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Research Article

Impact of tenecteplase in intermediate and high risk pulmonary embolism

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ABSTRACT

Background: Pulmonary embolism (PE) is a 3rd most common lethal cardiovascular disease. The objective was to study the outcome of high and intermediate risk acute pulmonary embolism (PE) with special reference to Tenecteplase.
Methods: Retrospective observational study of clinical features and outcome of high and intermediate risk patients with acute pulmonary embolism treated with Tenecteplase from January 2008 to January 2016.
Results: 40 patients who were newly diagnosed to have PE with a mean age of 54 years were included in the study. Dyspnea and syncope were the predominant symptoms in both IR and HR. Most sensitive parameter i.e. D-dimer was positive among all 40 cases but cardiac biomarker troponin was positive in 56.8% cases only. Evidence of RV dysfunction was present all cases with 65% cases had presented with severe pulmonary arterial hypertension. Diagnosis of acute pulmonary embolism was confirmed by MDCT of lung. All confirmed cases of acute PE were administered dose adjusted intravenous tenectaplse. Of the 40 patients, 39 were discharged and were under regular follow up for 6 months. In hospital mortality of HR and IR 11% &3.2% respectively but 2 more cases expired within a span of 7 days after discharge due to sepsis and neurological shock. Major bleeding manifestations more in HR as compared to IR group.
Conclusions: Tenectaplase is a potent thrombolytic agent which can be used as the drug of choice for acute PE of usual causes without many complications. Prompt diagnosis and treatment of PE with potent thrombolytics can be life-saving.

Keywords: Acute pulmonary embolism, High risk, Intermediate risk group, Tenecteplase

INTRODUCTION

Pulmonary embolism (PE) is a 3rd most common lethal cardiovascular disease. Most patients who succumb to PE do so within few hours of the event. Ten percent of PE is fatal in the first hour.[1] Annual incidence of PE is around 100-200/lakh PE can be asymptomatic. But its diagnosis may be an incidental finding in 34% cases of SCD. Only 7% of the patients who die early with PE are confirmed cases of PE before death.

Major anatomical characterization of acute PE is into central or peripheral, depending on the location or the arterial branch involved. The central vascular zones include the main pulmonary artery, the left and right main pulmonary arteries, the anterior trunk, the right and left interlobar arteries, and lobar arteries. Peripheral vascular zones include the segmental and sub-segmental arteries. Clinical signs and symptoms for PE are nonspecific; therefore, patients suspected of having PE due to unexplained dyspnea, tachypnea, or chest pain. CT pulmonary angiogram (MDCT) is the gold standard

investigation of choice for early diagnosis and prompt treatment of PE. Although there are rapid advancements in the diagnosis and management of PE, it is rarely being reported. Most of the reports are limited to case reports, series and autopsy.[2] It is for the first time such a large trial from India studying in hospital outcomes, mortality and morbidity benefits in confirmed cases of intermediate and high risk acute PE after Tenecteplase.

METHODS

Patients admitted with acute PTE at institute from January 2008 to January 2016 were selected for retrospective study. All patients diagnosed as acute PE who had no previous history of PE no pre-existing cardiac or pulmonary disease. Analysis of clinical presentation, investigation and management with Tenecteplase was done. A patient was diagnosed to have PE if there is evidence of thrombus in CT pulmonary angiogram (MDCT).

Inclusion criteria

- All High and intermediate risk acute pulmonary embolism who had no contraindications for use of Tenecteplase.

Exclusion criteria

- All High and intermediate risk acute pulmonary embolism who had contraindications for use of Tenecteplase.
- Low risk acute pulmonary embolism (no indication for use of Tenecteplase).
- Age less than 18-years.

Patients with PE were classified as high risk (massive) if there was evidence of hemodynamic compromise (defined as systolic BP <90 mmHg) and as intermediate risk (submassive) if there was right ventricular dysfunction on echocardiography with no hemodynamic compromise. Patients without any evidence of these features were labeled as low risk PE. D-dimer testing was done using enzyme linked fluorescent assay. The normal value is 0-500 ng/ml. Any value greater than 500 ng/ml is considered positive. Troponin I was done using electro-chemiluminescence method and a value greater than 0.03 was considered abnormal. Echocardiogram was done using GE machine VIVID. Pulmonary arterial pressure was calculated by TR jet velocity using Bernoulli's method (P=4v2) and RV function was assessed by eyeball method.

Pulmonary hypertension was categorized as mild, moderate, or severe based on pulmonary artery systolic pressures (mild: 40-45 mmHg, moderate: 46-60 mmHg, or severe >60 mmHg). CT pulmonary angiogram was done using GE 64 slice CT scanner. Apart from routine blood counts, hematological profile, all patients had a protein C, S values, antithrombin III, antiphospholipid antibody and homocysteine levels. Thrombolytic therapy with intravenous Tenecteplase bolus of 30/40 mg/kg was administered for diagnosed cases.

