The PERSEVERE Trial: Advancing Evidence in High-Risk PE

Global Principal Investigators discuss the design and impact of a randomized trial evaluating the FlowTriever System versus standard of care for high-risk pulmonary embolism.

With Stavros V. Konstantinides, MD, PhD, and Nicolas Meneveau, MD, PhD

Stavros V. Konstantinides, MD, PhD
Center for Thrombosis and Hemostasis (CTH)
University Medical Center of the Johannes Gutenberg-University Mainz
Mainz, Germany
stavros.konstantinides@unimedizin-mainz.de

Nicolas Meneveau, MD, PhD
Department of Cardiology
University Hospital Besançon Franche-Comté
Besançon, France
SINERGIES, University Marie & Louis Pasteur
Besançon, France
F-CRIN, INNOVTE Network
nicolas.meneveau@univ-fcomte.fr

The PERSEVERE trial is enrolling patients with high-risk, or massive, pulmonary embolism (PE). As the Global Principal Investigators for PERSEVERE, please explain the unmet need behind the study. What are the gaps in existing literature that you are aiming to address, and why is a randomized trial in this patient population important?

Prof. Konstantinides: High-risk PE is classically defined by "hemodynamic instability" based on persistently low arterial blood pressure or collapse, necessitating cardiopulmonary resuscitation. It is associated with a very unfavorable early prognosis, with in-hospital mortality rates ranging from 20% to 50%, and rising to almost 85% if cardiac arrest occurs. Of all patients with acute PE, these are the patients who most urgently need effective life-saving treatment, but this is also the PE risk class with the largest knowledge gaps regarding optimal management to date. The only "high-level" evidence to back existing guideline recommendations in this risk category comes from a single randomized, prematurely terminated trial of eight patients, published in 1995, which claimed superiority of intravenous streptokinase (a thrombolytic agent no longer used in most countries) compared to unfractionated heparin.[1] This is totally insufficient and outdated, and should not be accepted as "evidence" in the second quarter of the 21st century. Moreover, many patients with high-risk PE also have contraindications against thrombolytic drugs and consequently do not receive any advanced reperfusion treatment in the real world, with physicians hoping that anticoagulation alone and catecholamines will save the life of the affected patient.

Today, the most important unanswered questions concerning the science and the practice of high-risk PE management are:

- How is high-risk PE best defined? Is the old, blood pressure–based definition of the European Society of Cardiology (ESC) dating back to 2019 adequate,[2] or should the definition of shock expand to include threatening decompensation and so-called "normotensive shock," as is already the case for other forms of cardiogenic shock? Should we place more focus on early signs of tissue hypoxia instead of waiting for the systemic blood pressure to fall?
- Is intravenous alteplase treatment effective and safe in patients with PE and shock (risk classes E1-E2 in the latest American Heart Association [AHA]/American College of Cardiology [ACC]

guidelines[3])? If yes, which regimen is better: 100 mg over 2 hours or 0.6 mg/kg (with a maximum of 50 mg) over 10 to 15 minutes?
- Large-bore mechanical thrombectomy (LBMT) has been demonstrated to effectively remove the bulk of proximal thrombus in massive PE, but can it improve the early clinical outcome of patients with high-risk PE? Can it perhaps also improve long-term outcomes in terms of persisting symptoms, late PE sequelae, functional status, quality of life, and return to work/previous activities?
- Can up-front integration of extracorporeal membrane oxygenation (ECMO) into the management strategy further contribute to improving early outcomes?
- What is the best way to design and execute a contemporary, state-of-the-art randomized controlled trial (RCT) to evaluate and define the success of a modern advanced treatment strategy in high-risk PE, apart from simply comparing 7-day or 30-day mortality?

As the first landmark RCT in this critical setting, in which every minute counts, PERSEVERE was designed to specifically address these clinical and scientific questions.

