

# A Positive Outcome Post Alteplase, ECMO and Emergent Surgery in a Case of Massive Pulmonary Embolism Cardiac Arrest Complicated by Intra-Abdominal Bleeding

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## ABSTRACT

Acute pulmonary embolism is stratified into three groups: low-risk, moderate-risk, and high-risk. High-risk PE, also known as massive pulmonary embolism (MPE), is defined as an acute PE with sustained hypotension, pulselessness, and persistent bradycardia. Herein, we present a case of a 44-year-old female presenting to the emergency department with shortness of breath, chest discomfort, and central cyanosis. She was found to have MPE and arrested twice during which she received alteplase and Advanced Cardiac Life Support. In the ICU, she arrested for the third time, was resuscitated, and a decision to initiate extracorporeal membrane oxygenation deemed reasonable. The patient deteriorated and was rushed to the operating room after detecting major intra-abdominal bleeding on FAST exam. Hepatic injury was suspected and liver packing was initiated. Patient was safely discharged home neurologically intact after a prolonged hospital stay.

**Key words:** bleeding; ECMO, massive pulmonary embolism, resuscitation, thrombolytic therapy

## INTRODUCTION

Acute pulmonary embolism (PE) is stratified, according to severity, into three different groups. The low-risk PE group includes hemodynamically stable patients with normal right ventricular (RV) function and without excessive hypoxemia or tachycardia. The moderate-risk (submassive) PE includes hemodynamically stable patients with evidence of RV dysfunction. The last group is the high-risk PE group. It is also known as the massive pulmonary embolism (MPE) and continues to have a vague definition. According to the American

Heart Association, MPE is defined as an acute PE with sustained hypotension, pulselessness and/ or persistent profound bradycardia.<sup>1,2</sup>

The short-term mortality from MPE ranges from 25% to 65%.<sup>3</sup> Accordingly, any patient presenting with hypotension, in the setting of elevated central venous pressure, should be evaluated for MPE. This should be done while concurrently ruling out cardiac tamponade, tension pneumothorax, acute myocardial infarction, and new-onset arrhythmias, among other life-threatening conditions.<sup>3</sup> Immediate diagnosis and management of MPE is crucial as 50%, 70% and more than 85% die within 30 minutes, one hour, and six hours of the onset of symptoms.<sup>4</sup>

To establish a diagnosis of MPE, pulmonary angiography and spiral computed tomography angiography are the gold standard studies in hemodynamically stable patients.<sup>5</sup> However, in hemodynamically unstable patients, where obtaining

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confirmatory studies might delay management, bedside transthoracic echocardiography (TTE) could be used.<sup>6</sup> In fact, TTE was shown to have high specificity in the diagnosis of PE, making it an adequate diagnostic tool to rule MPE in.<sup>6</sup>

When it comes to the management of MPE, different approaches exist. The first thing to be addressed is hypotension. Hypotensive patients with MPE should receive intravenous (IV) fluids, vasopressors and oxygen therapy to correct hypoxemia. Additionally, patients with MPE should be started on anticoagulation therapy, even when planned to receive more advanced therapeutic options.<sup>3</sup> Moreover, thrombolytic therapy is the first-line treatment in hemodynamically unstable patients with MPE.<sup>7</sup> Thrombolytic therapy was shown to decrease all-cause mortality and mortality due to recurrent venous thromboembolism in this population, with benefits outweighing the potential risks.<sup>8</sup> However, two major considerations should be taken into account. The first is weighing the benefit of thrombolytic agents against the risk of major bleeding and intracranial hemorrhage. This risk/benefit assessment should be agreed upon on individual basis.<sup>9</sup> Secondly, the high-risk (MPE) group is in fact a heterogenous group.

Unconscious hypotensive patients who have not yet arrested are the most ideal candidates for thrombolytic therapy from the MPE group. However, indications are still ambiguous when it comes to patients on both ends of the spectrum within the MPE group: the alert, persistently hypotensive patients and those who have already arrested.<sup>10</sup> The main concern among those who arrested is the absence of adequate blood flow for effective thrombolytic therapy.<sup>3</sup> It was shown, nevertheless, that the chances of return of spontaneous circulation (ROSC) are higher in MPE patients who receive thrombolytic therapy.<sup>11</sup>

What about the role of thrombolytic therapy in low-risk and intermediate-risk PE groups?