Statistical analysis

All the variables were expressed as mean standard deviation (SD). Skewed variables were also expressed as median. For paired data, student's t-test was used to determine the significance of differences in RV function parameters pre- and post-lysis. Echocardiographic inter-observer variability was assessed by two persons one of them being blinded. There was minimum inter observer varability in entire course of study. For variables, which were not normally distributed, Wilcoxon signed rank test was used. The differences in means of the parameters between patients with IR and HR were analyzed using unpaired student's t-test for normally distributed variables and Manne Whitney U-test for skewed variables. A p-value of 0.05 was considered statistically significant. Statistical analyses were done by using software was R 3.2.

RESULTS

40 patients who were newly diagnosed to have acute pulmonary embolism were included in the study. Out of the 40 patients 31 were intermediate risk (IR) and 9 were from high risk group (HR).Their mean age was 54 years. Among 40 patients, 14 (37.2%) were males and 26 (62.8%) were females. Average age in HR and IR were 48.44±21.02 and 55.65±12.80 respectively.

Table 1: Baseline parameters.

Baseline characters	IR (31)	HR (9)	p-value
Family history	1 (3.2%)	1 (11.1%)	0.381
Smoking	1 (3.2%)	0	0.472
Obesity	13 (41.9%)	4 (44.4%)	0.894
HTN	9 (29%)	3 (33.3%)	0.806
DLP	6 (19.4%)	1 (11.1%)	0.550
Sx GA	7 (22.6%)	2 (22.2%)	0.982
Sx SA	4 (12.9%)	2 (22.2%)	0.507
Immobilisation	2 (6.5%)	0	0.306
OCP	4 (12.9%)	0	0.141
HRT	3 (9.7%)	0	0.206
Malignancy type	2 (6.5%)	0	0.306
Malignancy AC	3 (9.7%)	0	0.206
Malignancy NONAC	1 (3.2%)	0	0.472

Out of 40 patients, 15 (37.5%) patients developed pulmonary embolism following surgical procedure of which (60% under general anaesthesia (GA) rest via spinal anaesthesia (SA). 17 cases had documented obesity 13 from IR group and remaining 4 from HR. 2 patients of IR group had a history of immobilization for a minimum of 2 weeks, 3 patients had carcinoma, 2 patients had

confirmed homocystenimia, 3 cases had hypothyroidism (Table 1). Most predominant blood group was B-positive.

The most common clinical presentation was dyspnea followed by syncope in both IR and HR group. The other major symptom is being pleuritic chest pain. Cardiac arrest occurred in 2 patients as the presenting symptom in high risk group (Table 2). The mean duration of symptom onset to hospitalization was 6.2 days. Although tachypnea followed by tachycardia were the predominat signs and equally present in both IR and HR group. Syncope was a significant sign in HR group which occurred as major independent predictor of mortality in the study.

Table 2: Distribution of cases according to ECG findings.

ECG findings	Group		p-value
	Intermediate risk (31)	High risk (9)	
ECG ST	5 (16.1%)	2 (22.2%)	0.679
ECG AF	0	1 (11.1%)	0.080
ECG S1Q3T3	9 (29%)	3 (33.3%)	0.806
ECG RBBB	2 (6.5%)	4 (44.4%)	0.010
ECG QR in V1	7 (22.6%)	0	0.046

D-dimer was positive in all 40 patients. Mean d-dimer was 5965±2504 ng/ml and 6822±2749 ng/ml in IR and HR group respectively which was done immediately as an early sensitive index of pulmonary embolism but statistically insignificant. Among 40 patients, 24 (68.5%) had positive troponin values.

Predominant electrocardiographic (ECG) was S1Q3T3 pattern was seen in 29%in IR group and 33% in high risk group and RBBB (44.4%) in HR group which was statistically significant (Table 2). Major sign in chest x-ray was wedge shaped opacity in 77.8% cases of HR group (p-0.057), while normal in 54.8% cases of IR group (Table 3).

Table 3: Distribution of cases according to chest radiographic findings.

Chest x-ray	Group	
	Intermediate risk (31)	High risk (9)
Normal	17 (54.8%)	2 (22.2%)
WO	11 (35.5%)	4 (44.4%)
PE	1 (3.2%)	2 (22.2%)
W/P	2 (6.5%)	1 (11.1%)

Echocardiography showed RV dilatation in all patients (Figure 1). 65% of patients in the study had severe pulmonary artery hypertension (PAH) (Figure 2). Although all cases in HR group had severe PAH, only 54.8% cases of IR group had severe PAH (p 0.018).

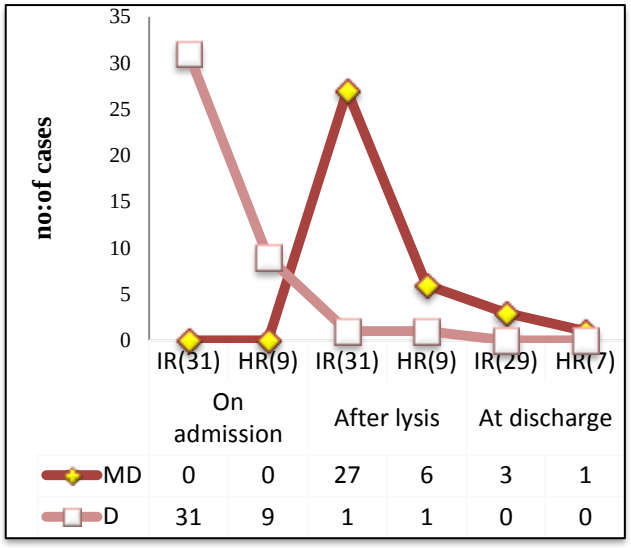

Figure 1: Distribution of cases according to RV dilation.

