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Original Article

Impact of catheter fragmentation followed by local intrapulmonary thrombolysis in acute high risk pulmonary embolism as primary therapy

Bishav Mohan [a,*], *Naved Aslam* [a], *Anil Kumar Mehra* [b], *Shibba Takkar Chhabra* [a], *Praneet Wander* [a], *Rohit Tandon* [a], *Gurpreet Singh Wander* [a]

[a] *Department of Cardiology, Dayanand Medical College & Hospital Unit Hero DMC Heart Institute, Ludhiana 141001, Punjab, India*

[b] *Department of Medicine, Keck School of Medicine, LAC-USC Medical Center, 1200 North State Street, Los Angeles, CA 90033, USA*

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ABSTRACT

Background: Pulmonary embolism (PE) with more than 50% compromise of pulmonary circulation results significant right ventricular (RV) afterload leading to progressive RV failure, systemic hypotension and shock. Prompt restoration of thrombolysis, surgical embolectomy, or percutaneous mechanical thrombectomy (PMT) prevents progressive hemodynamic decline. We report our single center experience in high risk PE patients treated with standard pigtail catheter mechanical fragmentation followed by intra-pulmonary thrombolysis as a primary therapy.

Methods: 50 consecutive patients with diagnosis of high risk PE defined as having shock index >1 with angiographic evidence of >50% pulmonary arterial occlusion are included in the present study. All patients underwent emergent cardiac catheterization. After ensuring flow across pulmonary artery with mechanical breakdown of embolus by rotating 5F pigtail catheter; bolus dose of urokinase (4400 IU/kg) followed by infusion for 24 h was given in the thrombus. Hemodynamic parameters were recorded and follow up pulmonary angiogram was done. Clinical and echo follow up was done for one year.

Results: Pigtail rotational mechanical thrombectomy restored antegrade flow in all patients. The mean pulmonary artery pressure, Miller score, Shock index decreased significantly from 41 ± 8 mmHg, 20 ± 5, 1.32 ± 0.3 to 24.52 ± 6.89, 5.35 ± 2.16, 0.79 ± 0.21 respectively ($p < 0.0001$). In-hospital major complications were seen in 4 patients. There was a statistically significant reduction of PA pressures from 62 ± 11 mmHg to 23 ± 6 mmHg on follow up.

Conclusions: Rapid reperfusion of pulmonary arteries with mechanical fragmentation by pigtail catheter followed by intrapulmonary thrombolysis results in excellent immediate and intermediate term outcomes in patients presenting with high risk pulmonary embolism.

* *Corresponding author.*
E-mail address: bishavmohan68@gmail.com (B. Mohan).

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Acute pulmonary embolism (PE) is common, but has clinically highly variable presentation ranging from asymptomatic to massive PE. Massive PEs are those that cause more than 50% pulmonary arterial compromise, leading to right ventricular failure, circulatory collapse, hypotension, and/or shock. Mortality rate without treatment from massive PE is approximately 30 percent; usually within the first few hours of the initial event.[1–3]

The goal of therapy in patients presenting with massive PE is rapid recanalization of pulmonary arteries with thrombolysis or embolectomy; to decrease right ventricular afterload and reverse right ventricular failure and shock, decrease the risk of recurrence, and prevent chronic thromboembolic pulmonary hypertension.[4,5] Intravenous Thrombolytic therapy is the first-line treatment in patients with high risk PE presenting with cardiogenic shock and/or persistent arterial hypotension.[6] A substantial proportion of patients, however, may not be eligible for Intravenous thrombolysis because of major contraindications.[7] Surgical embolectomy is an alternative therapeutic option in patients in whom thrombolysis is absolutely contraindicated or has failed. However number of experienced tertiary care centers with around-the-clock availability of emergency surgical embolectomy are limited.[8,9] Percutaneous catheter embolectomy or mechanical fragmentation of proximal pulmonary arterial clots followed by local thrombolytic therapy may be considered as a very attractive alternative to surgical embolectomy and systemic thrombolysis because of their capacity to establish pulmonary blood flow rapidly. Several reports have shown that mechanical fragmentation combined with local thrombolysis is a good therapeutic option for restoring pulmonary flow and decreasing PAP; with comparable short term outcomes to systemic thrombolysis.[10,11] However information on long term outcomes are limited in literature. We report here our single center experience in high risk PE patients treated with standard pigtail catheter mechanical fragmentation followed by intrapulmonary thrombolysis on immediate and long term hemodynamic and clinical outcomes.

