

# Management of Right Ventricular Failure in Acute Pulmonary Embolism

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The management of acute right ventricular (RV) failure in acute pulmonary embolism (PE) differs from RV failure in chronic forms of pulmonary hypertension (PH) such as pulmonary arterial hypertension (PAH). In PE, RV failure generally occurs suddenly and there is far less ability to acutely compensate. Parameters that reflect RV function help predict outcome in PE. The mortality in acute PE leading to shock is very high; when cardiopulmonary arrest occurs, it approaches 100%.

Patients with acute PE must be risk stratified, but no perfect algorithm exists. Certain parameters are predictive of a poor prognosis and should be considered. Treatment decisions for the extremes of presentation are relatively straightforward. Patients with small clot burdens, ie, few segmental or solely subsegmental acute PE, particularly with minimal or no residual deep vein thrombosis (DVT) should be treated with anticoagulation alone. Those with massive PE and shock or significant hypotension should receive aggressive measures, including consideration for thrombolysis. Submassive, or "intermediate-risk" PE, ie, without hemodynamic compromise, has been more controversial. Our focus will be the management of RV failure causing hemodynamic compromise.

## DEFINITIONS

**Massive ("high-risk") PE** is defined by resulting hemodynamic compromise.<sup>1</sup> This is most evident with shock or hypotension requiring pressor therapy. Profound bradycardia may be present. Still, the definition of massive PE includes patients with a systolic blood pressure <90 mm Hg for  $\geq 15$  minutes or a drop in systolic pressure by at least 40 mm Hg from baseline. Thus, massive PE cases vary in severity, ranging from hypotension responding to fluids, to shock with cardiopulmonary arrest.

**Submassive ("intermediate-/moderate-risk") PE:** These patients are normotensive, with evidence of RV dysfunction.

**Nonmassive/minor ("low-risk") PE:** The term "nonmassive" is less than ideal, but implies neither massive nor submassive. (None of these definitions incorporates residual DVT.)

## RISK STRATIFICATION

A comprehensive review is beyond our scope, but it should be emphasized that it has been repeatedly demonstrated that RV dysfunction is a predictor of mortality in acute PE.<sup>2-4</sup> The shock index (defined as heart rate divided by systolic blood pressure) of  $\geq 1$ , has been shown to be an independent predictor of 30-day mortality in acute PE, and may be a

better predictor than systolic blood pressure.<sup>5</sup> Mortality is markedly increased when the pulmonary artery obstruction index is greater than 40%.<sup>6</sup> Brain natriuretic peptide (BNP)/NT-pro-BNP, and troponin reflect RV function, and elevations predict a poorer outcome.<sup>7-8</sup> Not surprisingly, concomitant leg DVT appears to predict higher mortality.<sup>9</sup> Combining these prognostic markers may more reliably predict poor prognosis in acute PE.<sup>10</sup> While controversies regarding aggressive treatment of *submassive* PE patients beyond anticoagulation alone have persisted for decades, taking an aggressive approach for massive PE is not controversial.

We believe that "submassive" PE patients, however, with profound RV enlargement and significant tachycardia likely have a prognosis that more resembles that of massive PE. Those with "submassive" PE, characterized by only mild RV enlargement/hypokinesis and with no residual leg DVT, likely have a much better prognosis.

## RECOGNIZING MASSIVE PE WITH RV FAILURE

Patients with massive PE may merely have hypotension without extreme symptoms. Very extensive PE, eg, saddle emboli, are often associated with severe dyspnea, anxiety, lightheadedness, and syncope. The physical examination can

reveal hypotension, tachycardia, tachypnea, or cyanosis. Signs of acute RV dysfunction include distended neck veins, a parasternal heave, an accentuated P2, and a tricuspid regurgitation murmur. The EKG will often show sinus tachycardia, an S1Q3T3 pattern, T-wave inversions in V<sub>1</sub> to V<sub>4</sub>, or a pseudoinfarction pattern in lead V<sub>1</sub>. A firm diagnosis by lung imaging is ideal, but sometimes therapy is predicated on the clinical setting alone when time does not allow for imaging or other ancillary testing. In all patients with acute PE, rapid, weight-based parenteral anticoagulation should be initiated unless contraindicated.

The general approach to RV failure in acute massive PE includes: (1) supportive therapy and (2) directly addressing the embolic burden. These goals are addressed in tandem as dictated by the clinical setting.

## SUPPORTIVE THERAPY

Supportive therapy consists of fluid and vasopressor management, oxygenation, and when necessary, intubation and mechanical ventilation. Intravenous access should be obtained immediately and oxygen placed and adjusted appropriately. Fluid should be initially administered as a bolus (often 500 to 1000 mL), with the amount determined by perceived hydration status and concomitant cardiovascular disease. Caution is warranted, as excessive fluid administration can worsen RV wall stress and ischemia.<sup>11</sup> Intubation is delayed when possible, as positive pressure can also worsen RV function acutely.

