Role of catheter-directed therapies in the treatment of acute pulmonary embolism. Expert opinion of the Polish PERT Initiative, Working Group on Pulmonary Circulation, Association of Cardiovascular Interventions, and Association of Intensive Cardiac Care of the Polish Cardiac Society

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ABSTRACT

Thanks to advances in interventional cardiology technologies, catheter-directed treatment has become recently a viable therapeutic option in the treatment of patients with acute pulmonary embolism at high risk of early mortality. Current transcatheter techniques allow for local fibrinolysis or embolectomy with minimal risk of complications. Therefore, these procedures can be considered in high-risk patients as an alternative to surgical pulmonary embolectomy when systemic thrombolysis is contraindicated or ineffective. They are also considered in patients with intermediate-high-risk pulmonary embolism who do not improve or deteriorate clinically despite anticoagulation. The purpose of this article is to present the role of transcatheter techniques in the treatment of patients with acute pulmonary embolism. We describe current knowledge and expert opinions in this field. Interventional treatment is described in the broader context of patient care organization and therapeutic modalities. We present the organization and responsibilities of pulmonary embolism response team, role of pre-procedural imaging, periprocedural anticoagulation, patient selection, timing of intervention, and intensive care support. Currently available catheter-directed therapies are discussed in detail including standardized protocols and definitions of procedural success and failure. This expert opinion has been developed in collaboration with experts from various Polish scientific societies, which highlights the role of teamwork in caring for patients with acute pulmonary embolism.

Key words: acute pulmonary embolism, intensive care, ineffective anticoagulation, ineffective systemic thrombolysis, interventional treatment, local fibrinolysis, percutaneous techniques, pulmonary embolectomy, pulmonary embolism response team, transcatheter techniques

INTRODUCTION

This expert opinion has been initiated by the Polish Pulmonary Embolism Response Team (PERT) Initiative [1] and developed in collaboration with experts of the Polish Cardiac Society representing the Working Group on Pulmonary Circulation, Association of Intensive Cardiac Care, and Association of Cardiovascular Interventions. The interdisciplinary approach signifies the role of teamwork in caring for patients with acute pulmonary embolism (PE).

As per the European Society of Cardiology (ESC) guidelines, the first-line treatment in patients with acute high-risk PE is primary reperfusion, preferentially systemic thrombolysis (ST). However, approximately 50% of this population do not receive this treatment due to contraindications or increased risk of bleeding [2]. Moreover, ST is associated with a nearly 2% risk of intracranial hemorrhage [3] and is ineffective in some patients [4]. Catheter-directed treatment (CDT) became a viable therapeutic option thanks to advances in interventional cardiology technologies.

This article aims to present the role of developing interventional cardiology technologies in the treatment of acute PE. We refer to 2 recently published European documents: the ESC guidelines for the diagnosis and management of acute PE [5] and a consensus statement on the interventional treatment of PE by 2 ESC groups, that is, the Working Group on Pulmonary Circulation and Right Ventricular Function and the European Association of Percutaneous Cardiovascular Interventions [2].

The Delphi method was used for the selection of issues presented in the article [6]. Firstly, 3 experts (GK, AA, and MK) suggested 62 questions that were sent to all the authors of this document, who, in turn, had to assess the relevance of each topic for this article. The topics were rated on a scale from 1 (irrelevant) to 10 (especially relevant). Issues with an average score greater than 7.0 were arbitrarily accepted. Issues with an average score of 3.0 or less were rejected. The remaining issues were reassessed by the authors as 0 (irrelevant) or 1 (relevant). Ultimately, 55 topics from the initial list were accepted. An additional 4 issues were proposed in the first round of the Delphi survey and accepted in the second round.

TASKS OF A PULMONARY EMBOLISM RESPONSE TEAM

A PERT is composed of specialists from various medical disciplines who cooperate in real-time and provide optimal and coordinated care for patients with acute PE. PERT members stratify patients according to their health risk status and assess their eligibility for anticoagulation, reperfusion including ST, CDT, or surgical pulmonary embolectomy (SPE) as well as supportive treatment, including extracorporeal membrane oxygenation (ECMO), Impella RP, or inferior vena cava (IVC) filter [7]. Each specialist contributes their knowledge, skills, experience, and unique approach to the treatment of acute PE.