1. Patients and methods

1.1. *Patient population*

This was an open labeled, noncomparative, single center experience. Approval for the study was obtained from local Institutional Ethics Committee. Prospectively consecutive patients presenting with clinical diagnosis of pulmonary embolism and shock index[12] (heart rate in beats per minute divided by systolic blood pressure in mm of mercury, HR/SBP) >1 from July 2006–July 2009 were enrolled in the trial. The patients were admitted to ICU and written informed consent was obtained. Bed side transthoracic echocardiography was done to confirm the suspicion of pulmonary embolism, to estimate pulmonary arterial pressure and to exclude right atrial or ventricular thrombi. All patients underwent emergent right heart catheterization and pulmonary angiography. Patients who showed a rapid deterioration of their cardiopulmonary condition were put on oxygen supplementation with noninvasive pressure support or intubation. Positive inotropic and vasoactive support was initiated according to the hemodynamic conditions. All patients underwent emergent right heart catheterization and pulmonary angiography.

Inclusion criteria for the study were: Patients with angiographically confirmed acute massive pulmonary embolism with shock index >1, pulmonary arterial occlusion with >50% involvement of the central (main and/or lobar) pulmonary arteries (Miller index >0.5),[13] and pulmonary hypertension (mean pulmonary artery pressure >25 mmHg.

Exclusion criteria included patients with echocardiographically confirmed right sided thrombi, Acute gastrointestinal bleeding, Electrolyte imbalance, Anticoagulation with international normalized ratio >1.8 or severe coagulopathy, Anaphylactoid reaction to contrast media, Acute stroke, Acute renal failure or severe chronic nondialysis dependent kidney disease, Unexplained fever or untreated active infection, Severe anemia, Uncooperative patient.

A total of 50 consecutive patients (9 females, 41 males) with average age of 47 ± 12 years were included in this study.

2. Methodology

All pulmonary angiograms and therapeutic interventional procedures were performed in cardiac catheterization laboratory (Phillips Medical Systems; Netherlands). After giving local anesthesia; 5F sheath was introduced in the femoral vein for procedure. Initially 5F multipurpose catheter was advanced over 0.035-inch Teflon-coated guide wires under fluoroscopic guidance and was used to measure right heart and pulmonary artery pressures. Subsequently, 5F standard pigtail catheter was used to obtain initial pulmonary angiography with an injected volume of 30–40 mL using cine mode with a frame rate of 25/s. Angiographic quantification of degree of pulmonary artery involvement was assessed by the Miller score. Miller score is calculated as the sum of obstruction and perfusion scores, ranging from 0 (best) to 34 (worst). Calculation of the Miller obstruction score ranges from 0 to 16: 9 major segmental branches in the right PA (3 in the upper lobe, 2 in the middle lobe, 4 in the lower lobe) and 7 major branches in the left PA (2 in the upper lobe, 2 in the lingual, 3 in the lower lobe). The presence of filling defect in any of these branches is scored 1 point. The perfusion is scored by dividing each lung into 3 zones (upper, middle, and lower), and the flow into each zone is characterized as absent (3 points), severely reduced (2 points), mildly reduced (1 point), or normal (0 points.) A Miller score of 17 or more indicates a greater than 50% obstruction of pulmonary vascular bed and forms an angiographic definition of a massive PE. The Miller index is Miller score divided by 34 (range 0–1.0).

After confirming the inclusion criteria, mechanical catheter thrombectomy was initiated using a pigtail catheter. The catheter was quickly spun manually so as to fragment the central thrombus and establish initial flow into pulmonary artery (Fig. 1). After ensuring initial flow, the pigtail was left in place inside the same large proximal embolus for subsequent local thrombolytic therapy. Initial bolus dose of Urokinase (4400 IU/kg body weight) was given over 10 min followed by continuous infusion of 4400 IU/kg/hr for 24 h. All patients were monitored continuously for clinical and hemodynamic

