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Efficacy and safety of reduced-dose and slow-infusion intravenous alteplase regimen in patients with acute pulmonary embolism at intermediate-high-risk

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Background: In patients with intermediate-high-risk (IHR) pulmonary embolism (PE), full-dose systemic thrombolytic treatment (STT) has been documented to lower the risk of hemodynamic decompensation and mortality, at the expense of an elevated risk of life-threatening bleeding. In this study, we aimed to evaluate the safety of reduced-dose STT regimen while maintaining effective reperfusion.

Methods: This single-center study comprised 124 retrospectively evaluated patients (female 58.9 % and mean age 55.4+15.8 years) diagnosed with acute PE at IHR status in accordance with European Society of Cardiology (ESC) 2019 acute PE guidelines in whom intravenous (i.v.) alteplase treatments were utilized. Patients fulfilling at least one of the following criteria have been included in the study: systolic blood pressure ≤ 110 mm Hg, heart rate > 100 bpm, SaO2 < 90 % on room air, respiratory rate > 20 breaths per minute, or serum lactate > 2 mmol/L. Exclusion criteria were any contraindication for STT and symptom onset > 14 days. Standard protocol for initial STT was i.v. infusion of alteplase of 25 mg over 4-6 hours. After completion of the infusion, a second STT in the same manner if one of the following criteria were present; heart rate > 100 bpm, SaO2 < 90 % or signs of organ hypoperfusion.

Results: Syncope and concomitant deep vein thrombosis were documented in 27.4 % and 49.2 % of patients, respectively. Baseline vital measures were as follows; heart rate: 112 +16.6 bpm, systolic blood pressure: 123+14.9 mm Hg, SaO2: 89 % (85-93), serum lactate 2.35 (1.6-2.9) mmol/L. Median alteplase dose and infusion duration were 50 (25-50) mg and 6 (4-10) hours, respectively. There were significant improvements in clinical parameters, pulmonary thrombus burden, pressure strain and right ventricular size and function as assessed by computed tomography and echocardiography (p< 0.001 for all). Minor and major bleeding events occurred in 3.2 % and 4.8 % of patients, respectively. One major bleed was due to cerebellar hemorrhage, but did not require surgery and patient was discharged without sequela. There were 6 (4.8 %) in-hospital deaths in which 2 were attributed to major hemorrhages and 4 due to hemodynamic decompensation.

Conclusion: In patients with acute IHR PE, reduced-dose and slow-infusion i.v. alteplase regimen seems to be a clinically relevant and safe reperfusion alternative to full-dose STT protocols associated with well-known major bleeding risks.

Variables	Before IV tPA	After IV tPA	Mean Change	p
PASP (mm Hg)	50.9 ± 13.3	34.4 ± 12.6	17.7	<0.001
RV/LV ratio	1.26 ± 0.21	0.89 ± 0.13	0.369	<0.001
RA/LA ratio	1.31 ± 0.26	1.02 ± 0.18	0.301	<0.001
TAPSE (cm)	1.81 ± 0.39	2.3 ± 0.3	0.46	<0.001
S' (cm/sec)	11.2 ± 2.74	14.1 ± 2.5	3.05	<0.001
Qanadli score	20 (18-23)	9 (6.75-13)	10	<0.001
Main PA diameter (mm)	30.4 (28-32)	28 (25.3-30)	2.31	<0.001
Heart rate (bpm)	112 ± 18.6	82.2 ± 11.3	29.7	<0.001
Systolic BP (mm Hg)	123 ± 14.9	127 ± 21.9	5	0.015
Oxygen saturation (%)	89 (85-93)	96 (94-97.3)	6.5	<0.001
Shock index	0.902 ± 0.22	0.682 ± 0.15	0.183	<0.001
Modified shock index	1.02 ± 0.26	0.702 ± 0.13	0.26	<0.001