






# Mechanical circulatory support in acute pulmonary embolism

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## KEYWORDS

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Acute pulmonary embolism (PE) is a life-threatening condition caused by the thromboembolic obstruction of pulmonary arteries, which often leads to haemodynamic instability, right ventricular failure, and potentially death. Patients with massive or high-risk PE are particularly vulnerable and may not respond to conventional treatments, necessitating the implementation of mechanical circulatory support. Here, we discuss recent advancements in the diagnosis and multidisciplinary management of patients with high-risk PE and highlight the need for rapid and personalized treatment strategies.

## Introduction

Acute pulmonary embolism (PE) is a common, life-threatening condition caused by the obstruction of pulmonary arteries, most often due to blood clots. The clinical presentation of PE varies widely, ranging from asymptomatic to severe cases involving shock and, in some instances, sudden death. Annual incidence rates of

overall PE cases according to epidemiological data range from 39–137 per 100 000 population per year and have been going up during the last decades.<sup>1–3</sup> In epidemiological studies in the USA, an increase in proportion of high-risk cases from 3.4% (1999) up to 7.2% (2014) of all hospitalized cases has been reported, while in Germany, it remained stable around 8.9% (2005–15).<sup>2,3</sup> Patients are classified as high-risk when their acute PE is accompanied by haemodynamic instability, such as cardiac arrest, obstructive shock, systolic blood pressure below 90 mmHg, or the requirement of vasopressors to maintain blood pressure. In cases where patients with

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high-risk PE cannot be stabilized by conventional therapies, mechanical circulatory support (MCS) becomes crucial. Mechanical circulatory support devices, including extracorporeal membrane oxygenation (ECMO) or percutaneous mechanical pumps, provide temporary circulatory and respiratory support while definitive treatments such as thrombolysis, interventional embolectomy, or surgical embolectomy are planned or performed. Here, we discuss recent advancements in the diagnosis and management of patients with high-risk PE, with an emphasis on emerging strategies and clinical structures that enhance patient outcomes.

### Pathophysiology of pulmonary embolism-mediated shock

Acute PE is most frequently caused by the thrombo-embolic obstruction of pulmonary arterial vessels, with the majority of emboli stemming from the deep veins of the lower extremities. This obstruction interferes with both circulation and gas exchange.<sup>4</sup> Clinical symptoms usually manifest once the occlusion blocks a significant fraction of the cross-sectional area of pulmonary arteries (30–50%), which leads to a marked increase in pulmonary artery pressure (PAP). This is further exacerbated by the subsequent release of vasoactive mediators such as thromboxane A<sub>2</sub> and serotonin,<sup>5</sup> and hypoxic vasoconstriction triggered by the Euler-Liljestrand mechanism. Collectively, these events cause an abrupt increase in pulmonary vascular resistance and, consequently, right ventricular (RV) afterload.<sup>6</sup>

The ability of the right ventricle to adapt to acute volume and pressure overload is limited, as it can only generate a mean PAP around 40 mmHg.<sup>4</sup> To compensate, the RV prolongs its contraction time and a neurohormonal release triggers inotropy and chronotropy by increasing wall tension and myocyte stretch. However, the heightened oxygen demand and prolonged dilation ultimately induces RV ischaemia and myocardial inflammation, resulting in a significant decrease in RV output. Elevated biomarkers like NT-pro-BNP and troponin have been identified as reliable diagnostic indicators of myocardial stress during acute PE and are associated with adverse early mortality.<sup>7</sup>

Given that left ventricular (LV) preload is directly dependent on RV output, ongoing RV failure leads to decreased LV filling and consequently, diminished cardiac output (CO).<sup>4</sup> In invasive diagnostics, this decline can be shown by cardiac index (CI) deterioration. Clinically, this systemic hypotension acts as a key haemodynamic measure and indicator of obstructive shock and, if left untreated, can progress to loss of circulation, cardiac arrest, and ultimately death. These adverse outcomes in acute PE can be further aggravated by gas exchange disturbances and respiratory failure that are primarily driven by reduced cardiac output, increased venous blood desaturation, and hypoxaemia caused by a ventilation/perfusion mismatch in the lungs.<sup>8</sup>