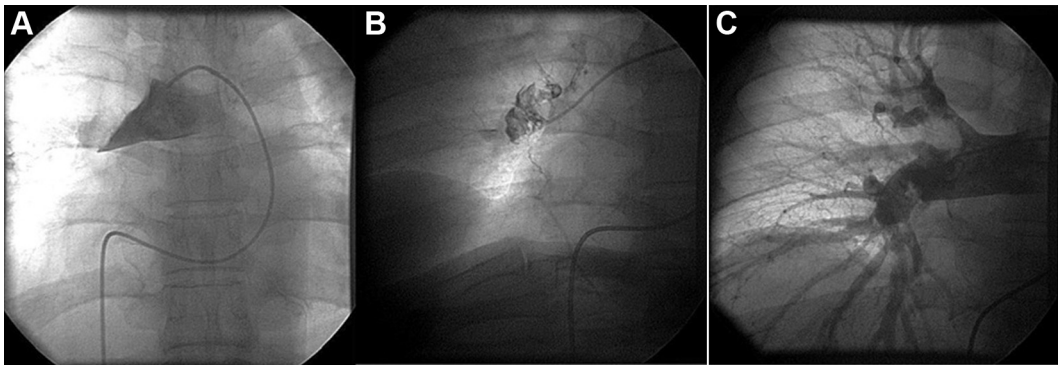

Fig. 1 – Pulmonary angiography revealing A) total cut off of right pulmonary artery B) mechanical breakdown and intrapulmonary urokinase administration and C) post procedural pulmonary angiography revealing restoration of pulmonary flow in right pulmonary artery and its branches.

status in the ICU. Systemic blood pressure and heart rate were recorded and shock index was calculated hourly for 24 h along with arterial oxygen saturations by finger oximetry and pulmonary arterial pressures to determine clinical success. All patients returned to the catheterization laboratory after 24 h of urokinase therapy for repeat pulmonary angiography followed by removal of pigtail catheter and femoral venous sheath. Follow up Miller scores at 24 h were calculated to define angiographic success.

All major complications such as a perforation of the pulmonary artery or cardiac structures, cardiac tamponade, cerebral vascular accident, or death were recorded. Cardiovascular mortality was defined as death secondary to PE, acute myocardial infarction, cerebral vascular accident, or sudden death. Bleeding complications were considered major if any GI or genitourinary bleeding associated with a 10% drop of hematocrit or need for transfusion, or intracerebral and retroperitoneal bleeding.

In-hospital management and long term follow up: after 24 h all patients were treated with intravenous heparin therapy followed by oral anticoagulation therapy with Coumadin prior to hospital discharge. After hospital discharge, all patients were followed every 3 months. Outcomes analysis included recurrent PE, hospital readmission or occurrence of cardiovascular death. Repeat transthoracic echocardiography was done at follow up of 3, 6 and 12 months to document right ventricular size and function as well as pulmonary artery pressures.

2.1. *Statistical analysis*

Continuous variables are expressed as mean with SD, and nominal variables in frequencies and percentages. Values before and after treatment were compared using the Wilcoxon nonparametric test; $p < 0.05$ was considered significant. We compared heart rate, oxygen saturation, pulmonary artery (PA) systolic blood pressure (BP), PA diastolic BP, PA mean BP, SBP, DBP, MBP, Shock Index and Miller index before and after the procedure using mean and standard deviation. *p*-Value was calculated using paired *t*-test. We used analysis of variance to see the trend in shock index and mean PA pressure, at various time intervals after the procedure. *p*value for linear trend was calculated using linear regression models. All statistical analyses were done using SAS 9.2.

3. Results

There were total of 50 patients (82% males, 18% females) with mean age 47 ± 12 years. Baseline characteristics of the patients are described in Table 1. The most frequent risk factors for pulmonary embolism were recent immobilization within prior 4 weeks (44%) and development of DVT (70%). Commonest clinical manifestations were acute onset dyspnea (100%) for ½ h to 15 days prior to admission associated with tachycardia (100%). Mean heart rate was 126 beats/min; mean systemic systolic BP was 101 mmHg, with calculated mean shock index of 1.32. Forty percent of patients had SBP <90 mmHg at the time of admission (Table 2). Other clinical signs/symptoms were nonspecific EKG findings revealed sinus tachycardia in all patients and S1Q3T3 pattern in 52% patients. Bed side Transthoracic Echocardiogram (TTE) was done within 30 min of presentation and revealed RV dilation, RV hypokinesis and/or moderate/severe TR in all patients. Classic MCcullen's sign was seen in 76% of patients. Estimated mean right ventricular systolic pressure was 62 ± 11 mm of Hg. Thirty six percent of patients required vasopressor drugs for hemodynamic support. Seventy two percent of patient had arterial oxygen saturation of equal to or less than 95% with respiratory distress on admission. Twenty four percent were managed with positive pressure ventilation while 4% required mechanical ventilation (Table 1).

Ninety four percent of patients were taken to the catheterization laboratory within 2 h of presentation. Initial pulmonary angiograms performed revealed bilateral pulmonary artery involvement in 86% of patients and sub total occlusion of main pulmonary artery in 4% of patients.