Prof. Meneveau: The PERSEVERE trial was designed to address a major therapeutic gap in the management of acute high-risk, or massive, PE. Although current international guidelines recommend systemic thrombolysis as the standard reperfusion strategy for high-risk PE, the evidence base supporting this recommendation remains surprisingly limited.[2] This creates a clear mismatch between the severity of the condition and the strength of the data guiding treatment.

Another major gap is that systemic thrombolysis is often underused in real-world practice because of bleeding concerns, especially intracranial hemorrhage, and contraindications (eg, recent surgery, advanced age, active cancer, active bleeding). As a result, only a minority of unstable patients actually receive thrombolysis, leaving a majority of patients undertreated. At the same time, LBMT has emerged as a promising catheter-based alternative that may achieve rapid clot removal and right ventricular unloading with potentially less bleeding, but the available data have mostly come from registries, single-arm studies, or nonrandomized comparisons.

PERSEVERE is an ambitious study that faces numerous challenges, particularly the difficulty of conducting a randomized trial in a population of unstable patients. The urgent need to coordinate care and the issue of obtaining consent from patients who may be on respiratory or circulatory support have led to significant reluctance to include them in such a prospective study. The very definition of high-risk PE encompasses a broad spectrum of clinical presentations, ranging from arterial hypotension to cardiac arrest, including obstructive cardiogenic shock. It is therefore essential to best define the population that is likely to benefit from a pulmonary revascularization strategy in combination with hemodynamic support therapies, including circulatory assistance. Furthermore, the multidisciplinary care of these patients complicates the implementation of such a strategy. All of these challenges have dampened enthusiasm for conducting a randomized trial in the setting of high-risk PE. Promising preliminary data on a percutaneous thromboaspiration approach offer a unique opportunity to make progress in this field, as no randomized trials have been conducted in this context for 30 years.

PERSEVERE is therefore important because it is the first adequately powered RCT specifically focused on high-risk PE. It aims to provide robust comparative evidence on both efficacy and safety, helping clinicians move beyond expert opinion and observational data toward a more evidence-based treatment strategy for this critically ill population.

The rationale and design of the trial were recently published in *American Heart Journal*.[4] Can you describe the design of the PERSEVERE study? What arms will patients be randomized to, and how long is the follow-up?

Prof. Meneveau: PERSEVERE is a multinational, open-label, randomized controlled superiority trial evaluating whether LBMT with the FlowTriever System (Stryker Peripheral Vascular) is superior to standard of care in patients with acute high-risk PE.[4] The trial plans to enroll approximately 200 patients across up to 40 sites in Europe and the United States, with randomization in a 1:1 ratio. Although the treatment assignment is known to investigators and treating teams, the adjudication of the primary and safety outcomes is performed by a blinded clinical events committee, and safety is further overseen by an independent data safety monitoring board.

Eligible patients are adults with acute proximal PE of recent onset, evidence of right ventricular dysfunction, and features consistent with high-risk disease (eg, hypotension, vasopressor requirement, markedly elevated lactate with signs of obstructive shock, need for ECMO, resuscitated cardiac arrest). After randomization, all patients receive therapeutic anticoagulation in addition to their allocated treatment strategy. The study's target population covers the broad spectrum of the clinical presentations of high-risk PE and incorporates the most advanced circulatory support strategies. In particular,

patients on ECMO are not excluded, which should allow for evaluation of therapeutic strategies combining reperfusion and hemodynamic support. Once again, the inherent difficulties of conducting a randomized trial in unstable patients requiring urgent care led us to limit exclusions to cases of refractory cardiac arrest with a low Glasgow Coma Scale score or those at very high risk of bleeding so as not to disadvantage the control group. The approach is pragmatic and closely aligned with everyday clinical situations.

The two treatment arms are straightforward. In the experimental arm, patients undergo LBMT using the FlowTriever System. In the control arm, patients receive standard of care according to local practice, which may include systemic thrombolysis, surgical embolectomy, ECMO as stand-alone therapy, or anticoagulation alone. Importantly, catheter-directed thrombolysis (CDT) is not allowed as an initial therapy in the control arm, although it may be used as bailout treatment if needed.