Acute RV failure, as described above, often leads to rapid deterioration of patient health.<sup>9</sup> Therefore, patients presenting with suspected PE plus haemodynamic instability (defined by one of the following: cardiac arrest; obstructive shock; systolic blood pressure < 90 mmHg or requirement of vasopressors to stay at  $\geq 90$  mmHg) are

classified as high-risk PE cases. In these potentially life-threatening instances, rapid and reliable diagnostic and therapeutic strategies are essential for patient survival.

### Disease-oriented diagnostics and immediate monitoring of pulmonary embolism

Effective management of PE also relies heavily on precise diagnostics and vigilant monitoring. Due to its rapid onset and potentially life-threatening nature, a systematic approach is essential to promptly identify and treat PE to ultimately improve patient outcomes. While reviewing patient history and conducting a physical examination are critical in identifying risk factors and clinical signs of PE during the initial assessment, specific diagnostic tools are also fundamental for accurate patient stratification and guiding appropriate therapy.<sup>4</sup>

Computed tomography (CT) is the gold standard of imaging and offers high sensitivity and specificity for diagnosing PE. As such, CT allows for direct visualization of clots within the pulmonary arteries and can assess the extent of these embolisms.<sup>10</sup> Importantly, CT can also provide key information regarding risk stratification via the RV/LV ratio. An RV/LV ratio > 1 is associated with a two- to three-fold increase in one-month mortality risk.<sup>11</sup>

Trans-thoracic echocardiography (TTE) serves as another valuable imaging tool for patients with suspected PE as it allows for the immediate assessment of RV function.<sup>12</sup> Similar to CT, an RV/LV ratio > 1 via echocardiography correlates with an increased one-month death risk, together with a tricuspid annular plane systolic excursion (TAPSE) value below 16 mm.<sup>13</sup> Given the speed with which ultrasound imaging, such as TTE, can assess RV function, these tools are particularly advantageous in critical, time-sensitive situations and influence acute patient management and decision-making. Furthermore, TTE and/or transoesophageal echo are potentially superior in situations when in-transit thrombi are present that require specific interventions.<sup>4</sup> Bedside echocardiography is also vital during intermediate high-risk re-evaluation at 24–48 h post-PE onset. According to the recent European Association of Percutaneous Cardiovascular Interventions consensus, a TAPSE value below 16 mm and/or an RV/LV ratio value > 1 observed during the 24–48 h re-evaluation may indicate the need for interventional treatments such as catheter-directed therapy (CDT).<sup>14,15</sup>

Serial assessment of biomarkers such as troponins, B-type natriuretic peptide (BNP), and lactate, can provide additional prognostic information for PE risk stratification and monitoring treatment response. Lactate (arterial or venous) is an important surrogate marker of cardiogenic shock and should be evaluated to distinguish between intermediate-high- and high-risk patients. This marker is also key in evaluating the efficacy of thrombolytic treatments.<sup>16</sup>

Lastly, although invasive haemodynamic monitoring is usually not a part of routine practice, it can play an important role in guiding interventional treatment. Extended haemodynamic monitoring is particularly useful for differentiating between acute PE and acute on chronic pulmonary hypertension, especially in patients

with chronic obstructive pulmonary disease. It also helps with interpreting the mismatch between thrombus burden in CT imaging and RV function. Finally, MCS also relies heavily on invasive haemodynamic parameters during the weaning process.<sup>17</sup>

### **Role of the Heart Team/Pulmonary Embolism Response Team in decision-making in patients with intermediate/high-risk pulmonary embolism and pre-shock**

Effective management of intermediate- and high-risk PE, especially in patients presenting with pre-shock or shock, necessitates a multidisciplinary approach to optimize patient outcomes.<sup>18</sup> The Pulmonary Embolism Response Team (PERT) and the Heart Team play pivotal roles in this process by fostering collaboration among specialists from various medical fields to provide comprehensive and individualized patient care.

