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Techniques in Vascular and Interventional Radiology

Catheter-Directed Thrombolysis for Pulmonary Embolism: The State of Practice

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Acute pulmonary embolism (PE) is a major public health problem. It is the third most common cause of death in hospitalized patients. In the United States, there are up to 600,000 cases diagnosed per year with 100,000-180,000 acute PE-related deaths. Common risk factors include underlying genetic conditions, acquired conditions, and acquired hypercoagulable states. Acute PE increases the pulmonary vascular resistance and the load on the right ventricle (RV). Increased RV loading causes compensatory RV dilation, impaired contractility, tachycardia, and sympathetic activation. RV dilation and increased intramural pressure decrease diastolic coronary blood flow, leading to RV ischemia and myocardial necrosis. Ultimately, insufficient cardiac output from the RV causes left ventricular under-filling which results in systemic hypotension and cardiovascular collapse. Current prognostic stratification strategy separates acute PE into massive, submassive, and low-risk by presence or absence of sustained hypotension, RV dysfunction, and myocardial necrosis. Massive, submassive, and low-risk acute PE have mortality rates of 25%-65%, 3%, and <1%, respectively. Current PE management includes the use of anticoagulation alone, systemic thrombolysis, catheter-directed thrombolysis, and surgical embolectomy. This article will describe the current state of practice for catheter-directed thrombolysis and its role in the management of acute PE.

KEYWORDS pulmonary embolism, venous thromboembolic disease, massive pulmonary embolism, submassive pulmonary embolism, pulmonary embolism severity index, catheter-directed lysis, catheter-directed therapy, embolectomy

Clinical Evaluation of the Patient

The most common clinical presentation of symptomatic pulmonary embolism (PE) is dyspnea, followed by pleuritic chest pain, cough, substernal chest pain, hemoptysis, and syncope.[1-4] Approximately, one-fourth of patients may have associated leg swelling. Several clinical features are predictive of 30-day mortality.[5] These factors are aggregated into scoring schemes, one of them being the PE severity index (PESI) (Table 1).[5] PESI consists of 11 parameters, and if the tallied score places the patient in class 3 or greater, the 30-day mortality risk ranges from 3%-25%. In 2010, a simplified PESI scale was described and validated with single points attributed to age greater than 80 years, presence of heart failure or pulmonary disease, heart rate greater than 110 beats per minute, systolic blood pressure less than 100 mmHg, and oxygen saturation on room air less than 90%.[6] Zero points implies an excellent 30-day prognosis (mortality < 1%). One point or more shows significantly increased 30-day risk.

Based on clinical data that showed higher mortality in acute PE with hypotension and RV dysfunction, the *American Heart Association* issued a guidance document in 2011 that defined the terms massive, submassive, and low-risk PE (Fig. 1).[3] A massive PE is one that causes sustained hypotension (<90 mmHg systolic for >15 minutes), or requires vasopressor support. A submassive PE is one that causes right heart strain, dilation, dysfunction, or ischemia. RV function may be assessed on echocardiography (ECHO). Right ventricle (RV) dilation (RV/left ventricle ratio >0.9) may be assessed on either computed tomography (CT) or ECHO. Elevation in biomarkers (brain natriuretic peptide or troponin) or specific electrocardiographic changes (eg, new complete

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Table Original PESI and Simplified PESI (sPESI) Scales

Parameter	Original PESI (Number of Points)	Simplified PESI (Number of Points)
Age	Actual age #	1 (If greater than 80 years)
Male sex	10	–
Cancer	30	1
Chronic heart failure	10	*
Chronic pulmonary disease	10	*
Pulse > 110 beats/min	20	1
Systolic blood pressure < 100 mm HG	30	1
Respiratory rate > 30 breaths/min	20	–
Temperature < 36°C	20	–
Altered mental status	60	–
Arterial oxygen saturation < 90%	20	1

Classification of original PESI: Class I is less than 65 points, very low 30-day mortality; Class II is between 66 and 85 points, low 30-day morality; Class III is between 86 and 105 points, moderate 30-day mortality; Class IV is between 106 and 125 points, high 30-day morality; Class V is greater than 125 points, very high 30-day morality. Classification of sPESI: 0 points, only 1% mortality; 1 point or more, at least 10% 30-day mortality. *These 2 variables from original PESI are combined into a single parameter in the sPESI, and earn a total of 1 point if at least one is present. The original reference is from Jimenez et al.[6]

or partial right bundle branch block, anteroseptal ST changes, or anteroseptal T-wave inversion), also qualify PE as submassive. A low-risk PE is one that has no associated hypotension or right heart dysfunction or dilation.

Absent in the stratification algorithm is the mention of thrombus location and burden. Central thrombus in the right or left main pulmonary arteries correlates with RV dysfunction and high rate of 30-day mortality.[7] Thrombus burden does not seem to correlate with adverse outcomes.[8]

Indications for Intervention

Current management of acute PE includes anticoagulation alone, systemic thrombolysis with anticoagulation, catheter-directed thrombolysis (CDT) with anticoagulation, or surgical embolectomy. Anticoagulation alone is the treatment of choice for low-risk PE. Treatment escalation in the form of systemic thrombolysis, surgical embolectomy, or CDT is used for massive patients with PE and for select submassive patients with PE. A detailed discussion of surgical embolectomy is outside the scope of this article.

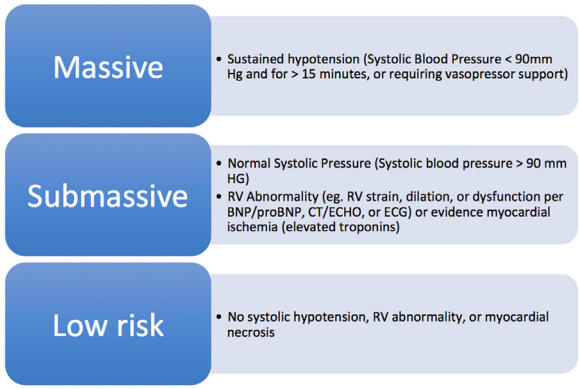

Figure 1 Definition of massive, submassive, and low-risk PE per American Heart Association.[3] Massive, submassive, and low-risk PE are associated with 25%-65%, 3%, and <1% mortality, respectively.

Systemic Thrombolysis

Systemic thrombolysis (ST) refers to the administration of a fibrinolytic drug via a peripheral intravenous line. The most common regimen in the United States is 100 mg of alteplase (tissue plasminogen activator [tPA] infused intravenously over 2 hours.[9] The most widely accepted indication is cardiogenic shock from acute PE. The advantage of ST is its ease of administration.

Data for Systemic Thrombolysis in Massive PE

In a large meta-analysis, systemic thrombolysis in acute massive PE was associated with lower all-cause mortality versus anticoagulation alone.[4] There was, however, also a higher risk of major bleeding and hemorrhagic stroke.

Data for Systemic Thrombolysis in Submassive PE

The *Pulmonary Embolism THrOmbolysis* (PEITHO) study was a randomized controlled trial with 1005 patients with submassive PE.[10] It compared systemic thrombolysis (bolus tenecteplase) and anticoagulation to placebo and anticoagulation. In PEITHO, systemic thrombolysis reduced the risk of hemodynamic decompensation but also increased major hemorrhage and stroke.

Tenecteplase or Placebo: Cardiopulmonary Outcomes At 3 Months (TOPCOAT) was a randomized controlled trial of 83 patients with submassive PE.[11] It compared systemic thrombolysis and anticoagulation to placebo and