The primary endpoint is assessed through hospital discharge or 7 days after randomization, whichever comes first. Patients are then followed for 3 months to capture mortality, functional recovery, quality of life, readmissions, and post-PE impairment.

Prof. Konstantinides: In PERSEVERE, patients are randomized 1:1 to LBMT using the FlowTriever System or standard of care (including systemic thrombolysis, surgical embolectomy, or possibly anticoagulation alone). Key inclusion criteria include a proximal pulmonary filling defect and at least one of the following: (1) persistent systolic hypotension or need for vasopressors, (2) tissue hypoxia as indicated by venous lactate ≥ 4 mmol/L along with clinical signs suggesting obstructive shock, or (3) need for ECMO support prior to randomization. Patients with resuscitated cardiac arrest and return of spontaneous circulation may also be included if they have regained consciousness and have no evident persistent neurological deficits.

The trial's primary composite outcome includes (1) all-cause mortality, (2) cardiac arrest necessitating cardiopulmonary resuscitation, (3) bailout to an alternative therapeutic strategy, and (4) major bleeding, all occurring until hospital discharge or day 7 after randomization (whichever comes first), as well as (5) ECMO in place on day 7 after randomization. Follow-up over 90 to 120 days ensures a comprehensive assessment of dyspnea severity and the patient's functional status and quality of life using established, standardized scales and questionnaires. In addition, 6-minute walking distance, postpulmonary impairment, and return to work or previous status are prospectively documented at the end of the follow-up period.

Patients in the standard-of-care arm can receive a few different primary therapies. How was it decided which therapies would be allowed? Is there a reason CDT was not included as a primary therapy option?

Prof. Konstantinides: The explicit aim of PERSEVERE is to compare LBMT with the current standard of care in patients in the high-risk class of acute PE. Although an increasing number of centers in the United States, Europe, and globally do choose to perform LBMT in patients with acute high-risk PE, systemic thrombolysis remains the standard of care in high-risk PE, at least in patients without absolute contraindications to this type of treatment. Theoretically, intravenous thrombolysis offers several important advantages as it is broadly available and standardized and can be initiated within minutes, requiring neither specific operator skills and experience nor emergency mobilization of qualified personnel and hospital equipment. On the other hand, and as emphasized above, patients with high-risk PE often have contraindications against thrombolytics and consequently do not receive reperfusion treatment. This fact was also taken into account in defining the standard-of-care treatment arm in PERSEVERE.

CDT is usually given over 7 to 24 hours depending on local protocols, and this treatment duration may be too long for patients with overt hemodynamic instability and collapse.

Prof. Meneveau: The standard-of-care arm in PERSEVERE was intentionally designed to reflect contemporary real-world management of high-risk PE rather than an artificially narrow comparator. In practice, although systemic thrombolysis is the guideline-recommended first-line reperfusion strategy, clinicians frequently individualize treatment according to bleeding risk, local expertise, surgical availability, severity of shock, and whether extracorporeal support is needed. For that reason, the control arm permits the therapies that are already accepted in routine care and supported by current guideline frameworks: systemic thrombolysis, surgical embolectomy, anticoagulation alone, and ECMO as a stand-alone support strategy. This design increases the external validity of the trial and makes the comparison more clinically relevant across a broad range of hospitals and health care systems.

The decision to not include CDT as a primary therapy option appears deliberate and methodologically important. First, the study specifically aims to compare LBMT against current standard of care in high-risk PE, not against every catheter-based technology. Because CDT is itself a device-based reperfusion strategy, including it as a routine primary option in the control arm would

blur the mechanistic distinction between the two strategies and make the trial harder to interpret. Second, CDT is not a standard primary approach in this protocol, although it remains available as bailout therapy if the patient deteriorates or fails to improve.

This approach preserves a cleaner comparison: LBMT as the tested interventional strategy versus conventional accepted management. It also ensures that escalation to CDT is still possible for patient safety, while counting such escalation as a clinically meaningful failure of the initial assigned treatment.

