

# Aggressive Treatment of Intermediate-Risk Patients with Acute Symptomatic Pulmonary Embolism



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## KEYWORDS

• Pulmonary embolism • Submassive • Intermediate-risk • Thrombolysis • Reperfusion • Prognosis

## KEY POINTS

- Intermediate-risk pulmonary embolism (PE) is defined by hemodynamic stability but the presence of right ventricular dysfunction, myocardial injury, or both.
- Most patients with intermediate-risk PE who receive standard anticoagulation and monitoring have an excellent short-term prognosis.
- Accumulation of factors indicating worse outcomes from PE or early deterioration on standard anticoagulation might alter the risk–benefit assessment in favor of thrombolytic therapy before the development of hemodynamic instability.

## INTRODUCTION

Pulmonary embolism (PE) remains a worldwide major health issue.<sup>1</sup> PE is the most common cause of vascular death after myocardial infarction and stroke, and is the leading preventable cause of death in hospitalized patients.<sup>2</sup> Although contemporary observational data indicate significant reductions in all-cause and PE-related mortality over time,<sup>3,4</sup> the overall short-term mortality rate continues to remain significant and many nonfatal

long-term complications may arise. Guidelines recommend risk stratification of patients with acute symptomatic PE.<sup>5,6</sup> Early prognostication allows clinicians to better determine the level of care (eg, intensive care vs step-down, regular floor, or outpatient treatment) and associated ancillary therapies.

From this perspective, this article provides an overview of the current definition of intermediate-risk PE, followed by a discussion of the available treatments for these patients, focusing on

Disclosure Statements: None.

Declaration of Interests: D. Jimenez has nothing to disclose. B. Bikdeli is supported by the National Heart, Lung, and Blood Institute, National Institutes of Health (NIH), through grant number T32 HL007854. The content is solely the responsibility of the authors and does not necessarily represent the official views of the NIH. B. Bikdeli reports that he serves as an expert (on behalf of the plaintiff) for litigation related to inferior vena cava filters. The content of the current article is not directly related to that litigation.

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Clin Chest Med 39 (2018) 569–581

<https://doi.org/10.1016/j.ccm.2018.04.011>

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thrombolytic therapy. Recently completed and ongoing clinical studies for the treatment of patients with intermediate-risk PE are included. Finally, a practical clinical algorithm that integrates risk stratification and management alternatives is provided.

### DEFINITION OF INTERMEDIATE-RISK PULMONARY EMBOLISM

The definition of intermediate-risk (or submassive) PE has evolved over time (Table 1). The classic

definition of intermediate-risk PE is the presence of either right ventricular (RV) dysfunction or myocardial injury in acute PE without systemic hypotension (systolic blood pressure  $\geq 90$  mm Hg).<sup>6</sup> However, observational studies have suggested that concomitant use of blood biomarkers and imaging markers of RV dysfunction improve the prognostic value over use of either alone.<sup>7-10</sup> Scridon and colleagues<sup>7</sup> enrolled 141 subjects with acute PE and found that those with echocardiographic RV enlargement and elevated troponin

**Table 1**  
Definitions used for stratification of pulmonary embolism

	Definition	Major Studies Using the Definition	Comment
Massive PE or ESC high	Persistent systolic hypotension (systolic blood pressure $< 90$ mm Hg) or cardiogenic shock	Almost all studies	Initial appropriate management, including adequate use of intravenous fluids should be attempted before hypotension is attributed to acute PE
Submassive PE	Presence of RV dysfunction evidence by increased RV/LV ratio on CT or echocardiography	Tenecteplase or Placebo: Cardiopulmonary Outcomes at 3 Months (TOPCOAT) Ultrasound Accelerated Thrombolysis of Pulmonary Embolism (ULTIMA) AINEP Randomized Trial of Inhaled Nitric Oxide to Treat Acute Pulmonary Embolism (INOPE)	Some studies have raised concerns about the prognostic utility of some of the echocardiographic factors, in isolation
Submassive PE	Defined by echocardiography or CT plus biomarkers	Pulmonary Embolism Thrombolysis Trial (PEITHO)	Mortality rate within the first 30 d after randomization of only 3.2% in the placebo group
Moderate PE	Defined by imaging findings	Moderate Pulmonary Embolism Treated with Thrombolysis (MOPETT)	Needs further validation on impact on prognosis
ESC intermediate-high	Absence of hypotension, positive PESI or sPESI but presence of RV dysfunction plus myocardial injury		Needs validation in a management study or RCT
ESC intermediate-low	Absence of hypotension, positive PESI or sPESI, but presence of RV dysfunction or myocardial injury or none		The difference in the risk of death in patients at intermediate to high and intermediate-low risk is not pronounced <sup>146</sup>

*Abbreviations:* AINEP, antiinflamatorios no esteroideos para la embolia pulmonar; ESC, European Society of Cardiology; LV, left ventricle; PESI, Pulmonary Embolism Severity Index; RCT, randomized controlled trial; RV, right ventricle; sPESI, simplified PESI.

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