Pulmonary Embolism Response Team is typically composed of cardiologists, pulmonologists, intensivists, emergency medicine physicians, haematologists, radiologists, and vascular surgeons.<sup>18,19</sup> This diverse group of healthcare professionals allows for the rapid and coordinated response that is required for the acute management of PE. In acute emergency scenarios or outside of typical office hours, the immediate availability of multiple specialists is often limited. In current clinical practice, these decisions are, therefore, frequently made by smaller teams or even single members of the PERT. While some institutions apply a step-by-step approach of involving different specialties, they still adhere to response algorithms pre-implemented by PERT for a rapidly coordinated, personalized care. Comparably, the Heart Team, traditionally involved in the management of complex cardiac conditions such as coronary artery disease and valvular heart disease, consists of cardiologists, cardiothoracic surgeons, anaesthesiologists, and often intensivists. Given the significant overlap in medical expertise, the Heart Team concept is now also being applied to manage severe PE cases.

Upon presentation, patients with suspected PE undergo an initial assessment involving clinical evaluation, imaging (e.g. computed tomography pulmonary angiography), and laboratory tests (e.g. D-dimer levels).<sup>4</sup> The European Society of Cardiology (ESC) and the American Heart Association guidelines stratify PE into low-, intermediate-, and high-risk categories based on clinical presentation and RV function. Intermediate-risk PE is characterized by RV dysfunction without haemodynamic instability, while high-risk PE involves haemodynamic instability, such as shock or hypotension. In these cases, timely decision-making is critical for improving patient outcomes. Thus, both PERT and the Heart Team engage in multidisciplinary discussions to evaluate patient condition, review diagnostic findings, assess risk factors, and consider comorbid conditions. This collaborative approach ensures thorough evaluation of patient health status, consideration of all potential treatment options, and selection of individualized approaches that are tailored to patient risk profiles and clinical presentations.

Treatment options for intermediate and high-risk PE include anticoagulation, systemic thrombolysis, CDT, surgical embolectomy, or implementation of MCS.<sup>4</sup> In

patients with pre-shock or shock, rapid intervention is crucial. The Heart Team or PERT can expedite decision-making and facilitate immediate access to advanced therapies, which might include MCS as a bridge to more definitive treatment or urgent CDT or surgical embolectomy.<sup>20</sup>

Research indicates that implementing PERT and Heart Team approaches in PE management leads to improved outcomes.<sup>20</sup> Benefits that have been identified include:

