Case Report

Intrapulmonary Artery Thrombolysis in Acute Pulmonary Embolism: Case Series from King Chulalongkorn Memorial Hospital Experience

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Acute pulmonary embolism (PE) is a life-threatening condition. In patient who has contraindication for systemic thrombolysis and inappropriate for surgical embolectomy, there is a role of catheter interventions. However, the data are limited. The aim of the present report was to assess a role of intrapulmonary artery thrombolysis bolus in acute PE. A retrospective review of the use of intrapulmonary artery thrombolysis in acute PE. The data were collected from 14 patients with massive or submassive PE who had contraindication or inappropriate for systemic thrombolysis and unsuitable for surgical embolectomy. After intrapulmonary thrombolysis was given, patients were followed clinically and hemodynamically until discharged and after 1 month. Pulmonary pressure was collected at pre and post intervention. Of the 14 patients (age 59±19 years, 78.6% female), 86% were diagnosed as submassive PE. Mean dose of tissue plasminogen activator (rt-PA) was 28±14 mg given as bolus and continuous infusion (19±10 hours). One patient died after completion of intrapulmonary infusion rt-PA at day 90, which did not relate to PE and the treatment. After intervention, mean PA pressure was significantly reduced from 32.3±6.0 to 21.0±4.3 mmHg (p<0.001). Three patients (21%) had minor bleeding (hematoma at access site). The present case series showed that intrapulmonary infusion of rt-PA was effective and safe in patient with massive and submassive PE who had contraindication or inappropriate to systemic thrombolysis or inoperable surgical thrombectomy.

Keywords: Acute pulmonary embolism; Intrapulmonary thrombolysis; Tissue plasminogen activator; Surgical thrombectomy

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Acute pulmonary embolism (PE) is a life-threatening condition. The overall mortality rate is estimated 15% at 3 month[1]. The prognosis varied by a spectrum of clinical syndrome. In massive PE, the hospital mortality rate may exceed 50%[2]. Submassive PE, the hospital mortality ranges between 6% to 8%[3]. From scientific guideline statement of the American Heart Association recommended on management of acute massive PE, included using of reperfusion therapy i.e., systemic thrombolysis, catheter interventions, and surgical embolectomy[4]. In patient who has contraindication for systemic thrombolysis and inappropriate for surgical embolectomy (such as severe co-morbidity disease etc.), there is a role of catheter interventions[5]. In submassive PE, there are still some controversies about systemic thrombolysis, surgical embolectomy or intravenous anticoagulant. Catheter intervention may be the role in this situation because of the effectiveness and less bleeding complication. Contemporary catheter intervention techniques can be devided into 6 categories[5,6]: thrombus fragmentation[7,8], rheolytic thrombectomy[9,10], suction thrombectomy[11], rotational thrombectomy, conventional catheter-directed thrombolysis[12,13], and pharmaco-mechanical thrombolysis. From the previous systematic review on mechanical interventions with or without catheter-directed thrombolysis, the pool clinical success rate was 86%[5]. The aim of the present report was to assess the effectiveness of the intrapulmonary artery thrombolysis in acute PE.

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Case Report

The authors enrolled 14 patients with massive or submassive PE who had contraindication or inappropriate for systemic thrombolysis and unsuitable for surgical embolectomy. The diagnosis

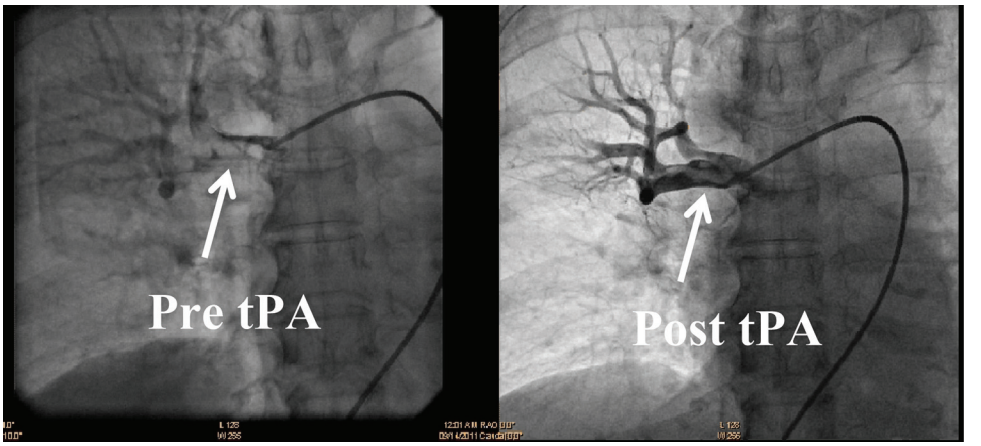

Figure 1. Left-hand side shows the large filling defect in right upper pulmonary artery (PA) before infusion of tissue plasminogen activator and after tPA shows in the right-hand side.