Globally, the role of PERT in making individualized therapeutic decisions in acute PE has been increasing considerably over the past decade [8]. This applies especially to hemodynamically unstable patients with absolute contraindications to ST or those with severe comorbidities (including cancer) as well as patients with acute intermediate-high-risk PE with no improvement on anticoagulation. The current ESC guidelines recommend formation of PERTs in individual hospitals depending on the local resources and access to specialists (ESC class IIa recommendation; C

Table 1. Typical clinical scenarios warranting PERT consultation

Acute high-risk PE with contraindications to ST or after ineffective ST
Acute intermediate-high-risk PE with clinical and hemodynamic deterioration during anticoagulant treatment — clinical, imaging, and/or laboratory data indicating worsening of PE (Table 4)
Acute intermediate-high-risk PE without clinical and hemodynamic improvement despite anticoagulant therapy—clinical, imaging, and/or laboratory data indicating persistence of PE (Table 4)
Acute intermediate-high-risk PE with absolute contraindications to ST
Acute PE with a thrombus in the RV, the so-called thrombus in transit, including the presence of a thrombus passing through the PFO/ASD
Acute PE with coexisting symptoms of paradoxical embolism such as acute myocardial infarction, ischemic stroke
Acute high-risk or intermediate-high-risk PE in a pregnant patient
Acute nonthrombotic PE (e.g., fat embolism, amniotic fluid, iatrogenic embolism)
Acute PE superimposed on chronic thromboembolic pulmonary hypertension
Acute PE with existing contraindications/complications of anticoagulant treatment

Abbreviations: ASD, atrial septal defect; PE, pulmonary embolism, PFO, patent foramen ovale; RV, right ventricle; ST, systemic thrombolysis

level of evidence) [5]. Establishing a PERT has been shown to significantly improve access to invasive therapy of acute PE and facilitate rapid patient qualification for such treatment, which subsequently leads to improved efficacy owing to increased experience of intervention teams [9, 10]. At Massachusetts General Hospital (Boston, MA, US), where the first PERT was created, a considerable increase in the use of CDT among patients with acute PE (mainly in patients with acute intermediate-high-risk PE) was observed over several years [10]. Moreover, accurate risk stratification, patient selection, and improved treatment availability were factors that led to significant mortality reduction when periods before and after PERT creation were compared [11, 12]. Typical clinical scenarios that warrant a PERT consultation are shown in Table 1.

Details on PERT organization and procedures are presented in an earlier publication by the Polish PERT Initiative [1].

In brief, the organization and operation of PERT are based on a coordinator and specialist team members. The PERT coordinator should be available at all times (in the so-called 24/7 mode) at a dedicated phone number and, upon receiving the notification, should be able to arrange quick consultations (<30 minutes) with relevant specialists. These consultations may take the form of a teleconference during which all participants have access to the patient's medical and imaging data. Treatment recommendations should result from joint decision-making by the PERT members. The PERT coordinator (or a designated person) simultaneously acts as a secretary who collects the necessary clinical and imaging data and provides PERT recommendations to the physician currently caring for the patient. Information communication technology tools (dedicated applications, instant messaging) can be a significant facilitator in sharing and collecting patient information; however, care must be taken to protect patients' personal data.

The PERT should include specialists with practical experience in various treatment strategies for acute PE as well as experts who could assist the team in case of complications or comorbidities that require modification of standard treatment protocols for acute PE. We believe that the PERT's "core" should include a physician experienced in cardiovascular interventions, a cardiac surgeon or thoracic surgeon, and a physician experienced in intensive care, who, if necessary, should be supported by specialists in anesthesiology, angiology, vascular surgery, radiology, emergency medicine, neurology, neurosurgery, oncology, hematology, and pulmonology [1]. The coordinator activates the PERT after obtaining the necessary information on the patient's condition, including results of additional examinations. The activation is usually phased over a period necessary to obtain results and insights about the dynamics of the disease. In straightforward situations, the PERT coordinator can make decisions and recommendations independently without activating other team members. A detailed diagram of the proposed PERT organization is shown in Figure 1.