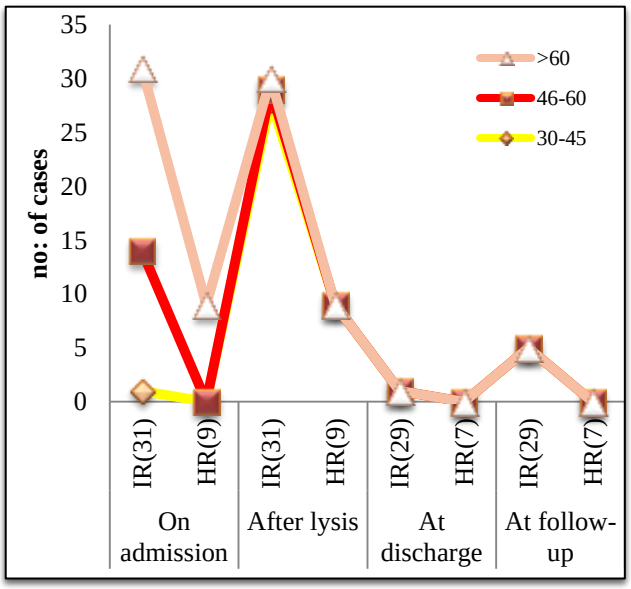

Figure 2: Distribution of cases according to pulmonary artery pressures.

CT pulmonary angiogram was done in all patients. Among 40 patients who underwent CTPA, 75% had bilateral massive pulmonary thrombus, rest of 25% had unilateral thrombus (Figure 3). Weight adjusted dose of Tenecteplase was given in all confirmed cases of acute PE. One patient underwent intravenous and catheter directed thrombolytic with Tenecteplase. Post thrombolysis, all patients were treated with LMWH and oral anticoagulants.

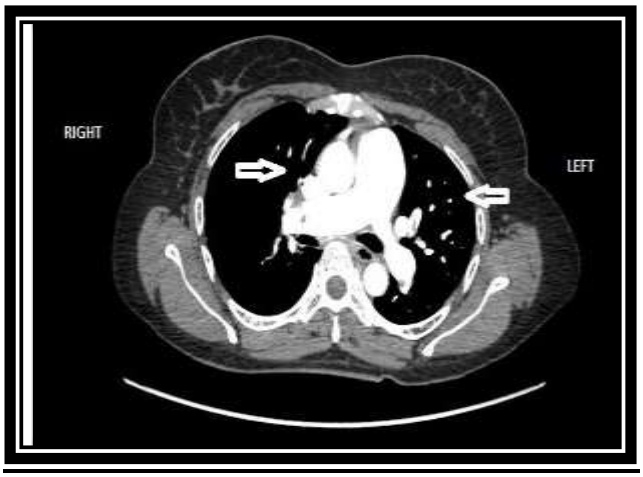

Figure 3: CT pulmonary angiography showing partial filling defects in right pulmonary artery extending into right and left segmental pulmonary arteries.

Major primary outcome studied was mortality which was 10% (both IR and HR). Mortality data suggested that 6.5% in IR and 22.2% in HR scummed to death. Although in hospital mortality in HR and IR was11% and 3.2% respectively. Fatal bleeding after thrombolysis occurred in 3 patients. Survival was better in IR group (93.5%) as compared to HR group (77.7%) which was statistically significant. In present study 84% and 55.5% cases in IR and HR group respectively had no major complication immediately after lysis, at discharge and during follow up and was statistically significant. Clinical symptomatic improvement was noticed in majority of patients with 90.3% improvement in dyspnea.

Assessment of echocardiographic improvement was done immediately, post lysis, at discharge and after 6 months. In the study we assessed pulmonary artery pressures (PAP) and RV dilatation. Severe pulmonary artery hypertension (PAH) with significant RA/RV dilation was seen in all cases of high risk PE while only in 54.8% cases in IR group on admission. The mean pulmonary artery pressures in IR and HR group on admission, after lysis, at discharge and follow up was 61.62 mmHg, 40.25 mmHg, 30.31 mmHg, 30.63 mmHg respectively which was statistically significant. IR group patients in the present study who had moderate to severe PAH (97.6%) improved within 24 hours with only mild PAH (90.3%) as compared to all HR group (100%) who had mild PAH after lysis. In present study IR group patients had mild RV dilatation in 87.1%, 10.3% cases as compared to HR group 66.7%, 14.3% cases respectively after lysis and at discharge.