Hemodynamic and angiographic parameters prior to and following percutaneous mechanical fragmentation followed by 24 h of local thrombolytic therapy with urokinase are shown in Table 2 and Fig. 2. Prior to mechanical catheter fragmentation and thrombolytic therapy tachycardia was

Table 1 – Baseline characteristics at diagnosis.

Characteristics	Data
Patients	50
Age, years	47 ± 12
Gender	41 male/9 female
Comorbidities:	
Malignancy	0
Tuberculosis	5 (10%)
Intravenous drug addict	2 (4%)
Recent immobilization (last 4 weeks)	22 (44%)
Leg fracture	9 (18%)
Postoperative	3 (6%)
Febrile illness	10 (20%)
Presenting symptoms:	
Dyspnea	50 (100%)
Chest pain	9 (18%)
Syncope	4 (8%)
Cough	4 (8%)
Hemoptysis	2 (4%)
Duration of symptoms (h)	84 (0.5–360)
Presenting Signs:	
Tachycardia	50 (100%)
Systolic BP <90 mmHg	20 (40%)
Electrocardiographic findings:	
Sinus tachycardia	50 (100%)
S1Q3T3	26 (52%)
Right axis deviation	23 (42%)
T- wave inversion V1–V4	12 (24%)
Atrial flutter	2 (4%)
Deep vein thrombosis:	35 (70%)
Echocardiographic findings:	
Right ventricular hypokinesis	50 (100%)
Right ventricular/left ventricular (ratio >1)	50 (100%)
McCullen's sign	38 (76%)
Thrombus in RVOT	2 (4%)
Moderate to severe TR	50 (100%)
Pulmonary artery systolic pressure (mmHg)	62 ± (11)
Time-hospital admission to initial fragmentation	
<1 h	12 (24%)
1–2 h	35 (70%)
>2 h	3 (6%)
Treatment:	
Positive pressure ventilation	12 (24%)
Intubation/mechanical ventilation	2 (4%)
Hemodynamic support with vasopressor drugs	18 (36%)

*Data are presented as mean _ SD or no. (%) unless otherwise.

seen in 100% of patients; shock index was more than one in 94% patients, and pulmonary hypertension (mean PAP >25 mm of Hg) was present in 100% of patients.

After 24 h of therapy, a significant increase of both MBP and Sao2 was observed (78.3 ± 11.8 mmHg vs. 92.3 ± 10.4. mmHg, $p < 0.0001$; and 90.3 ± 6.7 mmHg vs. 98.1 ± 2.1%, $p < 0.0001$), as were a significant decrease in the shock index (1.32 ± 0.31 vs. 0.79 ± 0.21, $p < 0.0001$), Miller score (20.2 ± 4.8 vs. 5.3 ± 2.1, $p < 0.0001$), and mPAP (41.2 ± 8.0 mmHg vs. 24.5 ± 6.8 mmHg, $p < 0.0001$). Fig. 3 shows the 2 hourly trend in the shock index after initiation of therapy. Shock index improved rapidly to less than one after 8 h of initiation of thrombolytic therapy although statistically significant improvement was initially noted at 4 h of follow up from 1.32 ± 0.31 at baseline to 1.12 ± 0.24, $p < 0.001$. The trend towards improvement continued over 24 h with statistically significant decline to index below 1 at 10 h and 22 h (0.98 ± 0.19 at 10 h and 0.81 ± 0.18 at 22 h) (Table 3).

3.1. *In-hospital outcome*

Hemodynamic success based on shock index was achieved in 92% of our patients along with clinical improvement in 96% patients. The major complication rate was 8% ($n = 4$): 2 deaths and 2 major hematoma requiring blood transfusion. Both patients died from persistent shock, severe metabolic acidosis and acute renal failure within 72 h of hospitalization. There were no other complications such as perforation of the pulmonary artery or right ventricle, cardiac tamponade, myocardial infarction, cerebrovascular accident or sudden deaths during the hospitalization phase. Minor complications were seen in 10% ($n = 5$) of patients: local hematoma in 4 patients (8%), femoral artery pseudoaneurysm in one patient.

3.1.1. *Long-term clinical outcome*

During the follow up period, 100% of the surviving patients were discharged on oral anticoagulation. 2 patients developed upper GI bleed and oral anticoagulation was stopped with placement of IVC filter. One of these patients developed recurrent fatal pulmonary embolism after 18 months of initial presentation. At one year of follow up another 3 patients were noncompliant with their regimen of anticoagulation. One of these had recurrent pulmonary embolism.

Table 2 – Pre and 24 h post procedure measurements in 50 patients.