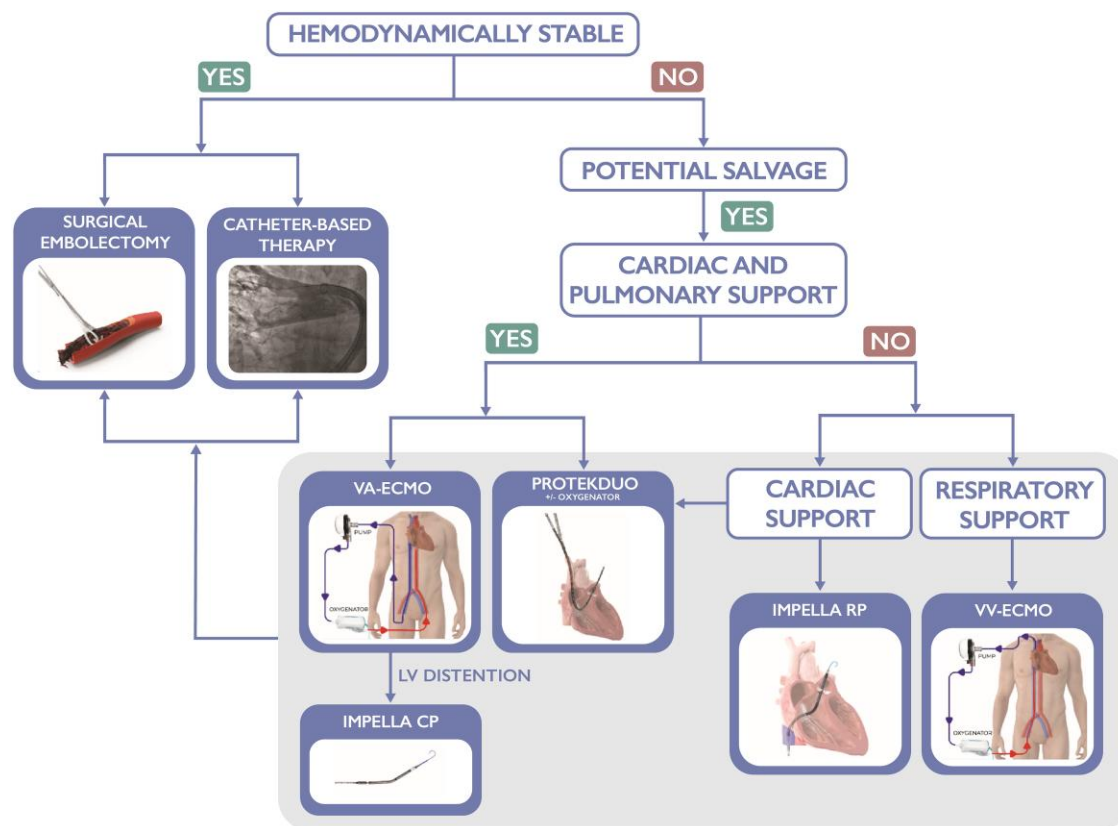
- Reduced mortality: prompt, co-ordinated care reduces the time to definitive treatment, decreasing mortality rates.
- Improved utilization of advanced therapies: multidisciplinary teams are more likely to employ advanced therapies appropriately.
- Personalized care: a team-based approach ensures that treatment is tailored to the specific needs and risk profiles of individual patients.

However, despite the clear benefits of PERT and the Heart Team, there are still challenges that prevent widespread implementation of these collaborative groups. First of all, not every institution has the resources to establish such teams and as previously mentioned, reducing acute decision-making to few specialists might be necessary and beneficial in extremely urgent situations. Second, communication and co-ordination among team members are crucial but can be challenging, especially in fast-paced clinical environments. Lastly, standardizing training and developing protocols for team operation are essential for consistent, effective team operation, and widespread implementation, which is still lacking.

Future directions include expanding the use of telemedicine for remote consultations, conducting further research on the efficacy of different treatment modalities, and developing predictive models to better stratify patients. Moreover, as healthcare continues to evolve, the integration of team-based approaches will be crucial in managing complex medical conditions like PE. Together, the Heart Team and PERT have clearly demonstrated an essential role in the management of intermediate/high-risk PE and patients in pre-shock or shock. Their multidisciplinary approach enhances decision-making, optimizes treatment strategies, and improves patient outcomes (*Figure 1*).

### **State of the art treatment options and decision-making**

Accurate diagnostics and vigilant monitoring have always been critical in guiding PE management, but their importance has grown as treatment decision-making has become increasingly complex over time. Historically, anticoagulation and reperfusion through systemic fibrinolytic treatment have been the cornerstones of therapy for acute PE, while catheter-directed treatment (CDT) and surgical embolectomy have been reserved only for specific high-risk situations. Recently, however, a paradigm shift has occurred with the growing availability of CDT options, adding difficulty to the decision-making-process in acute settings. In response to these developments, multidisciplinary PERT have gained popularity, optimizing decision-making in high-risk PE



**Figure 1** Pathway to decision-making in PE management. LV, left ventricle; PE, pulmonary embolism; VA-ECMO, veno-arterial extracorporeal membrane oxygenation; VV-ECMO, veno-venous extracorporeal membrane oxygenation. *Figure 1* created with BioRender.com.

