



## Case Report

## Multiple boluses of alteplase followed by extracorporeal membrane oxygenation for massive pulmonary embolism

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## ABSTRACT

Thrombolytics and extracorporeal membrane oxygenation (ECMO) are potential management options for massive pulmonary embolism (PE). There are early data supporting the use of repeated alteplase 50 mg bolus for massive PE. However, there is sparse literature addressing placement of ECMO catheters after systemic thrombolysis, and there are no reports of initiating ECMO after repeated bolus of alteplase. We present the case of a patient with massive PE who received two boluses of alteplase for recurrent cardiac arrest, followed by initiation of ECMO. The patient stabilized with these interventions, and ultimately had a good outcome with normal neurologic and functional status.

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Pulmonary embolism (PE) occurs in approximately 60–70 per 100,000 people annually. Those with a massive PE (systolic blood pressure <90 mmHg for ≥15 min, requiring inotropes or vasopressors, or pulselessness) have an increased mortality [1,2]. Kasper et al. found that in-hospital mortality was up to 65% in those requiring CPR [1].

Thrombolytics are one of the primary therapies used to treat massive PEs. However, some patients may have persistent hypoxia or hemodynamic instability after initial thrombolysis. There is literature describing the utilization of up to two boluses of alteplase 50 mg (code dose) for massive PE in patients that remain highly unstable or pulseless [3–5]. Another treatment option for massive PE with hemodynamic instability is extracorporeal membrane oxygenation (ECMO). Limited data suggest a mortality benefit with ECMO in the most severe cases of massive PE, those with circulatory collapse [6].

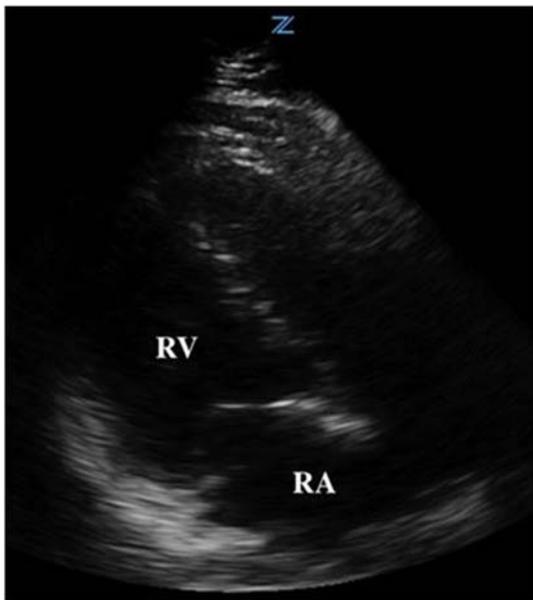
Although there is research describing double code dose alteplase and ECMO individually, little is known regarding the safety and efficacy of combining ECMO and systemic thrombolysis [7]. We present a patient with massive PE who received two boluses of alteplase 50 mg followed by initiation of ECMO.

A 65-year-old male presented to the ED with an oxygen saturation (SpO<sub>2</sub>) in the 80's on a non-rebreather mask, altered mental status, and mottled skin. He was on his fourth day of enoxaparin bridging to warfarin for a left lower extremity deep vein thrombosis and reportedly called 911 for new onset shortness of breath. Bedside ultrasound

showed right ventricular dilation and bowing of the interventricular septum (Fig. 1). The patient was intubated for respiratory distress, poor mental status and persistent hypoxia. Shortly after intubation he lost pulses and Advanced Cardiac Life Support (ACLS) was initiated. An alteplase bolus of 50 mg and epinephrine 1 mg were given via IV push (IVP), and return of spontaneous circulation (ROSC) was achieved after one round of CPR (2 min). An epinephrine infusion was started at 0.05 µg/kg/min for a pressure of 89/53, along with an infusion of alteplase 50 mg over 1 h. Within a few minutes, the patient lost pulses again. ACLS was resumed and the alteplase infusion was converted to a second 50 mg IVP dose. The patient had ROSC again after one round of CPR (2 min), but his SpO<sub>2</sub> was persistently in the 50's despite correct endotracheal tube placement confirmed on chest X-ray. Our "Pulmonary Embolism Response Team" (PERT) was activated. The PERT team consists of an attending from Emergency Medicine, Cardiothoracic Surgery, and Vascular Interventional Radiology. The team proceeded with veno-arterial cannulation while in the ED resuscitation bay. The patient was successfully started on ECMO 1 h and 20 min after arriving at the hospital. Major bleeding was a significant concern when our team decided to administer a repeat bolus of alteplase and to initiate ECMO afterwards. Fortunately, our patient did not require blood products for approximately 2 h that he was on ECMO while awaiting transport. He was then transferred to an outside hospital for further management, where he underwent thrombectomy. The patient had good neurologic and functional status after discharge. During a telephone interview four months later, the patient reported he was living independently at home with no marked disability. His primary complaint was bilateral thigh pain with ambulation, possibly related to his vascular access sites.

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**Fig. 1.** Bedside ultrasound showing a dilated right ventricle and bowed interventricular septum.

Massive PE is associated with high morbidity and mortality, and definitive treatment (thrombectomy) is often limited by profound hemodynamic instability in this patient population [1]. Therefore, management strategies that increase successful stabilization to thrombectomy may significantly decrease mortality. In our patient with recurrent cardiac arrest, we utilized repeat alteplase boluses followed by ECMO. Although repeat code dose alteplase is described in the literature, it is not widely established [3–5]. Furthermore, the use of ECMO with systemic thrombolysis is rare.

There have been cases describing systemic thrombolysis with ECMO already in place [7,8]. We also found two cases of successful venoarterial cannulation and ECMO after systemic thrombolysis. Chon et al. cannulated 1 h after an infusion of alteplase 100 mg over 2 h, and Fernandes et al. cannulated less than an hour after two boluses of tenecteplase 50 mg IVP [9,10].

Although bleeding risk remains an important consideration, there are select patients where the benefits outweigh the risks. When a patient is too hemodynamically unstable for thrombectomy, this case suggests that a repeat alteplase bolus can be beneficial, and that prior thrombolytics, such as code dose alteplase, should not be considered an absolute contraindication to ECMO.

Based on this outcome, we suggest that repeat bolus doses of systemic thrombolysis followed by ECMO can be a safe and effective

treatment for massive PE in patients with severe persistent circulatory collapse.

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### Declaration of Competing Interest

None.

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