Measurement	Mean (±SD)			p^* value
	Before	After	Difference	
HR (BPM)	125.18 (±17.83)	93.28 (±13.31)	−31.9 (±15.06)	<0.0001
Saturation (%)	90.33 (±6.78)	98.18 (±2.1)	7.85 (±6.05)	<0.0001
PA SBP (mmHg)	65.1 (±10.39)	37.76 (±10.58)	−27.34 (±8.75)	<0.0001
PA DBP (mmHg)	29.26 (±8.53)	17.9 (±6.04)	−11.36 (±8.37)	<0.0001
PA MBP (mmHg)	41.21 (±8)	24.52 (±6.89)	−16.69 (±7.25)	<0.0001
SBP (mmHg)	100.52 (±19.15)	120.2 (±14.47)	19.68 (±18.92)	<0.0001
DBP (mmHg)	67.24 (±10.36)	78.48 (±9.94)	11.24 (±11.06)	<0.0001
MBP (mmHg)	78.33 (±11.89)	92.39 (±10.48)	14.05 (±12.19)	<0.0001
Shock index (HR/SBP)	1.32 (±0.31)	0.79 (±0.21)	−0.53 (±0.28)	<0.0001
Miller score	20.21 (±4.88)	5.35 (±2.16)	−14.85 (±4.33)	<0.0001

*P-value based on paired *t*-test.
Is statistically significant compared to the value at 6 h at the 0.05 level.

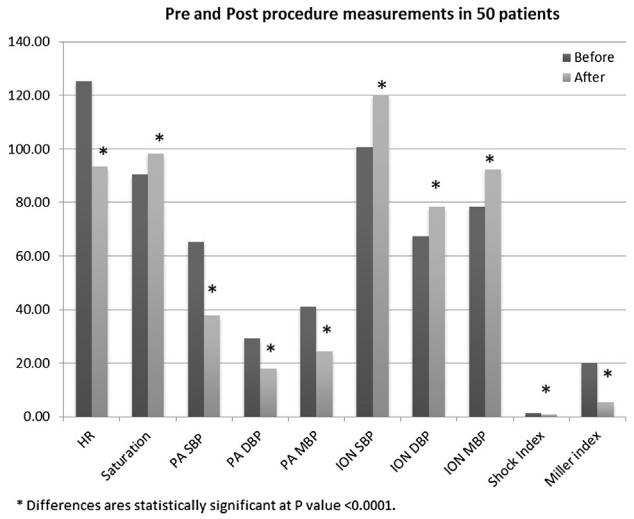

Fig. 2 – Comparison of hemodynamic data before and after 24 h of therapy.

Table 3 – Mean Shock Index (HR/SBP) by hours after treatment.

Time (h)	*n*	Mean shock index (±SD)
Baseline	50	1.32 (±0.31)
2	50	1.25 (±0.27)
4	50	1.12 (±0.24)[a]
6	50	1.08 (±0.22)
8	50	0.99 (±0.2)
10	50	0.98 (±0.19)[b]
12	50	0.95 (±0.19)
14	50	0.9 (±0.18)
16	50	0.88 (±0.17)
18	50	0.87 (±0.17)
20	50	0.85 (±0.19)
22	50	0.81 (±0.18)[c]
24	50	0.8 (±0.19)

[a] Difference is statistically significant compared to the value at baseline.
[b] Difference is statistically significant compared to the value at 4 h.
[c] Difference is statistically significant compared to the value at 10 h.

All patients were followed up for mean of 18 (12–30) months. All patients had sequential analysis of pulmonary artery systolic pressure (PASP) by TTE at 3 months; 6 months and one year follow up along with clinical assessment. As shown in Table 4, there was a significant reduction of pulmonary artery systolic pressure at three months by 26 mmHg from time of presentation (62.3 ± 11.1 to 36.6 ± 8.3 mmHg). There continues to be small but statistically significant drop in PASP even at 6 and 12 months from initial presentation (Fig. 4).

4. Discussion

Acute massive pulmonary embolism is life threatening and one of the most enigmatic diseases facing emergency medicine. Recent statement by AHA on management of pulmonary embolism define massive PE as patients with sustained systolic blood pressure <90 mmHg for at least 15 min or requiring inotropic support in absence of other identifiable causes. The document also defines submassive PE with strain as any hypotension (SBP <90 mmHg) or Shock index >1.0 or respiratory failure evidenced by clinical appearance distress with SaO2 <95% or Borg score>8 and evidence of RV dysfunction suggested by RV hypokinesis or estimated RVSP> 40 mmHg, elevated biomarker values (e.g., troponins, BNP > 100 pg/mL or pro-BNP >900 pg/mL).[14] Based on this definition, 40% of patients in our series were with massive PE and 60% of patients had submassive PE with significant RV strain.

