). In present study we confirm that TAPSE correlates well with RVFAC and ratio of E/A in patients with pulmonary embolism. Our findings in patients with acute pulmonary thromboembolism are consistent with those of Lopez-Candales A et al [27], who found a strong link between TAPSE and reduced RVFAC in patients undergoing routine transthoracic echocardiographic (TTE) examinations for a variety of clinical reasons. Schmid E et al.[28] reported similar TAPSE results to those of the current study. Our results indicate that TV annulus TDI (E/E') in patients with PTE was 7.63 ±2.34. TDI (E/E') was found to be negatively associated with ratio of RV/LV and E'. The systolic and diastolic tricuspid annular velocities were significantly lower in patients with PTE than in healthy controls, according to some studies.[29,30] The mean values of LVEDD and RVEDD in our study was reported to be 38.78 ±4.58 mm and 42.40 ±4.28 mm respectively, and RVEDD was found to be negatively associated with FAC & S'and positively associated with ratio of RV/LV. Ratio of E/A is positively associated with E'. Shahabi J et al [31] reported a lower RVEDD value of 3.41 ±0.09 cm in patients with pulmonary thromboembolism and 3.02 ±0.12 cm in controls, with significant differences in mean values between the groups. RVEDD was found to be positively associated with RVESD (Right ventricular end-diastolic diameter), RV fractional shortening, and negatively associated with the RV/LV ratio and PACTOIR in their study. As the present study was a cross-sectional single group observational study, without a control group, parameters of RV dysfunction including TAPSE, FAC etc. in the present study were compared with other epidemiological studies in the literature. The results of present study were comparable to literature regarding TAPSE, but the other markers of RV dysfunction including TDI, E', S' etc. are not studied by many researchers.

CONCLUSION

This study concluded that parameters of RV dysfunction other than TAPSE are statistically correlated and can help to point to a diagnosis of PE even if the gold standard test of CTPA is not available. Of course, all this is relevant in the presence of clinical features.

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