Regarding the eligibility criteria, PERSEVERE appears to allow for enrollment of patients with high lactate but who are hemodynamically stable, in contrast with the current ESC guideline definition of high-risk PE that requires hemodynamic instability.[2] What factors led to the inclusion of such patients?

Prof. Konstantinides: Although arterial hypotension is a clear sign of hemodynamic instability, it is not the only, and most of all, not the earliest sign of failing of the circulation. Before the human body "gives up" systemic blood pressure—its last line of defense for maintaining perfusion of vital organs—tissue hypoxia may already be present despite apparently normal blood pressure levels. These patients are *not* hemodynamically stable as often regarded in the past; rather, they are already manifesting early or "normotensive" shock, corresponding to class B in the updated Society for Cardiovascular Angiography & Interventions shock classification pyramid.[5] It is important to emphasize and make clear to the medical community that shock and, consequently, high-risk PE, or any other acute cardiovascular syndrome, are not all-or-none phenomena. It covers an entire spectrum of escalating circulatory insufficiency and, ultimately, overt failure and collapse. Besides testing LBMT with the FlowTriever System for patients with high-risk PE, the inclusion criteria of PERSEVERE help advance our understanding of what is really "high risk," evolving from the 2019 European guidelines definition[2] and learning from the evidence that has accumulated in recent years.

Prof. Meneveau: One of the most interesting features of PERSEVERE is that it broadens the operational definition of high-risk PE beyond overt hypotension alone. The trial allows enrollment of patients with a venous lactate level of ≥ 4 mmol/L plus clinical signs suggesting obstructive shock or hypoperfusion, even if blood pressure is still preserved. The rationale is that hemodynamic collapse in PE is often a continuum rather than a binary event. Some patients compensate temporarily and remain normotensive despite already having significant right ventricular failure, impaired cardiac output, and tissue hypoperfusion. If one waits for frank hypotension to occur, the opportunity for earlier reperfusion may be missed.

We deliberately chose a lactate threshold of 4 mmol/L, which is higher than the 2.5 mmol/L threshold referenced in current European guidelines.[2] Our reasoning is clearly explained in the design paper.[4] Data from the FLASH registry suggest that lactate values around 2.5 mmol/L are relatively common even among intermediate-risk PE patients and are not necessarily associated with the extreme risk profile targeted in this trial.[6] By contrast, lactate levels near 4 mmol/L have been associated with mortality in cardiogenic shock populations, making this threshold more specific for severe circulatory compromise.

We also note that a substantial proportion of patients with clinical obstructive shock may be normotensive at presentation. Including such patients therefore reflects the biological reality of high-risk PE and may identify a subgroup most likely to benefit from rapid reperfusion before irreversible decompensation occurs. In that sense, the eligibility criteria are designed to capture true severity earlier and more precisely than blood pressure alone.

What considerations contributed to the design of the primary endpoint in PERSEVERE?

Prof. Meneveau: The primary endpoint of PERSEVERE is a composite clinical endpoint assessed through the earlier of hospital discharge or 7 days after randomization. It includes five adjudicated components: all-cause death, cardiac arrest requiring cardiopulmonary resuscitation, bailout to an alternative therapeutic strategy, major bleeding defined by Bleeding Academic Research Consortium criteria, and ECMO still in place on day 7. This is a deliberately pragmatic and clinically rich endpoint that captures both efficacy and safety in a patient population where deterioration can occur rapidly and where treatment decisions often involve escalation of support.

Several design considerations shaped this endpoint. First, mortality alone would be too narrow and may underrepresent clinically important treatment failures, especially in a trial of feasible size. High-risk PE patients can survive yet still experience catastrophic deterioration, require bailout reperfusion, or remain dependent on ECMO. Including these events makes the endpoint more sensitive to meaningful differences between strategies. Second, major bleeding was incorporated because the trial is not simply testing whether one approach removes clot more effectively; it is also evaluating whether reperfusion can be achieved with an acceptable

safety profile. That is especially important when comparing a mechanical strategy to therapies such as systemic thrombolysis that carry substantial bleeding risk.