cases.<sup>21</sup> In line with increasing treatment complexity, a recent meta-analysis found that PERT involvement is associated with more frequent use of advanced PE treatments and shorter hospital stays.<sup>21</sup>

Multidisciplinary approaches and advanced treatments play a key role in managing high-risk patients with PE. As such, ~50% of patients with high-risk PE present after initial cardiopulmonary resuscitation, often with complicating factors like anaemia, malignancies, or thrombocytopenia that elevate bleeding risk.<sup>3,22</sup> Thus, systemic thrombolysis is frequently impeded. Two recent registry studies from the USA and Germany show that only 30% and 25% of patients with high-risk PE received systemic fibrinolytic treatment, respectively, despite a class IB recommendation in the current guidelines.<sup>3,22</sup> In contrast, CDT is an option for reperfusion treatment even for patients with elevated bleeding risk, contraindications for systemic thrombolysis, or those requiring MCS devices. Recent non-randomized data support the use of interventional therapy in intermediate-high<sup>22,23</sup> and high-risk PE cases,<sup>24</sup> showing reduced mortality after CDT. Additionally, large-bore thrombectomy seems to be associated with improved outcomes.<sup>25</sup> Similar to CDT, surgical embolectomy has demonstrated efficacy in treating PE,<sup>26</sup> but its use is limited to specialized centres with advanced expertise. Thus, until data from adequate randomized trials become available, PERTs will remain of particular importance for treatment decision-making in PE. Current

guidelines particularly encourage the use of MCS as a treatment or bridging option for high-risk PE, PE-related shock, or when complex interventional or surgical reperfusion is planned.<sup>4</sup>

### Mechanical circulatory support in acute pulmonary embolism

The recent ESC guidelines suggest that patients with high-risk PE who are experiencing circulatory collapse or cardiac arrest may benefit from the use of temporary MCS devices. These potential benefits are seen in survival rates, haemodynamic stabilization, and/or as a bridge to definitive therapy or recovery.<sup>4</sup> The primary objective of MCS in these cases is to manage acute RV failure and, in some instances, concomitant LV failure. Mechanical circulatory support is especially considered when these conditions present refractory to medical treatment.

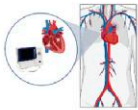



Mechanical circulatory support implementation decisions should be consensus-driven and guided by a multidisciplinary PERT.<sup>27,28</sup> When selecting the optimal MCS strategy, patients should benefit from an individually tailored approach that considers the specific characteristics of the given case. This approach must consider the nature of the PE (acute vs. acute-on-chronic), haemodynamic status, shock phenotype (isolated RV failure vs. biventricular failure), organ failure (respiratory and/or cardiac), the

availability and feasibility of other therapeutic options (e.g. thrombolysis or embolectomy), the experience of the operator and the institution, as well as patient comorbidities and life expectancy.<sup>29</sup>