was made by clinical, physical examination, echocardiogram and CT pulmonary angiogram. Cases were collected between July 2011 and March 2013 with intrapulmonary artery thrombolysis via catheter at King Chulalongkorn Memorial Hospital. Massive PE was defined as acute PE with sustained systemic arterial hypotension (SBP less than 90 mmHg), cardiogenic shock, or the need for cardiopulmonary resuscitation[4]. Submassive PE was defined as acute PE with preserved systemic arterial pressure, but with right ventricular dysfunction on echocardiography or with elevated cardiac biomarkers(4). The diagnoses were made by one cardiologist. After diagnosis, patient was sent to the catheterization laboratory. The intervention was performed via right femoral vein approach. Pulmonary pressure was documented by using 6 Fr multipurpose catheter. Then, selective pulmonary angiogram was done in anteroposterior (AP) view by manual contrast injection as Figure 1. After that, the local thrombolysis was initiated by bolus injection of rt-PA (alteplase). Then, the catheter was left in place with continuous infusion of rt-PA. The patient was sent to cardiac care unit (CCU) for intensive hemodynamic monitor. The follow up pulmonary angiogram was done after infusion of rt-PA 6 to 48 hours according to the clinical status and the amount of thrombus. After repeated pulmonary angiogram, rt-PA was continuous infused or terminated according to the clinical and hemodynamic responsive or concurrent bleeding complication. Then, patient was follow up clinically and hemodynamically until discharge and after 1 month.

Major bleeding was defined as a hemoglobin decrease more than 3 g/dL or need for blood transfusion or intracerebral hemorrhage.

Continuous variables were expressed as mean ± standard deviation (SD). Hemodynamic values between the 2 time points were compared using a paired Student's t-test. A p-value of less than 0.05 was considered significant. Statistical analysis was performed using SPSS Statistics, version 16.0 (SPSS Inc., Chicago, IL, USA). All patients had given consents before the intervention.

Results

The present case series included a total of 14 patients in King Chulalongkorn Memorial Hospital with a mean age 59±19 years. The baseline characteristics were show in Table 1. There were eleven females (78.6%). Two patients (14%) were diagnosed as massive PE and 12 (86%) diagnosed as submassive PE. There were 5 post-operative patients. The day from operation to the event varied from 2 to 6 days. Pre-intervention hemodynamics were showed in Table 2. The echocardiographies were done in 11 patients. And right ventricular dysfunction was diagnosed in 9 patients (81.8%). The rt-PA was given to all patients with a mean dose of 27.6±13.8 mg. Mean duration of continuous rt-PA in each patient was 19±10 hours. The changes of mean pulmonary artery (PA) pressure were shown in Table 2. After catheter infusion, mean PA pressure was significantly reduced from 32.3±6.0 mmHg to 21.0±4.3mmHg ($p<0.001$). None died at 30-day follow up. One female patient died in-hospital at day 90 as in Table 3. She was diagnosed as Krukenberg tumor, admitted for hysterectomy and bowel surgery due to

Table 1. Characteristics of the study population (n=14)

Variable	Value; mean±SD
Age (years)	59±19
Women (%)	78.6
Massive PE; n (%)	2 (14.3)
Submassive PE; n (%)	12 (85.7)
Systolic blood pressure (mmHg)	115±24
Diastolic blood pressure (mmHg)	72±17
Heart rate (beats/min)	110±12
Oxygen saturation room air at diagnosis (%)	86.9±8.5
PA systolic pressure (mmHg)	49.1±9.5
PA diastolic pressure (mmHg)	19.7±5.2
PA mean pressure (mmHg)	32.3±6.0
Impaired RV function from TTE (n=11); n (%)	9 (82.0)
Dose of rt-PA infusion (mg)	27.6±13.8
Duration of rt-PA infusion (hours)	19.0±10.0

PE=pulmonary embolism; PA=pulmonary artery; RV=right ventricular; TTE=transthoracic echocardiography; rt-PA=tissue plasminogen activator; SD=standard deviation

gut obstruction and developed acute submassive PE. The rt-PA was given via intrapulmonary continuous infusion. Her clinical was significantly improved after the treatment. The cause of death was sepsis from intra-abdominal infection.

Table 2. Pre and post intervention pulmonary artery pressure of the patients

Variable	Pre intervention; mean±SD	Post intervention; mean±SD	p-value
PA systolic pressure	49.1±9.5	33.5±5.8	<0.001
PA diastolic pressure	19.7±5.2	12.8±3.8	<0.001
PA mean pressure	32.3±6.0	21.0±4.3	<0.001

PA=pulmonary artery; SD=standard deviation

Three patients (21%) had minor bleeding (groin hematoma). One patient developed large hematoma at access site (10 cm) after 3 hours of intervention, the patient was sent to follow up imaging by computed tomography (CT) pulmonary angiogram showed resolution of the thrombus in right and left PA. Therefore, the rt-PA infusion was terminated. None of these patients had major bleeding or fatal bleeding.