DISCUSSION

Pulmonary embolism presents with a wide clinical spectrum from asymptomatic disease to life threatening High risk (massive) PE that causes hypotension and cardiogenic shock.[2,8]

Right ventricular failure due to pressure overload causes death in severe PE. PAP increased >30-50% total cross-sectional area of the pulmonary artery when it is occluded. PE-induced vasoconstriction, mediated by the release of thromboxane A_2 (TXA_2) and serotonin (STS), contributes to the initial increase in PVR proportional decrease in arterial compliance. Increase in PVR results in RV dilation, which alters the contractile properties of the RV myocardium via the Frank-Starling mechanism. Increase in RV pressure and volume leads to an increase in wall tension and myocyte stretch. RV contraction time is prolonged, while neurohumoral activation leads to inotropic and chronotropic stimulation. The prolongation of RV contraction time into early diastole leads to leftward bowing of the IVS. LV filling is impeded in early diastole, and this may lead to a decrease in CO and contribute systemic hypotension and haemodynamic instability. Together with systemic vasoconstriction, these compensatory mechanisms increase pulmonary artery pressure, improving flow through the obstructedpulmonary vascular bed and thus temporarily stabilize systemic blood pressure (BP) (Figure 4).[3] The extent of immediate adaptation is limited, since a non-preconditioned, thin-walled right ventricle (RV) is unable to generate a mean pulmonary artery pressure above 40 mmHg. As a result, left ventricular (LV) filling is impeded in early diastole, and this may lead to a reduction of the cardiac output and contribute to systemic hypotension and haemodynamic instability.[4]

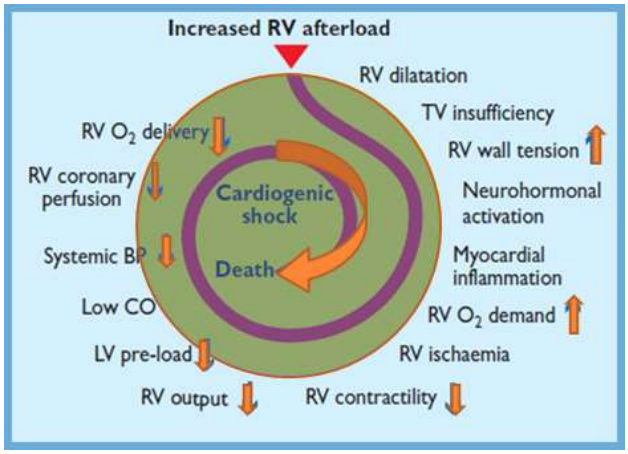

Figure 4: Pathophysiology of acute pulmonary embolism.[5]

The clinical presentation and the investigations including electrocardiography, chest radiography and analysis of arterial blood gases cannot be relied on to confirm or rule out PE because of lack of adequate specificity. Clinically pulmonary embolism is classified as massive PE (5-10%), sub massive PE (20-25%) and small-moderate PE (70%) (Table 4).[5]

Age is a statistically significant univariate predictor for PE. The frequency and recurrence of PE is increased in elderly patients but in our study mean age group was 54 years. In previous reported studies male predominance

was documented as compared to our study in which females 26 (62.8%) population was the dominating group.[8]

Table 4: Classification of pulmonary embolism as per esc guidelines 2014.[5]

Clinical class	Clinical indicators for diagnosis
Massive PE	Hypotension/RV dysfuntion/elevated biomarkers
Submassive PE	RV dysfuntion/elevated biomarkers
Small to moderate PE	Elevated biomarkers

Predisposing factors for venous thromboembolism and pulmonary embolism are well recognized. Usually predisposing factors are present in almost 96% of patients with confirmed venous thromboembolic disease.[6] There are 2 types of predisposing factors for pulmonary embolism namely provoked (temporary or reversible risk factors) and unprovoked (permanent or irreversible risk factors). Provoked predisposing factors are surgery, trauma, immobilization, pregnancy (*in-vitro* fertilization), oral contraceptive use, hormone replacement therapy, infections, blood transfusion, children due to indwelling catheter.[7,8] The most common risk factors in our patients was post-operative cases (15/40) and cases with obesity (17/40). Although maximum post-operative cases (44%) were from high risk group as compared to IR group. It is believed that diagnosis of PE is more difficult and debatable. Clinical suspicion of this PE is of paramount importance in guiding diagnostic testing.

Major clinical features include dyspnea, syncope (indicate massive PE), pleuritic/substernal chest pain, cough, heamptysis, fever, unilateral leg pain and signs of DVT.[31,32] In the study the most common clinical presentation was dyspnea followed by syncope in both IR and HR group. The other major symptom is being pleuritic chest pain. Cardiac arrest occurred in 2 patients as the presenting symptom in high risk group. Pleuritic chest pain usually signifies that the embolism is located in the distal pulmonary arterial system, near the pleural lining. Unexplained dyspnea and chest pain are the most frequent symptoms, and sudden onset dyspnea and pleuritic chest pain are the most typical.[31] In this study HR/IR group both significant improvement in symptoms after thrombolysis with tenectaplase. ECG can be used as a clinical parameter for physicians towards diagnosis. While no isolated ECG abnormality is definitively associated with PE, certain group of ECG abnormalities has been shown to be specific. Various types of described associations include: normal ECG, sinus tachycardia, complete and incomplete RBBB, axis changes, ST segment and T-wave changes, S1Q3T3 pattern, P-pulmonale and atrial arrhythmias.[9,10] The most common ECG finding in the study was S1Q3T3 pattern and RBBB which was similar to previous literatures. The desynchronization of the ventricles may be exacerbated by the development of right bundle branch block.