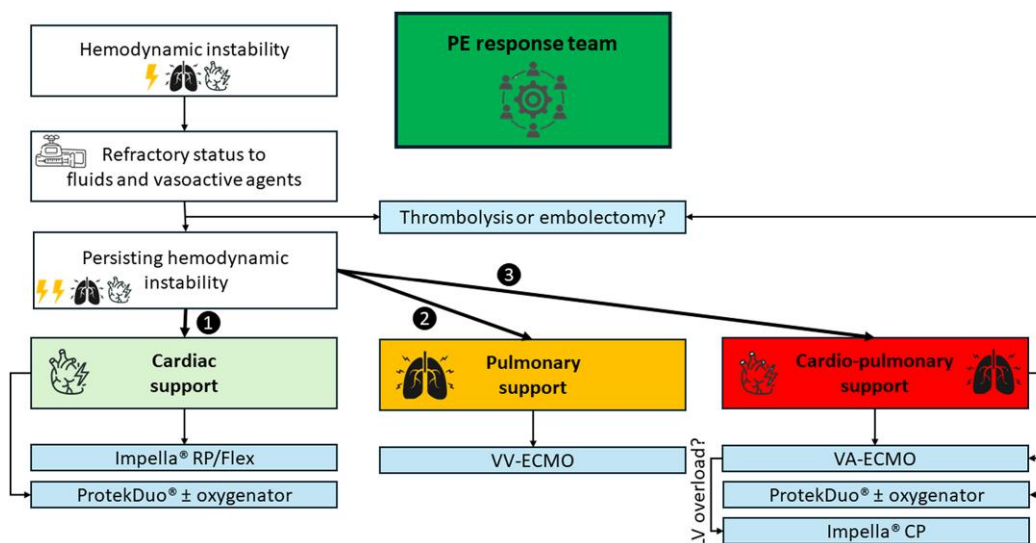
Currently, MCS options include right ventricular assist devices (RVADs), with or without an oxygenator, and veno-arterial extracorporeal membrane oxygenation (VA-ECMO) for biventricular support.<sup>30,31</sup> To date however, there are no randomized controlled trials (RCTs) evaluating the efficacy and safety of these devices in patients with high-risk PE, and there are no established selection criteria for use. Existing evidence demonstrates significant variations in applied MCS strategies with the majority of centres employing MCS as a rescue therapy during cardiac arrest, while others implement MCS prophylactically upon diagnosing high-risk PE.<sup>32</sup> Irrespective of the timing of MCS use, awareness of potential major complications, including bleeding, ischaemia, neurological injury, thromboembolism, and cannulation-related injury is critical for ensuring patient safety.<sup>33</sup>

More specifically, a benefit of using RVADs is the ability to bypass the RV thereby facilitating blood circulation from the right atrium to the pulmonary artery. This reduces central venous pressure (CVP), increases PAP, and enhances overall cardiac output. Percutaneous

RVADs include devices such as the Impella RP/Flex (Abiomed, Danvers, MA) and the ProtekDuo (CardiacAssist Inc., Pittsburgh, PA, USA), while surgical RVADs include devices like the CentriMag (Abbott Vascular, Green Oaks, IL, USA). The Impella RP/Flex (Abiomed, Danvers, MA) system lacks additional oxygenation capabilities and may be ineffective in severely obstructed pulmonary arteries, but other systems like ProtekDuo and CentriMag allow for additional oxygenation. However, the main limitation of RVAD use derives from the heightened risk of pulmonary haemorrhage, particularly in patients who have previously received thrombolytic therapy. Additionally, fluoroscopic guidance is required for interventional RVAD placement. However, a primary advantage of catheter-directed RVADs is that they require only venous access, avoiding the need for surgical procedures or large-bore arterial access and therefore offering a suitable option for patients with an already heightened bleeding risk. Nonetheless, existing data or large-scale studies on outcome after RVAD use in high-risk PE are scarce. One of the few multicentre studies, involving only 30 patients with RV failure, demonstrated adequate safety and haemodynamic stabilization with Impella RP.<sup>34</sup> A summary of MCS devices for use in PE is provided in [Figure 2](#).<sup>12</sup>

Percutaneous				Surgical
	Impella RP	ProtekDuo	VA-ECMO	RVAD
				
<b>Flow</b>	<4 L	4-6 L	4-6 L	4-6 L
<b>Mechanism of Action</b>	Microaxial Flow Pump	Centrifugal Pump	Centrifugal Pump	Centrifugal Pump
<b>Implantation</b>	<b>Sheath Size</b>	23 Fr	29 Fr 31 Fr	A: 15-19 Fr V: 21-25 Fr
	<b>Access Site</b>	Femoral Vein	Jugular Vein	Femoral/ Axillary Artery + Femoral/ Jugular Vein
<b>Visualization</b>	Fluoroscopy + Echocardiography	Fluoroscopy + Echocardiography	Echocardiography	-
<b>Respiratory Support</b>	No	Yes (Possible)	Yes	Yes (Possible)
<b>Mobilisation</b>	Partial	Full	Partial-Full	Partial-Full (if chest closed)
<b>Advantage</b>	Small venous only access	Venous only access	Biventricular support	Post-cardiotomy

**Figure 2** Mechanical circulatory system support devices in PE. A, artery; L, litre; PE, pulmonary embolism; RVAD, right ventricular assist device; VA-ECMO, veno-arterial extracorporeal membrane oxygenation; V, vein. [Figure 2](#) created with BioRender.com.