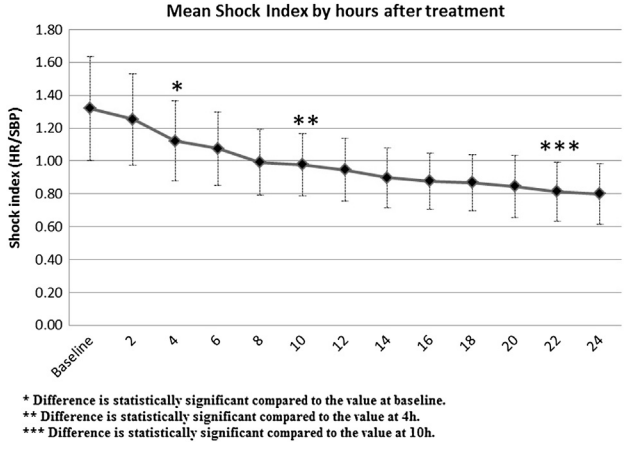

Fig. 3 – Trend of shock index over first 24 h of therapy.

The consensus statement recommends IV fibrinolytic therapy for patients with massive PE *(Class IIa; Level of Evidence B)* and for patients with submassive PE judged to have clinical evidence of adverse prognosis *(Class IIb; Level of Evidence C)* only in patients with low risk for bleeding complications which is significant limitation of Intravenous thrombolytic therapy. Up to fifty percent of patients presenting with massive PE may have absolute contraindications to IV thrombolysis.[7] As in our patient population 44% of patients would not have been able to receive IV thrombolysis due to contraindications. Mechanical thrombectomy or surgical thrombectomy are the alternatives. The guidelines recommend for patients with massive PE and contraindications to fibrinolysis or who remain unstable after receiving fibrinolysis fragmentation of clot in the main or lobar pulmonary arteries alone or followed by local thrombolysis as an alternative *(Class IIa; Level of Evidence C)* when emergency surgical thrombectomy is unavailable or not preferred.[14]

There is no randomized trial comparing mechanical thrombectomy with local intrapulmonary thrombolysis and IV thrombolytics. Pooled analysis of results from 13 Placebo-Controlled, Randomized Trials of various fibrinolytics vs. IV heparin alone to treat acute PE showed no advantage of fibrinolysis in reducing mortality or recurrent PE. However when the analysis was restricted to patients with massive PE only, a significant reduction in recurrent PE or death was observed from 19.0% with heparin alone to 9.4% with fibrinolysis (odds ratio 0.45, 95% CI 0.22–0.90).[15,16] Data from EMPEROR [Emergency Medicine Pulmonary Embolism in the Real-World Registry]and other registries indicate a trend

Table 4 – TTE estimated Mean PA Systolic pressure (mmHg) by months after treatment.

Time (month)	Mean PAS pressure (Mean ± SD)	p^*	Comparison set	Change in PA	p
0	62.33 (±11.1)		0–3	−26.29 (±6.88)	**
3	36.61 (±8.3)		3–6	−9.42 (±5.61)	**
6	28.29 (±7.41)		6–12	−5.32 (±6.19)	**
12	23.03 (±6.37)	<0.0001			

*p-value for linear trend.
**p value for difference in means based on analysis of variance (comparisons significant at the 0.05 level).

towards decrease in all cause mortality with IV thrombolysis in patients with massive PE.[3,7,17,18] In patients with submassive PE IV Thrombolysis has not been shown to improve mortality[19,20] and expected mortality rate in this subgroup of patients is around 3%.[18] However 10% of patients with submassive PE may develop hemodynamically significant right heart failure.[20] Limitations of thrombolytic therapies are several absolute and relative contraindications. Even when patients are pre-screened for absolute and relative contraindications, there is significantly high rate of hemorrhagic complications (up to 20%) including the risk of hemorrhagic stroke.[15,16] Another limitation of thrombolysis is the time (at least 2 h) which is needed to complete the recommended tPA infusion protocol and the delayed onset of lytic effect with its variable efficacy in the presence of organized venous thrombus in the pulmonary artery.