It is a fact, however, that one cannot depend on chest x-ray for the diagnosis of pulmonary embolism. In the study, lung field was clear in most of the patient in intermediate risk group and wedge shaped opacity was predominately seen in high risk group which was statistically significant. Stein et al found that the most common chest X-ray finding was parenchymal abnormality.[9] D-dimer levels are elevated in acute thromboembolism and result from the lysis of cross-linked fibrin within the thrombus.[2] D-dimer levels may however be elevated in other conditions that not pathognomonic for thromboembolic disease. D-dimer testing has been reported to have a sensitivity approximately 100 percent.[11,12] However, such high sensitivity often comes at the cost of low specificity. Retrospective analysis of a sequential series of 376 patients revealed that no patient with D-dimer of <275 ng/ml was diagnosed with pulmonary embolism, irrespective of clinical probability.[12] The D-dimer test, irrespective of the sensitivity of the assay, cannot be specific in isolation. In this study D-dimer was positive in all patients. Elevated D-dimer concentrations were associated with increased short-term mortality while levels, <1500 ng/mL had a negative predictive value of 99% for excluding three-month all-cause mortality.[13]

Serum troponin I is sensitive but not a specific marker of cardiac myocardial inflammation or injury. They are elevated in acute coronary syndrome and myocardial injury. The stretching of the right ventricle from pressure overload found with HR or IR. PE causes the release of troponins. Right ventricular dysfunction or elevated troponin levels in acute PE patient can predict short-term adverse outcome.[14] It has been proposed by current ESC guidelines that patients in IR group with <1 sPESI score and having cardiac biomarkers positive should be managed with thrombolytics because these patients are then categorized as IR to HR PE cases. This was substantiated by our study in which 63% cases in IR group had TropI positive as compared to HR group who had only 33% cases with TropI positive which was statistically significant.

Major thrombus originate from deep veins of the legs, Doppler examination of lower limb veins is an investigation in the diagnosis of provoked PE. Compression venous ultrasound is positive in 10-20 percent of all patients without leg symptoms or signs who undergo evaluation and in approximately 50 percent of patients with proven embolism.[15] Compression venous ultrasound has its value in situations where there is a high clinical probability of PE and the patient has no past history of venous thromboembolism.

2D echocardiographic feature of PE are dilated pulmonary artery, dilated right atrium, right ventricular hypokinesis, right ventricular enlargement, reduced left ventricular size, McConnell's sign, flattening of the intraventricular septum or paradoxical septal motion, direct visualization of thrombus in the right heart or

pulmonary artery and distention of the inferior vena cava with loss of normal respiratory variation.[16] Echocardiography is a useful in identifying patients with right ventricular dysfunction, free floating thrombus and persistent pulmonary hypertension. So all patients were underwent echocardiography. Evidence of pulmonary arterial hypertension was found in all patients.

Perfusion scan has been used for almost three decades for the diagnosis of PE and is a valuable tool. Respiratory failure in PE is predominantly a consequence of haemodynamic disturbances.[17] Low cardiac output results in desaturation of the mixed venous blood. In addition, zones of reduced flow in obstructed vessels, combined with zones of overflow in the capillary bed served by non-obstructed vessels, result in ventilation-perfusion mismatch, which contributes to hypoxaemia. But approximately 30-70% of scans are nondiagnostic and the clinician is left in a diagnostic dilemma.[18] Perfusion scans are insensitive in patients with preexisting lung diseases, especially the chronic obstructive lung disease.[19]

The use of spiral CTPA is a major tool in the diagnosis of PE. The sensitivity and specificity for detection of PE by CTPA at the main, lobar and segmental levels are greater than 90% with accuracy decreasing when isolated subsegmental vessels are involved.[18]

All HR PE cases had RV dysfunction and severe PAH on admission which was attributed to the fact that there will be severe RV contractile dysfunction and multiple massive bilateral microthrombus dislodgement in various levels of pulmonary artery, thus a vicious cycle of RV begets RV will prevail leading on to severity and fatality of PE in these group of patients.[28] The combination of RV dysfunction on the echocardiogram (or CT angiogram) with a positive cardiac troponin test has poor prognosis.

The ACCP and ESC guidelines recommends thrombolytic therapy in PE with evidence of hemodynamic compromise, although with absolute contraindications in cases with major active bleeding manifestations.[5,29,30] Thrombolytic therapy of acute PE restores pulmonary perfusion more rapidly than with UFH alone.[20,21] Thus intiation of a major thrombolytic agent early in course of disease can be lifesaving preserving both RV function and gradually decreasing elevated pulmonary artery pressures.[21] The haemodynamic benefits of thrombolysis are confined to the first few days. Tissue plasminogen activator (tPA) has a short infusion time so recommended as one of the best thrombolytics. Major studies demonstrate the superiority of thrombolytic therapy with respect to the resolution of hemodynamic abnormalities within the first 24 hours; this advantage disappears 7 days after treatment. Overall, 90% of patients appear to respond favorably to thrombolysis, as judged by clinical and echocardiographic improvement within 36 hours.[22] As in our study 95% cases improved within first 36 hours both clinically and by echo. The greatest benefit is observed when treatment is initiated within 48 hours of symptom onset, but thrombolysis can still be useful in patients who have had symptoms for 6-14 days.[23] Most contraindications to thrombolytic should be considered relative in patients with life-threatening, high-risk PE. We had thrombolyzed 40 patients with tenectaplase with a mean duration of 3±1.5 hours.