The bailout component is also highly relevant. In this setting, needing to switch therapies or urgently escalate support reflects failure of the initial strategy. Likewise, ECMO dependence at day 7 signals persistent severe cardiopulmonary compromise. Overall, the endpoint is well aligned with the realities of high-risk PE; it focuses on short-term, hard clinical events while balancing survival, hemodynamic stabilization, rescue interventions, and bleeding.

Prof. Konstantinides: When designing the PERSEVERE trial, particular attention was given to defining a composite primary endpoint that would both be scientifically rigorous and reflect and inform contemporary state-of-the-art treatment of acute high-risk PE. Thus, besides the "classic" outcomes of death, cardiac arrest necessitating cardiopulmonary resuscitation, and major bleeding, the primary endpoint also includes bailout to an alternative strategy and ECMO life support in place on day 7 after randomization. Bailout comprises (1) initiation of unplanned ECMO support at any time prior to or on day 7, or any ECMO use beginning > 6 hours after randomization; (2) unplanned use of additional mechanical, pharmacomechanical, or pharmacologic catheter-based therapies, systemic thrombolytics, or surgical thrombectomy; and (3) changing from the assigned treatment strategy (ie, between LBMT and systemic thrombolytics). ECMO use planned from the beginning as an adjunctive means to support LBMT or standard of care, depending on the randomly assigned treatment, is considered an endpoint *only* if it needs to be maintained at least 7 days postrandomization.

The choice of these outcomes criteria defining the primary endpoint supports a carefully planned, up-front multimodal treatment strategy and, at the same time, takes into account adjustments in the treatment plan that often need to be made early and fast in such a rapidly changing emergency situation. In this regard, it defines a time window after which the initially assigned treatment and adjunctive supportive measures can be considered to have failed to reverse the shock.

The meticulously elaborated criteria for reaching the primary endpoint are one of the greatest strengths of PERSEVERE and may set a standard for evaluating therapies in acute high-risk PE in future trials.

What are the potential impacts of the PERSEVERE trial on this patient population? How might the study change how patients with high-risk PE are managed?

Prof. Konstantinides: As explained previously, the trial's design, and particularly its primary endpoint, supports a carefully planned, up-front, state-of-the-art multimodal treatment strategy that accounts for and supports the treatment adjustments that must be made early and fast in a rapidly changing emergency situation. Thus, PERSEVERE is expected to inform and define the future standard of care in the management of acute high-risk PE, aiming at fast relief of right ventricular pressure overload and reversal of shock through catheter-based thrombus removal—to be aided, if necessary, by mechanical support of oxygenation and circulation.

Prof. Meneveau: If PERSEVERE shows that LBMT is superior to current standard care, its impact on the management of high-risk PE could be substantial. At present, clinicians treating these patients face a major dilemma. Systemic thrombolysis is recommended in guidelines, yet many patients are poor candidates because of bleeding risk or formal contraindications. As a result, treatment pathways vary widely across institutions, and decisions are often based on local expertise, availability of surgical or catheter-based teams, and clinician preference rather than high-level comparative evidence. A positive PERSEVERE trial could help reduce this uncertainty.

The most immediate effect would likely be on reperfusion strategy selection. If LBMT improves the composite of death, cardiac arrest, bailout therapy, major bleeding, and persistent ECMO dependence, it could become a more prominent first-line option for appropriately selected patients with high-risk PE, particularly those in whom thrombolysis is hazardous or unlikely to be used. Because the trial also evaluates longer-term outcomes such as quality of life, functional recovery, readmission, and post-PE impairment, it may also shift the field away from focusing only on short-term survival and toward a more comprehensive view of recovery.