Catheter based techniques which frequently combine mechanical and pharmacologic therapy have distinct advantages over IV thrombolysis. It offers an immediate predictable way to recanalize thrombus in the main pulmonary trunk or major pulmonary arteries without exposure to risks of IV thrombolysis or cardiopulmonary bypass.[21] Various angiographic or pigtail catheter devices have been used to break apart large centrally located emboli by direct mechanical action.[22] The pigtail catheter is universally available cheap and effective device. The goal of therapy is breakdown the large central fresh clot into multiple small fragments to achieve partial reperfusion for thrombolysis to act and not complete removal of thrombus. The proposed mechanisms of improved thrombolytic action are increased exposure of fresh clot surfaces caused by fragmentation accelerating the thrombolytic action. In addition when there is total occlusion of pulmonary artery occlusion by an embolus, any fluid infused will theoretically make only evanescent contact with thrombus and be washed into the nonoccluded ipsilateral and contralateral pulmonary artery. After fragmentation, infused thrombolytics will have greater contact with the distal thrombus throughout the pulmonary arterial tree.[23–27] Ninety four percent of patients in our series were treated in less than 2 h of presentation. Partial Pulmonary artery reperfusion with rotating pigtail catheter was achieved in all patients with immediate initial stabilization of pulmonary as well as systemic hemodynamics and arterial oxygen saturation. One disadvantage with catheter fragmentation techniques is the risk of embolization of clot fragments into distal pulmonary circulation with potential deterioration in hemodynamics.[28,29] However in our study, no evidence of macroembolisation leading to deterioration of hemodynamics or other complications as perforation of pulmonary artery, right ventricle or cardiac tamponade were noted during mechanical reperfusion.

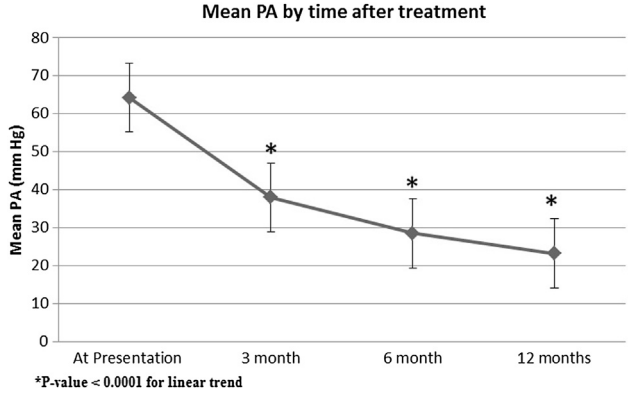

Fig. 4 – TTE estimated pulmonary artery systolic pressures (mmHg) on long term follow up.

All patients in our series received intrapulmonary thrombolysis for 24 h with repeated assessment of hemodynamics every 2 h. Pulmonary perfusion was assessed angiographically at 24 h. Although there was immediate improvement in oxygen saturation and pulmonary pressures with mechanical reperfusion alone, the shock index (systemic hemodynamics) showed a gradual decline with statistically significantly fall first seen only after 4 h and then a further decline to less than 1 at 10 h. At 24 h 98% of patients had improved systemic hemodynamics with 92% having shock index <1. We believe mechanical reperfusion needs to be followed by catheter directed thrombolysis to prevent progressive RV dysfunction and development of cardiogenic shock.[30] We also observed 41% reduction in mean pulmonary artery pressure at 24 h paralleling 74% reduction in lung perfusion defect (Millers score from 20.21 ± 4.88 to 5.35 ± 2.16). Although there are no randomized trials comparing catheter based interventions vs. IV thrombolysis, studies comparing IV fibrinolysis vs. heparin alone show 30%–35% reduction in total lung perfusion defect with fibrinolysis at 24 h compared to no substantial improvement in pulmonary blood flow with heparin alone. However, at 7 days, both heparin and fibrinolysis groups showed similar 65%–70% reduction in total lung perfusion defect indicating a continuous process of body's own autothrombolysis.[31] Our observations and previous studies using similar approach may suggest that catheter based therapies result in more rapid improvement in lung perfusion and pulmonary artery pressure compared to systemic thrombolysis and heparin alone.[32]

Although clinical success of catheter based techniques has not been compared in a randomized trial with systemic thrombolysis or anticoagulation alone, but it compares favorably with the available data for systemic thrombolysis.[11,30] Kuo et al[11] based on a recent meta-analysis of 594

patients from 35 nonrandomized studies (six prospective with 94 patients, 29 retrospective with 500 patients) reported pooled clinical success rate from catheter based therapy to be 86.5% (95% CI: 82.2%–90.2%) when clinical success was defined as hemodynamics stabilization, resolution of hypoxia, and survival at hospital discharge. The success rate was higher (91% vs. 83%) when local thrombolytic therapy was used after mechanical fragmentation. Rotating pigtail catheter was the most common device used for mechanical intervention in 69% of the total study group. All 50 patients in our series were treated with rotating pigtail fragmentation followed by 24 h infusion of local thrombolytic therapy. Using the same definition of clinical success, we observed a success rate of 96%.