Discussion

The authors review a series of patient who underwent treatment with intrapulmonary rt-PA. The present report showed that this novel treatment is effective and relatively safe with lower rates of major bleeding compared to the systemic thrombolysis

Table 3. Baseline characteristics of study populations

No.	Age (year)	Sex	Severity	Precipitating factors	rt-PA dose	Duration infusion (hour)	PAP pre intervention (mmHg)	PAP post intervention (mmHg)	In-hospital outcome	Complications
1	71	F	Submassive	DVT left leg	10	0	44/17/27	None	Alive	None
2	77	F	Submassive	Post spine surgery day 6	28	16	49/23/31	None	Alive	None
3	32	F	Massive	Post hysterectomy day 4	45	37	36/21/30	32/7/20	Alive	None
4	67	F	Submassive	History of idiopathic PE	25	18	57/15/32	28/7/16	Alive	Hematoma at access site
5	23	F	Submassive	No	20	15	None	None	Alive	None
6	64	F	Massive	Lung cancer, post surgery day 5	29	24	51/21/37	26/9/17	Alive	None
7	39	F	Submassive	Krukenberg tumor, post hysterectomy day 4	22	20	50/22/35	42/13/27	Death from intra-abdominal infection at day 90	None
8	67	M	Submassive	DVT left leg	20	20	49/13/29	34/12/19	Alive	None
9	94	F	Submassive	Bed ridden	5	3	42/16/27	36/16/24	Alive	Hematoma at access site
10	79	F	Submassive	Adrenocortical cancer	46	22	52/29/38	42/16/26	Alive	None
11	57	M	Submassive	Nasopharynx cancer	29	24	38/12/23	32/10/16	Alive	None
12	52	M	Submassive	DVT left leg	56	34	66/22/40	32/17/25	Alive	None
13	48	F	Submassive	Sacral chordoma, post surgery day 7	30	21	48/19/33	33/15/21	Alive	Hematoma at access site
14	57	F	Submassive	Breast cancer on tamoxifen	21	12	57/25/37	33/18/21	Alive	None

rt-PA=tissue plasminogen activator; PAP=pulmonary artery pressure; DVT=deep vein thrombosis; F=female; M=male; PE=pulmonary embolism

(0% in the present study versus 9% in a recent meta-analysis)[14]. In the previous cohort study, manual aspiration and application of prolonged thrombolytic (urokinase) in 63 patients are feasible and safe in patient with massive and submassive PE[15]. The mean PA pressure in that study was reduced from 32.3±6.0 to 21.0±4.3 mmHg ($p<0.001$)[15]. The mortality rate was 6%. Nine patients (14%) had major bleeding without fatal bleeds, slightly higher rates of major bleeding compared to systemic thrombolysis (14% in that study versus 9% in a recent meta-analysis)[15]. This may be contributed to less fibrin specific activity of urokinase and duration of the thrombolysis infusion.

Verstraete et al had previously demonstrated that intrapulmonary infusion of rt-PA did not offer a significant benefit over the intravenous route[16]. In that study, the dose of intrapulmonary infusion rt-PA was similar to the intravenous infusion dose (100 mg) and more patients with recent surgery were included in the intrapulmonary infusion rt-PA arm. These two factors may contribute to non-significant in bleeding complication. In contrast to our study, the dose of rt-PA was less than the previous study (27.6±13.8 mg in the present study versus 100 mg in previous study)[16], therefore, the major bleeding rate in the present study was lower than the previous study (0% in the present study versus 12%).

The present case series showed that intra-pulmonary infusion of rt-PA was effective in reduced PA pressure and improved mortality in patient with submassive PE and inoperable massive PE with contraindication to systemic thrombolysis. The major bleeding complication was also less than systemic route.

Limitation

First, the present study was done in small population in one center, this may not present variation of baseline characteristic. Second, the authors collected data from registries not randomization. Therefore, the authors had no data of systemic thrombolysis, surgical embolectomy or only unfractionatedheparin (UFH) to be compared. Third, by using the dose of rt-PA in 1 to 2 mg/hour, so, the authors did not know the truly effectiveness and safest dose of rt-PA infusion.

Conclusion

Intrapulmonary infusion of rt-PA is effective and safe in patient with submassive PE and massive PE who have contraindication to systemic thrombolysis or inoperable. The PA pressure was significant reduce after the infusion. Survival rate and complication rate was impressive.

What is already known on this topic?

Systemic thrombolysis is standard treatment for patients with massive PE, however, this modality of treatment contains high bleeding complications.

What this study adds?

Intrapulmonary thrombolysis in patients with massive or high risk submassive PE is feasible, safe and effective with less bleeding complication.

Conflicts of interest

The authors declare no conflict of interest.

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