The 3-step PERT activation process (the coordinator, core PERT, and regular PERT depending on the complexity of the clinical situation), usually used in currently existing teams, performs well in Poland, and moreover, it is easier to implement. However, the final composition of the PERT as well as its operation may vary from facility to facility, depending on the operation and experience of a given hospital. This is confirmed by data on PERTs from the US as well as recently published experiences from Polish centers [9, 13–16].

Choosing the optimal therapy (including, e.g., ST, CDT, SPE, and ECMO) is one of the most important tasks of the PERT in the setting of acute PE; therefore, the ideal organizational solution is to create PERTs in hospitals with all treatment options available in one location. If the PERT is established in a hospital without a cardiac surgery department, formal cooperation with a cardiac surgery center should be ensured to enable immediate transfer of patients for further treatment. According to experts, a consultation with a cardiac surgeon is not a prerequisite to qualify a patient for CDT, especially in emergencies. Nevertheless, every PERT should also have access to treatment with extracorporeal mechanical circulatory support (e.g., ECMO), which in Poland is usually associated with cardiac surgery units. In addition to the acute-phase treatment of acute PE, PERTs can play a role in optimizing patient management in the following months, including determination of the mode and duration of long-term anticoagulant treatment, potential implantation of an IVC filter, and patient follow-up for chronic thromboembolic pulmonary hypertension [17–22].

