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WHAT'S NEW IN INTENSIVE CARE

What's new in severe pulmonary embolism?

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Introduction

Severe pulmonary embolism (PE) remains a major cause of mortality. For intensivists managing the most "severe" forms of PE, we highlight the main recent advances in the care of such patients including risk stratification, diagnostic algorithms, general supportive care, and reperfusion therapy.

Quickly identify patients presenting with severe PE but also patients with intermediate-high-risk PE

Severe or high-risk PE is defined by cardiac arrest, or persistent hypotension (i.e., systolic blood pressure < 90 mmHg or a systolic pressure drop by 40 mmHg, for > 15 min, if not caused by new onset arrhythmia, hypovolemia, or sepsis) accompanied by signs of end-organ hypoperfusion [1–3]. High-risk PE represents less than 5% of all acute PE and constitutes a medical emergency, associated with a 15–50% risk of in-hospital death, particularly during the first hours after admission [1–3]. Among initially hemodynamically stable patients, about 10% may suffer early clinical and hemodynamic deterioration, with an overall in-hospital mortality risk close to 50% [3, 4]. Risk stratification of acute PE patients allows physicians to identify such patients with an elevated risk of death or major complications [4]. Advanced risk stratification with the combination of clinical variables (i.e., tachycardia, mild hypotension, hypoxemia, age, and previous cardiorespiratory disease) using the PE severity index (PESI) or its simplified version (sPESI) [4], biomarkers reflecting myocardial dysfunction or injury, and imaging of right ventricular (RV) dysfunction allows one to identify the clinically stable patients with the highest risk of subsequent deterioration (intermediate-high-risk patients) who might benefit from intensive monitoring and even recanalization procedures (Supplementary Fig. 1) [1–4].

Interpret isolated RV dilatation with caution

Computed tomography pulmonary angiography (CTPA) is principally recommended to confirm PE in patients presenting with shock and suspected PE. If CTPA is not immediately available or the patient is too unstable to be transferred to the radiology department, bedside transthoracic echocardiography is mandatory to rapidly diagnose signs of RV overload and potential thrombi in the right cavities. Isolated RV enlargement, however, should be interpreted with caution in patients admitted to the ICU who may have other causes of RV dilatation, especially mechanical ventilation [1, 3, 5]. Recent animal data suggest that RV dilatation is commonly diagnosed after cardiac arrest, irrespective of the cause (PE, hypoxia, or arrhythmia) [5].

Think about VAECMO and catheter-directed thrombolysis after discussion with multidisciplinary pulmonary embolism response teams (PERT)

The medical management principles of patients with severe PE are based upon support of the failing heart, prompt debulking and reperfusion therapy, anticoagulation by unfractionated heparin, all coordinated by the joint efforts of a multidisciplinary PERT (Fig. 1) [1–3, 6].

General supportive care

Despite the lack of clinical trials, guidelines recommend the following supportive care [3]:

1. First, to use volume expansion cautiously. Indeed, too much fluid may worsen acute RV failure by increasing RV overload and ischemia and left ven-

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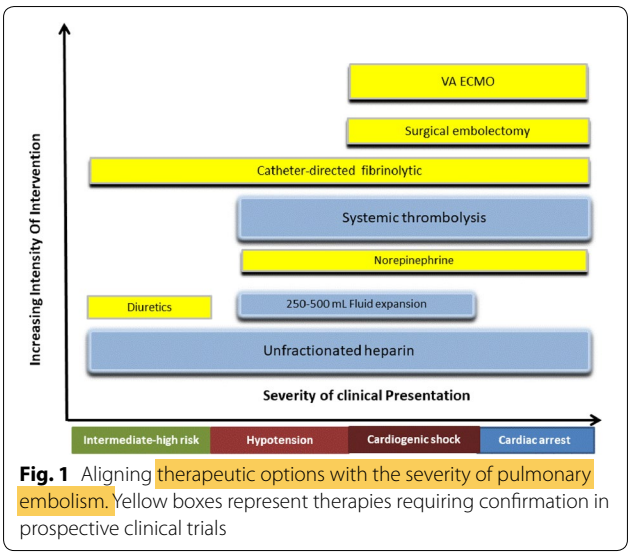

Fig. 1 Aligning therapeutic options with the severity of pulmonary embolism. Yellow boxes represent therapies requiring confirmation in prospective clinical trials

tricular compression by an enlarged RV. Furthermore, in intermediate-high-risk patients, it has been reported that diuretic treatment (compared with volume expansion) as initial management may improve RV function without increasing the risk of adverse clinical events [7]. A randomized multicentric trial (NCT02268903) is ongoing in intermediate-high-risk PE patients to assess the clinical benefit of diuretics on admission.

