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## REVIEW

# Update on the risk stratification of acute symptomatic pulmonary thromboembolism<sup>☆</sup>

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### KEYWORDS

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**Abstract** Early mortality in patients with pulmonary thromboembolism (PTE) varies from 2% in normotensive patients to 30% in patients with cardiogenic shock. The current risk stratification for symptomatic PTE includes 4 patient groups, and the recommended therapeutic strategies are based on this stratification. Patients who have hemodynamic instability are considered at high risk. Fibrinolytic treatment is recommended for these patients. In normotensive patients, risk stratification helps differentiate between those of low risk, intermediate-low risk and intermediate-high risk. There is currently insufficient evidence on the benefit of intensive monitoring and fibrinolytic treatment in patients with intermediate-high risk. For low-risk patients, standard anticoagulation is indicated. Early discharge with outpatient management may be considered, although its benefit has still not been firmly established.

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### PALABRAS CLAVE

Tromboembolismo pulmonar;  
Estratificación de riesgo;  
Pronóstico;  
Supervivencia

### Actualización en la estratificación de riesgo del tromboembolismo pulmonar agudo sintomático

**Resumen** La mortalidad precoz en pacientes con tromboembolia pulmonar (TEP) varía desde el 2% en pacientes normotensos al 30% en pacientes con shock cardiogénico. La estratificación actual de riesgo en la TEP sintomática incluye 4 grupos de pacientes y las estrategias terapéuticas recomendadas se basan en dicha estratificación. Los pacientes que se presentan con

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inestabilidad hemodinámica se consideran de alto riesgo y en ellos se recomienda el tratamiento fibrinolítico. En pacientes normotensos, la estratificación de riesgo ayuda a diferenciar entre aquellos de bajo riesgo, riesgo intermedio-bajo y riesgo intermedio-alto. Actualmente no existe suficiente evidencia sobre el beneficio de una monitorización intensiva y tratamiento fibrinolítico en pacientes con riesgo intermedio-alto. En pacientes de bajo riesgo, está indicada la anticoagulación estándar y podría considerarse la posibilidad de un alta precoz con manejo ambulatorio, aunque su beneficio no está todavía firmemente establecido.

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## Background

Pulmonary thromboembolism (PTE) results from the partial or total occlusion of the pulmonary vascular bed by a detached thrombus (embolus) of the deep venous system, usually of the legs.

Acute symptomatic PTE is the most severe manifestation of venous thromboembolism (VTE), whose overall incidence rate is 131 per 100,000 individuals/year, causing PTE in 45.9% of cases.<sup>1</sup> PTE causes 0.52% of hospital admissions, which represents a high healthcare cost in Spain.<sup>2</sup>

The clinical presentation of PTE can vary. The mortality of a PTE that starts as cardiopulmonary arrest (1% of cases) is 70%. If the PTE presents as shock or arterial hypotension requiring inotropic agents (5% of cases), the risk of mortality is 30%, while for normotensive patients the risk declines to 2%.<sup>3-5</sup>

A recent study of the Computerized Registry of Patients with Venous Thromboembolism (RIETE) assessed the mortality of acute PTE. In 23,858 patients treated during a 12-year period, an overall mortality rate at 30 days of 5.9% was observed, with a significant declining trend, both for secondary to any cause (from 6.6% between 2001 and 2005 to 4.9% between 2010 and 2013) and for PTE-induced (from 3.3% to 1.8% in the same periods).<sup>6</sup>

## Prognostic stratification of patients with pulmonary thromboembolism

To reduce PTE mortality, it is essential to differentiate patients at high risk of adverse events from those at low risk, to indicate the most effective and efficient therapeutic alternatives in each case. Therefore, the management guidelines for massive and submassive PTE of the American Heart Association (AHA),<sup>7</sup> the 9th edition of the antithrombotic therapy guidelines of the American College of Chest Physicians (ACCP)<sup>5</sup> and the latest guidelines of the European Society of Cardiology (ESC)<sup>8</sup> recommend stratifying patients according to their early mortality risk (in-hospital or during the first 30 days) into 3 categories: low, intermediate and high risk, depending on a number of risk markers and prognostic scales. The national consensus on the diagnosis, risk stratification and treatment of patients with PTE<sup>9</sup> was published in Spain in 2013 and supports these same recommendations.

The hemodynamic situation at the onset of PTE has the greatest prognostic significance for short-term mortality. Patients with hypotension<sup>5,7</sup> (systolic blood pressure <90 mm Hg) or hemodynamic shock are considered at high risk. Therefore, after confirming the diagnosis through transthoracic echocardiography or thoracic multidetector computed tomography angiography (CTA), the clinical guidelines and expert recommendations propose systemic fibrinolytic therapy if the hemorrhagic risk is not high.<sup>5,7,8</sup>

After confirming the PTE with a multidetector CTA or lung scintigraphy, clinical prognostic scales are employed for hemodynamically stable patients to stratify the risk, classifying patients into low to intermediate risk groups. For low-risk patients, standard anticoagulation is indicated. Early discharge with outpatient management may be considered.<sup>5,7,8</sup>

The most complex patient group to stratify is the intermediate risk group. These are hemodynamically stable patients in their presentation, who can undergo subsequent hemodynamic instability as a consequence of a thromboembolic recurrence or an impairment in right ventricular (RV) function. Therefore, risk stratification is currently focused on differentiating (within the normotensive patient group with intermediate risk) those at low risk of early complications (low-intermediate risk) from those at high risk of adverse events (intermediate-high risk).<sup>4,8,10-13</sup> The recommendation for intermediate risk patients is the combination of prognostic tools that assess RV dysfunction, myocardial ischemia, cardiomyocyte stress or thrombotic burden, to thereby identify those with intermediate-high risk who could benefit from intensive monitoring and reperfusion therapy (rescue fibrinolysis) if hemodynamic decompensation occurs.

## Prognostic clinical models

A number of prognostic tools are employed to stratify the risk for patients with acute symptomatic PTE, mainly clinical scales, biological markers and imaging tests. In particular, to identify patients with low-risk PTE, clinical prognostic scales have shown an excellent negative predictive value (NPV) and are inexpensive and simple to apply. The scales include clinical parameters that can be obtained quickly and require no special skills or training.

Two meta-analyses were published in 2012 and 2014 on the performance of clinical scales for predicting early mortality after PTE.<sup>12,14</sup> The meta-analyses analyzed 9 and 11

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