In patients with acute PE, thrombolytic therapy is only indicated in patients who have no bleeding risk with either sustained hypotension or continued deterioration despite anticoagulation.<sup>2</sup> Accordingly, thrombolytic therapy is not indicated in the low-

risk group.<sup>2</sup> The hardest patients are the submassive PE group. Several studies addressed this topic; some showed a mortality benefit with an increased bleeding risk,<sup>12</sup> while others demonstrated no mortality benefit with increased bleeding risk.<sup>13</sup> Accordingly, the best candidates for thrombolytic therapy among the submassive PE group are those who have a low bleeding risk but display clinical deterioration.<sup>2,14</sup> An ongoing trial is currently assessing role of half-dose thrombolytic therapy in the management of submassive PE.<sup>14</sup>

The mortality benefit of thrombolytics stems from its ability to reduce the obstruction from thromboembolism, pulmonary vascular resistance as well as RV overload and dysfunction.<sup>3</sup>

Other therapeutic options may be used in the management of MPE. These include inferior vena cava (IVC) filters, surgical pulmonary embolectomy, and extracorporeal membrane oxygenation (ECMO).<sup>3</sup> ECMO, for instance, is recommended in hemodynamically unstable patients with contraindication to systemic thrombolysis.<sup>15</sup> Also, ECMO was shown to be effective in MPE patients who arrest, especially when combined with systemic fibrinolytics or a catheter-directed therapeutic approach.<sup>15</sup> However, ECMO necessitates full anticoagulation; therefore, it is associated with an extensive bleeding risk.<sup>15</sup>

This case sheds the light on the importance of early initiation of thrombolysis to successfully resuscitate a patient with MPE. This is, to our knowledge, one of the very few reported cases in the literature showing a positive outcome after extensive resuscitative methods in a case of massive PE cardiac arrest complicated by major intra-abdominal bleed post single dose of alteplase. Our patient was adequately managed by ECMO and emergent surgery and discharged home neurologically intact, without any residual deficits.

## CASE REPORT

Herein, we present a case of a 44-year-old female that presented to the emergency department (ED) with worsening shortness of breath, chest discomfort and central cyanosis. The patient was on oral contraceptives and had a history of recent long

duration of travel. A few minutes after arrival, the patient had a cardiac arrest. She was immediately intubated and picked up after one cycle of cardiopulmonary resuscitation (CPR). Bedside TTE demonstrated the D-sign resulting from RV strain and a severely dilated RV, twice the size of the left ventricle (LV). A diagnosis of MPE was made. A few minutes later, the patient arrested again and was given a bolus of 100 mg of recombinant tissue type plasminogen activator (rt-PA/ alteplase) while resuming Advanced Cardiac Life Support (ACLS) until return of spontaneous circulation (ROSC) was achieved. Bedside TTE was repeated after rt-PA administration to reassess the RV size; progressive reduction in the size was noted. Major bleeding was a significant concern as the patient received a high dose of rt-PA. To be noted, during the whole resuscitation period and before ROSC was achieved, the patient's rhythm was PEA. The patient was transferred to the intensive care unit (ICU), where she arrested for the third time. She was resuscitated and was planned for VA ECMO given her persistent hypoxia and hypotension. After insertion of the ECMO, the patient developed severe hemodynamic instability with systolic blood pressure reaching 30 mmHg. Evidence of free fluid in the abdomen on bedside ultrasound was noted. The patient was rushed to the operating room for an emergent exploratory laparotomy. A deep lateral laceration over the right hepatic lobe with rupture of the hepatic capsule was detected. Laceration repair and liver packing were done. Intraoperatively, the patient suffered an estimated blood loss of 3500 ml. Patient was retransferred to the ICU and a revisit exploratory laparotomy was done 48 hours later. Complete resolution of the bleeding was noted. The patient's hemodynamics significantly improved during her ICU admission postoperatively. An IVC filter was inserted and a plan to re-initiate heparin after 10 days was drawn. She was later extubated and transferred to a regular floor for continuity of care. After ensuring clinical stability, the patient was safely discharged home.

## DISCUSSION

MPE is a major cause of morbidity and mortality.<sup>1</sup> As such, early diagnosis and effective treatment are

necessary. Thrombolytic therapy is the pillar of treatment in patients with MPE, in the absence of contraindications.<sup>3</sup> Although concerns have been raised regarding the effectiveness of thrombolytic therapy among those who arrest due to a possible or established acute PE, several studies highlighted its importance for ROSC.<sup>11</sup> In fact, patients with PEA were more likely to have better mortality outcomes upon receiving multiple doses of rt-PA.<sup>11</sup> Evidence regarding the administration of thrombolytic agents during cardiac arrest is still lacking. This is dependent upon the clinical sense of the physician and is individualized for each case.<sup>3</sup> In our case, after the diagnosis of MPE was made, the patient arrested for the second time. The time to achieve ROSC was prolonged. After administration of systemic fibrinolytic therapy, ROSC was achieved. Similar to our patient, multiple cases of successful use of thrombolytic therapy in cardiac arrest patients with MPE were previously reported in the literature.