**Figure 3** Proposed approach for managing patients with high-risk pulmonary embolism and circulatory collapse using mechanical circulatory support. ECMO, extracorporeal membrane oxygenation; LV, left ventricular; PE, pulmonary embolism; VA, veno-arterial; VV, veno-venous.

Currently, VA-ECMO is the most utilized MCS device in patients with high-risk PE. It redirects blood from the right atrium to the iliofemoral artery system, providing an indirect RV bypass, and resulting in reduced CVP and PAP, while facilitating biventricular support and oxygenation of blood. One benefit of utilizing VA-ECMO is the ability to deploy outside of the operating room and cardiac catheterization laboratory, making it an accessible device for timely haemodynamic stabilization. The primary drawback of VA-ECMO, however, is the requirement for large-bore arterial access, which potentially elevates risk of bleeding and limb ischaemia. A recent extensive meta-analysis revealed a 40% mortality rate in high-risk PE cases treated with VA-ECMO, with a better prognosis observed in patients undergoing concomitant surgical embolectomy.<sup>35,36</sup>

Weaning patients off these MCS devices poses a challenge and requires deliberate timing within a clinical context. If RV function fails to recover, patients risk progressing into a refractory state of shock. Weaning typically entails the incremental reduction of the device support level under close surveillance of haemodynamic and respiratory responses. During this process, parameters such as blood and pulse pressures, echocardiographic markers of RV and LV function, and invasive haemodynamic measurements (e.g. CVP, pulmonary capillary wedge pressure, pulmonary artery pulsatility index, CO, and/or CI) should be evaluated, as well as surrogates of systemic perfusion (e.g. lactate levels and/or urine output) and dependency on vasoactive agents.<sup>37</sup> Patients who remain stable with minimal mechanical support for several hours are considered ready for device removal.

In summary, the landscape of treating PE is evolving and MCS devices are currently the only option in rescuing haemodynamically unstable patients with high-risk PE. The choice of MCS device for high-risk PE patients should be made on a case-by-case basis, considering the unique clinical features and haemodynamic status of each patient (Figure 3). RVADs, such as the Impella RP/Flex and ProtekDuo, offer the advantage of venous access

and are effective in reducing CVP and improving cardiac output, but they lack oxygenation capabilities and carry risks like pulmonary haemorrhage, especially in patients with thrombolysis. Veno-arterial extracorporeal membrane oxygenation, on the other hand, provides comprehensive biventricular support and oxygenation, making it suitable for more severe cases, but it requires large-bore arterial access, which increases bleeding risk and limb ischaemia. While both devices have shown potential benefits in observational studies, the lack of large-scale RCTs leaves a gap in definitive evidence regarding their efficacy and safety. Future research, including robust RCTs, is essential to establish clear guidelines and improve outcomes for patients with high-risk PE requiring MCS devices.

## Conclusion

The management of acute PE, especially in high-risk patients with haemodynamic instability, continues to evolve with the advancement of diagnostic tools, multidisciplinary approaches, and MCS devices. Pulmonary Embolism Response Team and Heart Team collaborations have become essential in optimizing treatment strategies, expediting decision-making, and improving patient outcomes. Future research focused on refining MCS protocols and expanding the implementation of multidisciplinary care models will be crucial in improving the survival rates and recovery of these high-risk PE patients.

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## Data availability

No new data were generated or analysed in support of this research.

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