In addition, the meta-analysis of catheter derived therapy where majority of patients treated had contraindication to IV thrombolytic therapy show a comparably low risk of minor procedural complications rate of 7.9% (95% CI: 5.0%–11.3%) and major procedural complications rate of 2.4% (95% CI: 1.9%,–4.3%) with low incidence of intracranial bleeding.[11] In contrast, the summarized data from randomized trials show a relatively high 13% rate of major bleeding and a 1.8% rate of intracranial/fatal hemorrhage with fibrinolysis.[15,16] In our series, major hematoma requiring blood transfusion was seen in 4% ($n = 2$) and minor hematomas were seen in 8% ($n = 4$) of patients. None of our patients had intracranial hemorrhage, other major bleeding complications or pulmonary artery/RV injury. The observation reaffirms the low risk of major complications associated with catheter based reperfusion therapy for massive and high risk submassive pulmonary embolism compared to IV thrombolysis despite the theoretically potential higher risk.

In literature, there is no prior well designed study of catheter based therapy on its effect on right ventricular systolic pressure (RSVP) or estimated pulmonary artery pressure and the development of chronic thromboembolic pulmonary hypertension (CTEPH) at 1 year follow up. Some studies have shown significant 46% reduction in pulmonary artery pressures with no incidence of CTEPH at 3–6 months follow up.[32] Similarly pooled analysis of the 4 reported studies showed a significantly greater reduction in estimated pulmonary arterial pressures with fibrinolysis plus heparin compared to heparin alone (mean of 50% vs. 25% respectively) at 6 months follow up.[33–36] But more importantly the study by Kline et al [36] showed an increase in RVSP in 27% of the patients in heparin group compared to none in fibrinolysis group indicating a beneficial impact of thrombolysis on development of CTEPH. In our present study, all surviving patients had sequential follow up echocardiogram at 3, 6 & 12 months to assess RVSP. Our data show a marked reduction in systolic pulmonary artery pressures from 62.33 ± 11.1 at baseline to 28.29 ± 7.4 (55%) at 6 months follow up. On sequential analysis there was further statistically significant improvement in PA pressures at 1 year compared to at 6 months post therapy (28.29 ± 7.4 at 6 months to 23.03 ± 6.3 at 1 year $p < 0.0001$) indicating a continued long term pulmonary artery remodeling following initial injury and recanalization of pulmonary vasculature. This may suggest that an anticoagulation therapy may need to be continued for up to a year to prevent repeat injury to pulmonary arteries.

5. Conclusion

The data form our single center largest reported prospective study suggest that a rapid reperfusion of pulmonary arteries with mechanical fragmentation by universally available pigtail catheter followed by intrapulmonary thrombolysis over 24 h results in excellent immediate and intermediate term outcomes comparable to published results of IV thrombolysis in patients presenting with massive or high risk submassive pulmonary embolism. We believe a more aggressive invasive approach after rapid initial clinical and echocardiographic evaluation followed by immediate transfer to catheterization laboratory offers a prompt diagnostic and potentially lifesaving therapeutic approach in high risk group of patients with pulmonary embolism. In addition, the approach is applicable to larger group of patients with lower risk of complications compared to IV thrombolysis. It can be offered as a primary therapy in experienced centers, similar to approach with coronary revascularization, in high risk patients with pulmonary embolism.

5.1. *Limitation*

Ours is a nonrandomized study with small sample size where bias in choosing management options can not be ignored. The majority of our patients were less than 60 years of age with low risk for intracranial and other hemorrhagic complications.

Conflicts of interest

All authors have none to declare.

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Abbreviation used

PE: Pulmonary embolism
PAP: Pulmonary arterial pressure
HR: Heart rate
SBP: Systolic blood pressure
ICU: Intensive care unit
PA: Pulmonary artery
BP: Blood pressure
DBP: Diastolic blood pressure
MBP: Mean blood pressure
DVT: Deep vein thrombosis
EKG: Electrocardiogram
mPAP: Mean pulmonary artery pressure
PASP: Pulmonary artery systolic pressure
IVC: Inferior venacava
GI: Gastrointestinal
TTE: Transthoracic echocardiography
AHA: American Heart Association
RVSP: Right ventricular systolic pressure
BNP: Brain natriuretic Peptide
RV: Right ventricle
IV: Inferior venacava
CTPEH: Chronic thromboembolic pulmonary hypertension