



# Management of acute pulmonary embolism: towards a (truly) global reach

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The study by Z. Zhai and colleagues provides an overview of the developments observed as risk-adapted management strategies for acute pulmonary embolism have been progressively introduced and optimised in the Chinese healthcare system <https://bit.ly/3swGht2>

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The risk-adapted management of acute pulmonary embolism (PE) is a teenager transitioning into adulthood. Over the past 10 years, we have experienced a revolution in the way we treat this disease, as reflected by the evolving recommendations of the European guidelines on PE [1–3]. The most remarkable advances concerning the treatment of the acute stage of PE included the approval of new classes of oral anticoagulant drugs [4], the optimisation of clinical criteria to select patients for early discharge [5–7], novel evidence on systemic [8] and catheter-directed [9] thrombolysis, and the establishment of multidisciplinary pulmonary embolism response teams [10].

Albeit rapid, this process has not been homogeneous. Rather, it has predominantly involved a few high-income countries in Europe and Northern America, where novel management strategies were developed, introduced in clinical practice, and have been the subject of continuous optimisation. Indeed, encouraging signals of a decreasing PE-related mortality and fatality primarily came from high-income countries and regions [11–14]. Even within individual countries, these trends may have disproportionately affected the regions and institutions that applied novel evidence most readily, and the patient subgroups who had a better access to care [12, 15–17]. Consistently, the reported increase in PE incidence in several countries and regions [4] may paradoxically represent a positive signal, reflecting favourable developments that included growing awareness of venous thromboembolism among physicians, patients and policymakers, as well as more sensitive and timely diagnoses.

Inequalities in the prevention and management of other cardiovascular conditions have been targeted in global programmes to fill gaps in prevention and treatment [18]. In this respect, research and practice in acute PE have been lagging behind. Indeed, a necessary condition for large-scale programmes to be designed and implemented has not yet been fulfilled: no focused analyses of the distribution and magnitude of inequalities in management across world regions are available, and the global cause-specific burden of lost healthy life years and economic productivity remains unclear [19]. In this context, China may spearhead the development of the body of evidence needed to address this knowledge gap. Its dramatic social and economic development over the past decades makes this country well representative of similar fast-growing middle-income countries, both in Asia and other continents. Indeed, these developments have been mirrored by a massive increase in scientific production [20]. Only recently, however, and mostly thanks to the combination of national initiatives and the efforts of individual institutions and researchers, has this increased scientific output reached the field of PE management and outcomes.

The study by ZHAI *et al.* [21] represents one of the largest individual patient level analyses of practice-based data on acute PE in China. The authors analysed the trends in risk stratification,

management and outcomes of 7438 patients with acute PE admitted at more than 100 medical centres over 6 years. Its findings provide an overview of the developments observed as risk-adapted management strategies are progressively introduced and optimised in a healthcare system. This included broader use of diagnostic tools, fine-tuning the use of reperfusion treatment, and gradual establishment of the role of novel oral direct anticoagulants. These advances may have contributed to a progressive reduction of all-cause and PE-related fatality, similar to what was observed in some European countries [4].

This study provides an important piece of information concerning in-hospital fatality in patients with acute PE in China [21]. Considerable controversy was sparked by the question whether a similar trend observed in European countries, in the USA, and in China itself [22, 23] reflected more diagnoses of low-risk PE (such as incidental and subsegmental PE) secondary to a broader use of high-quality imaging tests, particularly in patients with cancer and chronic cardiopulmonary diseases. ZHAI *et al.* [21] demonstrated that this might have also been the case in China, with more low-risk patients, according to the simplified Pulmonary Embolism Severity Index, diagnosed over time. However, these authors also showed a similar increase in prevalence for patients belonging to the other extreme of the PE severity spectrum, namely those with haemodynamic instability. Indeed, these data on fatality are consistent with prior national estimates on PE-related fatality [23].

Some trends are strikingly similar or aligning to what has been described in some Western countries. The decreasing use of thrombolytic and reperfusion treatment, the predominant role of computed tomography angiography for PE diagnosis, and the progressively older age of PE patients at diagnosis all echo previous reports from other continents. A point of specific interest for practitioners is the confirmation of the prognostic significance of well-studied clinical factors and laboratory parameters reflecting the severity of PE and the burden of comorbidities. Despite not representing a formal validation, this is reassuring as regards the applicability of risk assessment models and algorithms for risk stratification of acute PE, in epidemiological and healthcare contexts as different from those so far explored as it gets.

The decrease in fatality rate was less evident among haemodynamically unstable patients, who represent a minority of the whole PE population but suffer from the highest mortality. How to better manage acute PE patients with (or at high risk of) haemodynamic decompensation remains one of the priorities of the global PE research agenda for the next decade [4]. Available evidence that contributed to set this course includes interventional studies initiated and conducted in China that studied the optimisation of systemic thrombolysis regimens for acute PE [24–26].

A number of devices and novel reperfusion strategies deemed to be as effective as and safer than standard-dose systemic thrombolysis are now available. These approaches proved to swiftly relieve the obstruction in the pulmonary circulation in acute PE patients with right ventricular dysfunction [27]. Their widespread use in Europe [28] and North America [29] anticipated the proof from large clinical trials, notably the Ultrasound-facilitated, Catheter-directed, Thrombolysis in Intermediate-high Risk Pulmonary Embolism (HI-PEITHO; NCT04790370) and the Pulmonary Embolism International Thrombolysis Study-3 (PEITHO-3; NCT04430569), which will test whether these strategies are able to improve important early and late clinical outcomes [27]. It will be interesting to observe how China and other developing economic powers will position themselves with respect to the development and implementation of these novel treatment strategies.

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