More broadly, the study could influence guideline updates, multidisciplinary PE response team algorithms, and hospital resource planning. It may encourage earlier recognition of obstructive shock, faster transfer to centers capable of advanced reperfusion, and more structured treatment pathways. Even if the trial does not definitively establish LBMT as superior, it should still provide a much stronger evidence base for comparing strategies in a population that has historically been managed with limited randomized data.

The field of PE is an area of active research, with several randomized trials currently underway. Are there any other PE studies that you are excited about right now?

Prof. Meneveau: This is a particularly exciting moment in PE research because the field is finally moving from registry-driven evidence and toward randomized comparative trials. Beyond PERSEVERE itself, one of the most important recent studies is PEERLESS, which compared LBMT with CDT in intermediate-risk PE.[7] Although that trial focused on a different risk category than PERSEVERE, it is highly relevant because it reflects the broader trend toward evaluating whether mechanical reperfusion can provide meaningful clinical advantages without increasing bleeding. The fact that PEERLESS demonstrated lower rates of clinical deterioration or bailout therapy and reduced intensive care unit utilization makes it an important signal for the field.

I am also encouraged by the continued maturation of the FLAME and FLASH data sets[6,8] These studies are not randomized in the same way as PERSEVERE, but they have been influential in showing that thrombectomy can be performed with acceptable safety and promising hemodynamic results, including in some patients with high-risk PE. They helped establish the biological plausibility and feasibility that made a trial like PERSEVERE possible.

Importantly, it has to be noted that at least two additional randomized trials in high-risk PE are ongoing (NCT06833827, NCT06672081). This is very encouraging because no single study will answer every question in such a complex population. Taken together, these efforts suggest that the next few years could transform PE management by clarifying which reperfusion strategy is best for which patient, and under what clinical circumstances.

Prof. Konstantinides: A number of major, guideline-relevant RCTs are currently underway that are evaluating different catheter-based procedures in patients with acute PE. In high-risk PE, the results of TORPEDO-NL and CATCH-PE are expected to support and complement those of PERSEVERE. In intermediate-risk PE, HI-PEITHO, PEERLESS II, PRAGUE-26, and PE-TRACT will help assess the benefits of CDT or mechanical thrombectomy, focusing on both early and long-term clinical outcomes. In only 2 to 3 years, the world of PE will be totally different!

What do you hope to see in the future regarding treatment guidelines and patient care in the PE space?

Prof. Konstantinides: I strongly hope and expect that PERSEVERE, together with the other major RCTs in intermediate- and high-risk PE currently underway, will inform future guidelines by helping validate not only individual catheter procedures but also integrated multimodal treatment strategies for the risk categories of severe PE as originally defined by the ESC guidelines in 2014 and 2019 and recently revisited by the 2026 ACC/AHA guidelines.[2,3,9] "Colorful" risk stratification tables in guideline texts are meaningless as standalone elements. They will become truly relevant and useful for clinicians only if they can be accompanied by strong evidence-based recommendations on how to treat patients in a given risk class, particularly when it comes to the risk classes that describe severe acute PE in which the patient's life directly depends on rapidly choosing the most effective and safest procedures and measures.

Prof. Meneveau: Looking ahead, I hope treatment guidelines in PE become both more evidence-based and more nuanced. For high-risk PE in particular, current recommendations still rely heavily on limited randomized evidence. As trials like PERSEVERE mature, guidelines should be able to move beyond broad statements and offer clearer patient-centered recommendations about when to choose systemic thrombolysis, MT, surgery, ECMO-supported strategies, or combinations of these approaches.

I also hope future guidance will better recognize that severe PE is not defined only by overt hypotension. The PERSEVERE design reflects an important clinical reality: Some patients have profound right ventricular dysfunction and tissue hypoperfusion before blood pressure falls. Incorporating markers such as lactate, shock physiology, right ventricular dysfunction, and early clinical trajectory into risk stratification could help identify patients who would benefit from earlier reperfusion, rather than waiting for frank collapse.