A very few randomized clinical trials have demonstrated a clear morbidity or mortality benefits. Controlled clinical trials in IR, PE demonstrated benefits in terms of reduced mortality rates or earlier resolution of symptoms when compared with heparin as per PEITHO trial. There are 2 major multicentric trials in which thrombolytic agent was Tenecteplase used in IR PE cases. In Topcoat and Peitho trial in hospital mortality was 2.6% and 2.5% in IR group cases as compared to our study in which it was 3.2%.[26,27] Although there are only 3 single centric trials of which this study is the latest showing almost similar mortality rates as compared to previous trials in IR group. While the HR group was never compared alone in various other studies but the benefits of thrombolytic agents was shown in our study in 89% HR cases (Table 5).

The role of thrombolytic therapy in the management of acute PE will remain controversial especially in HR PE as compared to IR PE since there are only proper evidence based support for use of thrombolytics in latter group.

Table 5: Various studies comparing mortality with use of tenecteplase as thrombolytic agent.

Study	Group	Centre	No. of cases	In hospital mortality
PEITHO Trial[26]	IR/SMPE	Multicentre	1005	2.6%
TOPCOAT[27]	IR/SMPE	Multicentre	83	2.5%
Bhubaneswar et al[33]	IR to HR PE	Single centric	30	3.3%
Anand et al[34]	IR to HR PE	Single centric	41	2.4%
Thrudeep et al	IR PE	Single centric	31	3.2%
Thrudeep et al	HR PE	Single centric	9	11%

Thrombolytic treatment carries a risk of major bleeding, including intracranial haemorrhage. Analysis of pooled data from trials using various thrombolytic agents and regimens reported intracranial bleeding rates between 1.9% to 2.2%.[24,25,34] Out of 40 patients thrombolyzed one patient died due to massive IC bleed and 2.5% cases had major bleeding manifestations. Intracranial bleed was most predominant in HR (11%) as compared to IR (3.2%) group which was statistically significant. The cause of increasing risk of bleeding in our study was due to increasing age and the presence of comorbidities which have been associated with a higher risk of bleeding complications. The Peitho trial showed a 2% incidence of haemorrhagic stroke after thrombolytic treatment with tenecteplase in patients with IR-HR PE. Major non-intracranial bleeding events increased in the tenecteplase group, compared with placebo (6.3% versus 1.5%; P <0.001).[26]

A patient with first episode of PE occurring in the setting of reversible risk factors should receive warfarin therapy for 3-6 months. The ACCP guidelines recommend that all patients with unprovoked PE should undergo an evaluation to determine if long-term therapy is needed. Long term treatment is recommended for those patients who do not have risk factors for bleeding and in whom accurate anticoagulant monitoring is possible.[6] Patients who have provoked PE and pre-existing irreversible risk factors, such as deficiency of antithrombin III, protein S and C, factor V Leiden mutation, or the presence of antiphospholipid antibodies, should be given on long term anticoagulation. According to progress and inference of study has leads to possible algorithm for approach to such group of patients in near future and for establishing guideline based recommendations supported with evidence based large multicentric RCTs.