Several thrombolytic agents have been studied in the management of MPE. First-generation agents, namely streptokinase and urokinase, are rarely used nowadays due to their prolonged infusion. The thrombolytic agent mostly used is rt-PA. It is FDA-approved for acute PE treatment.<sup>2,13</sup> Our patient was given a single dose of rt-PA.

The optimal dose of alteplase has always been a topic of debate. In a study by Kiser et al., the authors showed that half-dose (i.e., 50 mg) and full dose alteplase (i.e., 100 mg) for the management of pulmonary embolism were both associated with a similar rate of bleeding, but the need for treatment escalation was more likely in those who received half-dose alteplase.<sup>16</sup> Given the equivalent risk of bleeding, we were inclined to give our patient the 100 mg dose, assuming that full dose alteplase might be more effective, especially in the case of cardiac arrest post massive PE. Guidelines from both the European Society of Cardiology and American College of Chest Physicians recommend giving 100 mg of rt-PA as an infusion over 2 hours. A bolus of thrombolytic therapy can be given exceptionally in patients who arrest or are at risk of an imminent arrest.<sup>13</sup> This is why a single 100 mg dose of rt-PA was given to our patient as an IV bolus. In fact, bolus

infusions of thrombolytic therapy were shown to be effective without increasing the risk of bleeding.<sup>13</sup>

The mortality benefit of thrombolytic therapy should be always weighed against the bleeding risk. The mortality benefit of starting systemic fibrinolysis in MPE takes precedence over the risk of developing an intracranial hemorrhage or a major bleed. The major intra-abdominal bleeding that occurred in our case was an inevitable complication of the high-quality CPR performed on our patient after she received a high dose of rt-PA. Despite that, prompt surgical intervention to control the bleeding was initiated leaving our patient neurologically intact at discharge. Although intra-abdominal injuries are much less common than chest wall injuries resulting from chest compressions, they are a quite possible complication. In point of fact, high-quality CPR might result in liver and/or spleen lacerations, gastric dilatation and perforation, intestinal injury, intraperitoneal bleeding, and even retroperitoneal hematomas.<sup>17</sup> The most reported intra-abdominal injury associated with CPR is liver damage, more so in the left lobe, with an incidence of up to 3%.<sup>17, 18</sup>

Another form of advanced therapy used in MPE treatment is ECMO, especially in hemodynamically unstable patients with contraindication to systemic thrombolysis or those who arrest.<sup>15</sup> In fact, the role of ECMO in high risk PE has proven to be highly significant, as it was shown to allow for RV recovery, as well as to give physicians time to observe hemodynamic improvement.<sup>19</sup> ECMO following thrombolytic therapy continues to be a highly variable practice, wherein some studies admitted to cannulation one hour after an infusion of rt-PA 100 mg over two hours, whereas other cannulated less than an hour after two boluses of tenecteplase 50 mg IV push.<sup>15</sup> Further studies are needed to indicate the ideal time and setting for ECMO cannulation when used in conjunction with thrombolytic therapy. ECMO was also shown to be effective in MPE patients who arrest, particularly when combined with systemic fibrinolytics or a catheter-directed therapeutic approach.<sup>15</sup> However, ECMO necessitates full anticoagulation and is hence associated with an increased bleeding risk.<sup>15</sup> In such cases, pulmonary embolism response

teams (PERTs) might help emergency physicians decide upon the optimal therapeutic option for each individual, permitting optimization of PE management.<sup>3</sup> Nowadays, PERTs are being globally recognized as means to provide immediate and individualized expert-based care in cases of acute PE. As a matter of fact, early PERTs adopters have confirmed the feasibility of establishing such teams and advocated their role in facilitating patient access to advanced care.<sup>20</sup>

## CONCLUSION

This case sheds light on the necessity of immediate diagnosis and initiation of thrombolytic therapy in patients with PE, especially unconscious and hemodynamically unstable MPE patients. As for other patients with acute PE, each case must be studied individually with benefits of thrombolysis weighed against the risk of bleeding. In our patient, although we were aware of the risk of bleeding associated with the high dose of rt-PA administered as a bolus, this did not stop us from initiating thrombolysis. Having these bleeding complications in mind, the surgery team was informed and prepared for possible emergent surgical intervention. Missing a case of MPE is fatal and holding thrombolysis in a case as ours would have most probably been fatal too.

*This manuscript has a supplementary video which can be viewed online.*

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