From a patient-care perspective, I would like to see more standardized multidisciplinary pathways, especially through PE response teams, so that unstable patients can be assessed rapidly and routed toward the most appropriate therapy without delay. Just as important, I hope the field continues to expand its focus beyond in-hospital survival alone. Outcomes such as functional recovery, quality of life, post-PE impairment, and readmissions matter greatly to patients and should increasingly shape both trials and guidelines.

Ultimately, the goal is more personalized PE care: treatment strategies matched to bleeding risk, severity, anatomy, and local expertise, supported by robust randomized evidence rather than tradition alone. ■

1. Jerjes-Sanchez C, Ramírez-Rivera A, de Lourdes García M, et al. Streptokinase and heparin versus heparin alone in massive pulmonary embolism: a randomized controlled trial. J Thromb Thrombolysis. 1995;2:227-229. doi: 10.1007/BF01062714. PMID: 10608028.
2. Konstantinides SV, Meyer G, Becattini C, et al; ESC Scientific Document Group. 2019 ESC guidelines for the diagnosis and management of acute pulmonary embolism developed in collaboration with the European Respiratory Society (ERS). Eur Heart J. 2020;41:543-603. doi: 10.1093/eurheartj/ehz405

3. Creager MA, Barnes GD, Giri J, et al. 2026 AHA/ACC/ACCP/ACEP/CHEST/SCAI/SHM/SIR/SVM/SVN guideline for the evaluation and management of acute pulmonary embolism in adults: a report of the American College of Cardiology/American Heart Association joint committee on clinical practice guidelines. Circulation. Published online February 19, 2026. doi: 10.1161/CIR.0000000000001415
4. Chopard R, Hobohm L, Barco S, et al. Large-bore mechanical thrombectomy vs standard of care for acute high-risk pulmonary embolism: rationale and design of the PERSEVERE randomized controlled trial. Am Heart J. 2026;294:107331. doi: 10.1016/j.ahj.2025.107331
5. Naidu SS, Baran DA, Jentzer JC, et al. SCAI SHOCK stage classification expert consensus update: a review and incorporation of validation studies: this statement was endorsed by the American College of Cardiology (ACC), American College of Emergency Physicians (ACEP), American Heart Association (AHA), European Society of Cardiology (ESC) Association for Acute Cardiovascular Care (ACVC), International Society for Heart and Lung Transplantation (ISHLT), Society of Critical Care Medicine (SCCM), and Society of Thoracic Surgeons (STS) in December 2021. J Am Coll Cardiol. 2022;79:933-946. doi: 10.1016/j.jacc.2022.01.018
6. Bangalore S, Horowitz JM, Beam D, et al. Prevalence and predictors of cardiogenic shock in intermediate-risk pulmonary embolism. Insights from the FLASH registry. JACC Cardiovasc Interv. 2023;16:958-972. doi: 10.1016/j.jcin.2023.02.004
7. Jaber WA, Gonsalves CF, Stortecky S, et al. Large-bore mechanical thrombectomy versus catheter-directed thrombolysis in the management of intermediate-risk pulmonary embolism: primary results of the PEERLESS randomized controlled trial. Circulation. 2025;151:260-273. doi: 10.1161/CIRCULATIONAHA.124.072364
8. Silver MJ, Gibson MC, Giri J, et al. Outcomes in high-risk pulmonary embolism patients undergoing FlowTriever mechanical thrombectomy or other contemporary therapies: results from the FLAME study. Circ Cardiovasc Interv. 2023;16:e013406. doi: 10.1161/CIRCINTERVENTIONS.123.013406
9. Konstantinides SV, Torbicki A, Agnelli G, et al; Task Force for the diagnosis and management of acute pulmonary embolism of the European Society of Cardiology (ESC). 2014 ESC guidelines on the diagnosis and management of acute pulmonary embolism. Eur Heart J. 2014 ;35:3033-69, 3069a-3069k. Published corrections appear in Eur Heart J. 2015;36:2666 and Eur Heart J. 2015;36:2642. doi: 10.1093/eurheartj/ehu283

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