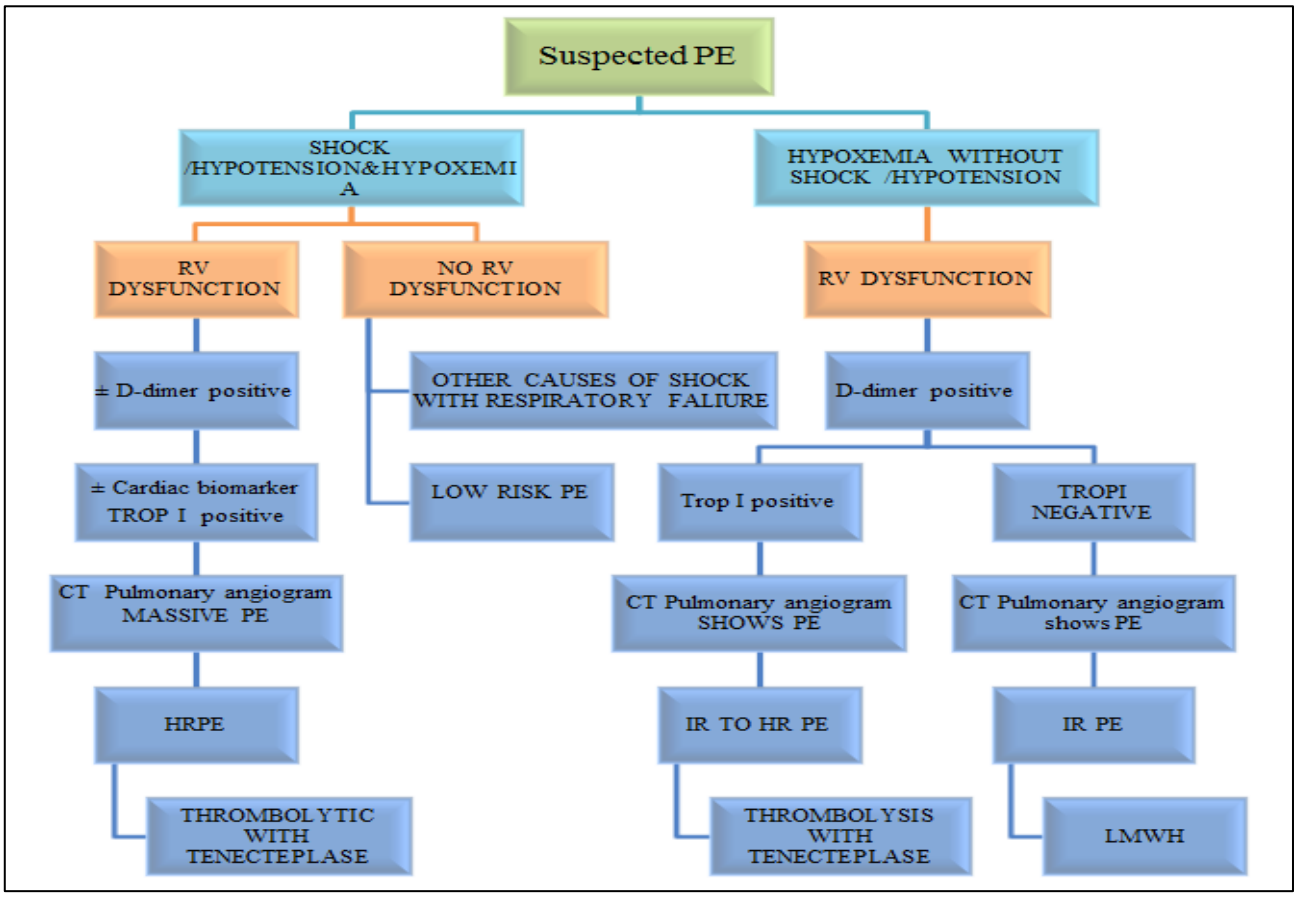

Figure 5: Proposed algorithm for management of acute pulmonary embolism.

Although the study was largest amongest the smallest but sample size was small, which is the main limitation of this study. To confirm these findings a study with larger sample size is required. Two dimensional RV imaging depend on adequate image quality, so suboptimal images in struggling patient with inter observer variability was a major issue in this study, although this percentage was small.

CONCLUSIONS

PE is a fatal clinical condition which is often masqueriding. The prompt uses of advanced imaging modalities are likely to improve the diagnosis of PE. Early diagnosis and aggressive management improves the outcome in this critically fatal condition.[33]