Vasopressor therapy should follow when hypotension persists. No randomized trials have determined the optimal vasopressor for patients with shock due to acute PE. Norepinephrine, dopamine, and epinephrine may be effective. We suggest norepinephrine as the initial agent.<sup>12</sup> Using a combination of dobutamine plus norepinephrine initially may increase myocardial contractility, while minimizing vasodilation and the risk of hypotension. At times, a pure  $\alpha$ -adrenergic receptor stimulant such as phenylephrine succeeds in otherwise refractory cases.

**Extracorporeal Membrane Oxygenation**  
Pulmonary and circulatory support may be required for severely ill patients with massive PE who remain hypotensive with inadequate oxygenation, or with cardiac arrest. Extracorporeal membrane oxygenation (ECMO) decreases RV volume and allows recovery of ventricular function, optimizing oxygen transport by improving cardiac output and oxygen content.<sup>13</sup> Recent systemic thrombolysis increases the risk of placement of ECMO access cannulas, but is not an absolute contraindication depending on the timing and dose. Patients are supported with ECMO with concomitant heparin administration. Importantly, ECMO can facilitate vortex/suction and surgical embolectomy. The time lag for recovery cannot be predicted and ECMO-related complications may occur. Thrombolysis may hasten hemodynamic improvement and enable more rapid weaning from ECMO. Ideally, a rapid response ECMO team is available.

## REDUCING THE EMBOLIC BURDEN

To effectively address severe RV dysfunction, the embolic burden must be acutely reduced. Choices include systemic thrombolysis, catheter-based extraction or clot disruption methods (which can include thrombolysis), and surgical embolectomy. These options depend on the degree of compromise, the rapidity at which deterioration occurs, and the resources available; thus, a case at one institution could be treated differently from an identical case at another facility. However, there are certain scenarios that favor one approach over others.

### *Systemic Thrombolysis*

The clearest indication for systemic thrombolysis is massive PE and shock on vasopressors when there are no absolute contraindications and the patient is too unstable to be moved. Absolute contraindications include scenarios in which incited bleeding could be fatal. The most concerning would be brain, spine, or major organ trauma or surgery. Risk/benefit in a critically ill PE patient may favor systemic thrombolysis despite relative contraindications. The

most common regimen is tissue-type plasminogen activator (tPA) at 100 mg intravenously over 2 hours. A 50 mg infusion has been studied and may be as effective, with less bleeding.<sup>14,15</sup> In patients with extreme shock in whom systemic thrombolysis cannot be given, ECMO should be considered (see below).

### *Catheter-Based Techniques*

A full discussion is beyond our scope. A number of techniques have been approved for clot extraction in certain specific settings, but not all are approved for acute PE. The EkoSonic Endovascular System (EKOS/BTG) was approved May 2014 for ultrasound-assisted thrombolysis, using a much lower thrombolytic dose than would be administered systemically. It is the most extensively studied technique; a randomized clinical trial of submassive PE patients demonstrated more rapid improvement in RV size than with anticoagulation alone (ULTIMA).<sup>16</sup> Another large nonrandomized study, which included predominantly submassive PE as well as cases of massive PE, also demonstrated that RV function was improved compared with baseline (SEATTLE II).<sup>17</sup> The infusion durations were 12 to 24 hours. In massive PE, the degree of illness and rapidity of deterioration must be weighed to determine whether or not a prolonged infusion should be considered.

The Angiovac catheter (Angio-Dynamics Inc.) received expanded FDA approval in March 2014 for venous thromboembolic disease. It utilizes vortex aspiration with a large-bore catheter that offers en bloc aspiration of large thromboemboli.<sup>18</sup> The 22 French cannula can be directed to the main pulmonary arteries, although more distal vessels are not easy to access. It is most commonly used for removing clots from the inferior vena cava and the right heart. This is a large-bore catheter technique and usually requires general anesthesia. A perfusionist and access for the bypass-type circuit are required, as enough blood is removed along with thrombus that recirculation is required. The procedure is generally done in the operating room.

### *Surgical Embolectomy*

In patients with massive PE and absolute contraindications to systemic thrombolysis, surgical embolectomy should be considered if the expertise is available. Recent systemic thrombolysis is a contraindication. In certain situations, such as massive PE with right heart clot-in-transit, surgical embolectomy or vortex clot extraction can be undertaken, although systemic thrombolysis may prove effective in this setting as well. Surgical embolectomy has not been compared to catheter embolectomy or systemic thrombolytic therapy.

In summary, there are several options to reduce the clot burden in massive PE and RV failure. These depend on the degree of RV failure and compromise, and the expertise and resources available.

### **EMPLOYING CLINICAL STRATEGIES: THE PE RESPONSE TEAM**

The PE response team (PERT) is a combined team that rapidly responds to selected acute PE cases, similar to how an ST segment elevation myocardial infarction (STEMI) response team reacts to STEMI.<sup>19</sup> Pulmonary critical care specialists, interventional cardiologists and radiologists, vascular medicine specialists, and dedicated cardiothoracic surgeons are often involved. These experts serve to integrate the information collected by the patient and formulate a plan. When the possibility of massive or submassive PE arises, the team is activated. The decisions surrounding reducing clot burden and supportive care

can be determined in a multidisciplinary manner and may offer a more rapid, experienced, and effective approach.

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