2. To use norepinephrine infusion to improve RV function if necessary, when blood pressure is low. Some patients remain clinically unstable because they are not amenable to reperfusion therapies or do not improve after this treatment. In these situations of refractory cardiogenic shock, veno-arterial extracorporeal membrane (VAECMO) may optimize end-organ function as a bridge to recovery or pulmonary vascular recanalization [8–10]. Indeed, a few small-sized studies report overall survival rates up to 85% with VAECMO [8, 9]. The most recent study reported a 90-day survival rate of 95% in 20 patients with high-risk PE who received early VAECMO implantation [9]. These patients were critically ill and highly unstable: their median SOFA was 9.0 (6.5–12.5), 75% had mechanical ventilation, and 25% had cardiac arrest. Of note, among the 20 patients, 15 received reperfusion therapies. Prospective analyses are needed to further elucidate the role and timing of VAECMO for severe PE.

Reperfusion therapy is crucial

In high-risk PE, systemic thrombolysis, using conventional doses, is associated with a significant reduction in PE-related mortality (OR 0.15, 95% CI 0.03–0.78) and a significant reduction of the combined endpoint death or treatment escalation (OR 0.18, 95% CI 0.04–0.79) [10]. In a population-based study of high-risk PE presenting with cardiac arrest, thrombolysis was associated with increased survival (OR = 12.5, 95% CI 1.8–89.1, $P = 0.01$) [11]. For patients with severe PE at high risk of bleeding, clinicians might consider the use of low-dose thrombolytic therapy, catheter-directed thrombolysis, or surgical embolectomy if they have access to the required expertise and resources [1, 3, 6]. Of note, guidelines take into consideration both the risks but also the expected benefits of a treatment modality in a specific clinical setting, when proposing absolute or relative contraindications to its use [3, 6]. Catheter-directed thrombolysis has the potential to offer the advantage of systemic thrombolysis while minimizing bleeding risk. Several techniques representing promising options for clearing pulmonary thrombi from the larger arteries have been reported (Supplementary Table 1). However, most studies were observational and small in size. The size of the populations or the design of the studies did not allow any conclusion on mortality. Additional studies are warranted before the use of such systems can be routinely recommended.

Surgical pulmonary embolectomy remains an option; however, the need to transfer the patient in the operating theatre and the need for sternotomy have decreased the use of the technique. The most recent series on patients with severe and intermediate-high-risk PE report in-hospital survival rates ranging from 67.9% to 91.0%, even in patients presenting with cardiac arrest [12]. In intermediate-high-risk PE patients, catheter-directed therapies and thrombolytic therapy may be considered in case of clinical deterioration [1, 3, 6].

Decreasing role of inferior vena cava (IVC) filters

Non-randomized studies report that IVC filters improve survival in patients with hemodynamically unstable PE [1–3, 13, 14]. These findings were not confirmed in the most recent meta-analysis; the use of an IVC filter on top of anticoagulation did not decrease PE-related mortality nor all-cause mortality, compared to anticoagulation alone [13]. Thus, current evidence does not support the use of IVC filters in severe PE patients unless there is a contraindication to anticoagulation [13, 14].

Ask the PERT in difficult clinical cases

In patients with contraindication to systemic thrombolysis or with remaining cardiogenic shock despite systemic thrombolysis, optimal first-line therapy is difficult to define because of the lack of scientific evidence from specific trials. Working with PERT (combining expertise from interventional cardiology, interventional radiology, cardiac surgery, cardiac imaging, and critical care) will

help generate a consensual multidisciplinary approach in such difficult situations [13, 15].

Electronic supplementary material
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