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REFERENCES

1. Kearon C. Natural history of venous thromboembolism. Circulation. 2003;107:22-30.
2. Thrudeep S. Sharma G, George R, George G, Gopinath R, Jayakumar TG, et al. A rare association of pulmonary thromboembolism in non-obstructive cortriatriatum. Kerala Heart J. 2014:4(1):402.
3. Molloy WD, Lee KY, Girling L, Schick U, Prewitt RM. Treatment of shock in a canine model of pulmonary embolism. Am Rev Respir Dis. 1984;130(5):870-4.
4. Mauritz GJ, Marcus JT, Westerhof N, Postmus PE, Noordegraaf VA. Prolonged right ventricular post-systolic isovolumic period in pulmonary arterial hypertension is not a reflection of diastolic dysfunction. Heart. 2011;97(6):473-8.
5. Acute Pulmonary Embolism (Diagnosis and Management of). Available at http:// www.escardio.org/Guidelines-&-Education/ linical-Practice-Guidelines/ Acute-Pulmonary-Embolism-Diagnosis-and-Management-of. Accessed on 15 November 2014.
6. Anderson FA, Wheeler HB. Venous thromboembolism. Risk factors and prophylaxis. Clin Chest Med. 1995;16:235-51.
7. Samuel GZ. Risk factors of venous thromboembolism. J Am Coll Cardiol. 2010;56:1-7.
8. Davidsingh SC, Srinivasan N, Balaji P, Kalaichelvan U, Mullasaric AS. Study of clinical profile and management of patients with pulmonary embolism Single center study. Indian Heart J. 2014;66:97-202.
9. Stein PD, Terrin ML, Hales CA, Palvesky HI. Clinical, laboratory, roentgenographic and electrocardiographic findings in patients with acute pulmonary embolism and no preexisting cardiac or pulmonary disease. Chest. 1991;100:598-607.
10. Sinha N, Yalamanchili K, Sukhija R, Aronow WS. Role of 12-lead electrocardiogram in diagnosing pulmonary embolism. Cardiol Rev. 2005;13:46-9.
11. Bounameaux H, Moerloose P, Perrier A, Reber G. Plasma measurement of D-dimmer as diagnostic aid in suspected venous thromboembolism: an overview. Thromb Headmost. 1994;71:1-6.
12. Hammond CJ, Hassan TB. Screening for pulmonary embolism with a D-dimmer assay: do still need to assess clinical probability. JR Soc Med. 2005;98:54-8.
13. Egermayer P, Town GI, Turner JG, Heaton DC, Mee AL, Beard ME. Usefulness of D-dimer, blood gas, and respiratory rate measurements for excluding pulmonary embolism. Thorax. 1998;53:830-4.
14. Becattini C, Vedovati MC, Agnelli I. Prognostic value of troponins in acute pulmonary embolism a meta-analysis. Circulation. 2007;116:427-33.
15. Moser KM, Fedullo PF, LitteJohn JK, Crawford R. Frequent asymptomatic pulmonary embolism in patients with deep venous thrombosis. J Am Med Asso. 1994;271:223-5.
16. Goldhaber SZ. Echocardiography in the management of pulmonary embolism. Arch Intern Med. 2002;136:691-700.
17. Burrowes KS, Clark AR, Tawhai MH. Blood flow redistribution and ventilation perfusion mismatch during embolic pulmonary arterial occlusion. Pulm Circ. 2011;1(3):365-76.
18. Padley SPG. Lung scintigraphy vs spiral CT in the assessment of pulmonary emboli. Br J Radiol. 2002;75:5-8.
19. Hartmann IJ, Hagen PJ, Melissant CF, Postmus PE, Prins MH. Diagnosing acute pulmonary embolism: effect of COPD on performance of D-dimer testing, perfusion scintigraphy, spiral CT angiography and conventional angiography. ANTELOPE study group: advances in new technologies evaluating the localization of pulmonary embolism. Am J Respir Crit Care Med. 2000;162(6):2232-7.
20. Dalla VS, Palla A, Santolicandro A, Giuntini C, Pengo V, Visioli OG, et al. PAIMS 2: alteplase combined with heparin versus heparin in the treatment of acute pulmonary embolism. Plasminogen activator Italian multicenter study 2. J Am Coll Cardiol.1992;20(3):520-6.
21. Becattini C, Agnelli G, Salvi A, Grifoni S, Pancaldi LG, Enea I, et al. Bolus tenecteplase for right ventricle dysfunction in hemodynamically stable patients with pulmonary embolism. Thromb Res. 2010;125(3):82-6.
22. Meneveau N, Seronde MF, Blonde MC, Legalery P, Didier PK, Briand F, et al. Management of unsuccessful thrombolytic in acute massive pulmonary embolism. Chest. 2006;129(4):1043-50.
23. Daniels LB, Parker JA, Patel SR, Grodstein F, Goldhaber SZ. Relation of duration of symptoms with response to thrombolytic therapy in pulmonary embolism. Am J Cardiol.1997;80(2):184-8.
24. Kanter DS, Mikkola KM, Patel SR, Parker JA, Goldhaber SZ. Thrombolytic therapy for pulmonary embolism. Frequency of intracranial hemorrhage and associated risk factors. Chest.997;111(5):1241-5.

25. Levine MN, Goldhaber SZ, Gore JM, Hirsh J, Califf RM. Hemorrhagic complications of thrombolytic therapy in the treatment of myocardial infarction and venous thromboembolism. Chest. 1995;108(4):291-301.
26. Meyer G, Vicaut E, Danays T, Agnelli G, Becattini C, Westendorf JB, PEITHO trial Fibrinolysis for patients with intermediate-risk pulmonary embolism. N Engl J Med. 2014;370(15):1402-11.
27. Kline JA , Nordenholz KE, Courtney DM, Kabrhel C, Jones AE, Rondina MT. Treatment of submassive pulmonary embolism with tenecteplase or placebo: cardiopulmonary outcomes at three months (TOPCOAT): Multicenter double-blind, placebo-controlled randomized trial. J Thromb Haemost.2014;12(4):459-68.
28. Gowrinath K, Reddy GK. CT appearances in patient with pulmonary thromboembolism and infarction. Indian J Chest Dis Allied Sci.2003;45:116-20.
29. Kearon C, Akl EA, Comerota AJ, Prandoni P, Bounameaux H, Goldhaber SZ. Antithrombotic therapy for VTE disease: antithrombotic therapy and prevention of thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest. 2012;141(2):195-226.
30. Agarwal R, Gulati M, Mittal BR, Jindal SK. Clinical profile, diagnosis and management of patients presenting with symptomatic pulmonary embolism. Indian J Chest Dis Allied Sci. 2006;48:111-5.
31. Paul SD, Henry JW. Clinical characteristics of patients with acute pulmonary embolism stratified according to their presenting syndromes. Chest. 1997;112(4):974-9.
32. Stein PD, Matta F. Thrombolytic therapy in unstable patients with acute pulmonary embolism: saves lives but underused. Am J Med. 2012;125(5):465-70.
33. Bhuvaneswar JS, Premchand RK, Iyengar SS, Rajeev Khare, Chabra CB, Padmanabhan TN, et al. Tenectaplase in the treatment of acute pulmonary thrombo embolism. J Thromb Thrombolysis. 2011;31(4):445-8.
34. Shukla AN, Thakkar B, Jayaram AA, Madan TH, Gandhi GD. Efficacy and safety of Tenecteplase in acute pulmonary embolism. J Thromb Thrombolysis. 2014;38(1):24-9.

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