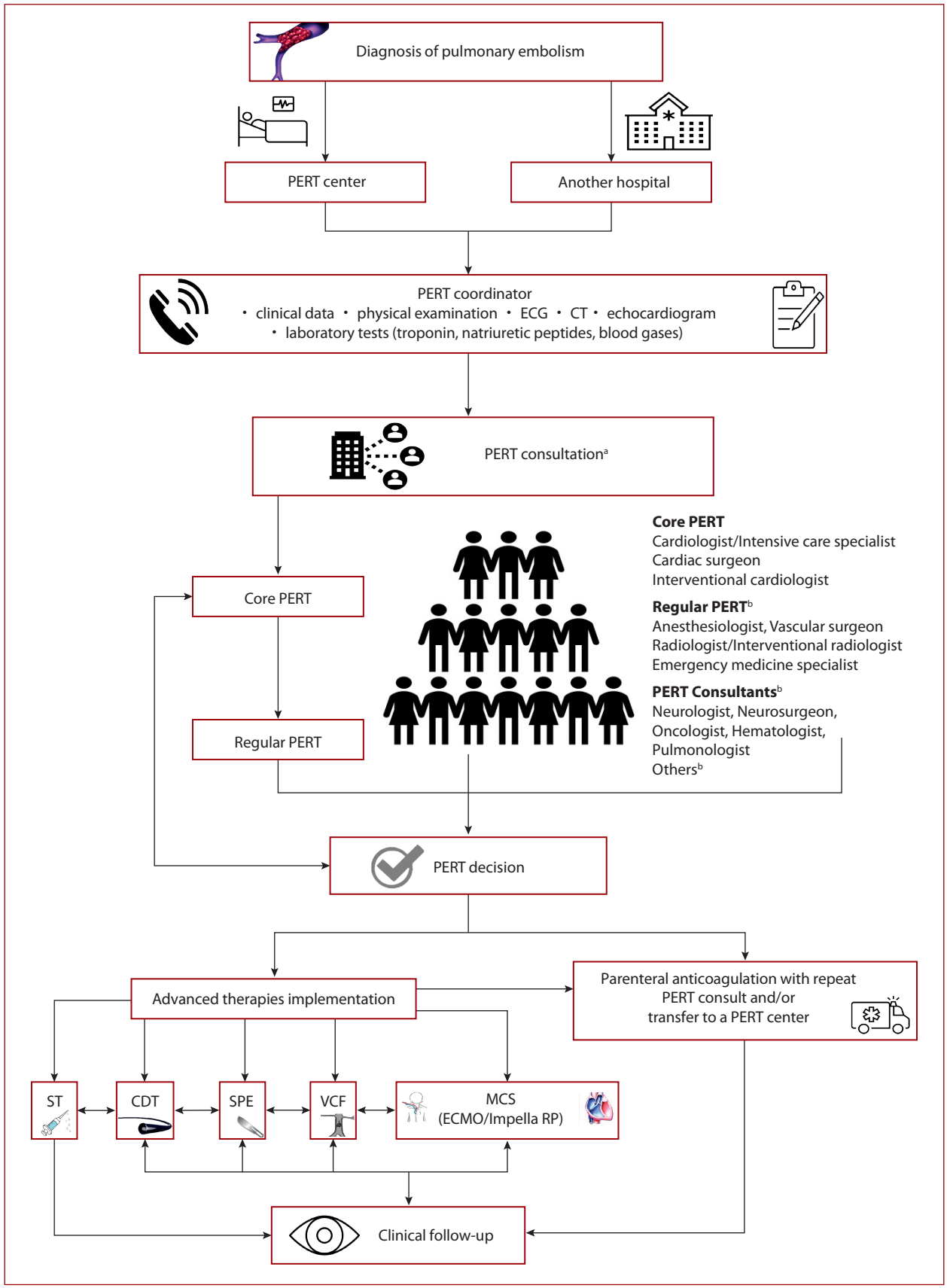

Figure 1. Detailed chart of PERT organization

Abbreviations: ECG, electrocardiogram; CDT, catheter-directed treatment; MCS, mechanical circulatory support; SPE, surgical pulmonary embolectomy; CT, computed tomography; VCF, vena cava filter; other — see Table 1

[a]Consultations are usually held with the use of telecommunications tools, including those enabling the transmission of imaging test results; [b]Additionally, as needed

Table 2. Key features to be assessed on computed tomography pulmonary angiography in patients with acute pulmonary embolism considered for catheter-directed therapy

Determination of direct symptoms of acute PE
Location of individual thrombi, central (main and lobar arteries)/peripheral (segmental and subsegmental arteries) embolism
Differentiation of acute/chronic embolism
Assessment of pulmonary artery trunk diameter
Features of right ventricular overload (the right ventricle/left ventricle diameter ratio, flattening or leftward shift of the interventricular septum, contrast agent pooling in the inferior vena cava and hepatic veins)
Presence of significant thoracic abnormalities, with particular emphasis on pulmonary parenchymal abnormalities

Abbreviations: see Table 1

IMAGING STUDIES TO DETERMINE ELIGIBILITY FOR INTERVENTIONAL TREATMENT OF ACUTE PULMONARY EMBOLISM

Computed tomography

Computed tomography (CT) pulmonary angiography is the gold standard in the diagnostic workup to confirm or exclude acute PE. It is commonly believed that the test should be performed on at least a 16-slice CT scanner. The ESC recommends emergency ST in cases of strongly suspected acute PE not confirmed on CT angiography when the clinical presentation is convincing, echocardiography shows signs of right ventricular (RV) pressure overload, and the patient's critical condition only allows bedside diagnostic tests [5].

CT angiography facilitates precise visualization of the pulmonary arterial tree at least to the segmental level as well as assessment of signs of pulmonary hypertension and RV pressure overload. It allows for accurate determination of the location, morphology, and size of thrombi, which is essential for assessing patients' eligibility for interventional treatment. Diagnostic efficacy depends on the technical quality of the test; nonetheless, the accuracy of eligibility assessment for interventional treatment of lesions located in the proximal pulmonary arteries (up to and including the level of the lobar arteries) is remarkably high [5].

The detailed description of the CT angiography should include all information listed in Table 2.

The physician drafting the report should first assess the image quality. There were attempts to assess the degree of pulmonary circulation obstruction more objectively by implementing time-consuming 3- or 5-point scales, but this has not been widely accepted in clinical practice.

The pulmonary trunk diameter is measured at the level of the bifurcation. Pulmonary hypertension is indicated by pulmonary trunk width greater than 29 mm or the ratio of the transverse diameter of the pulmonary trunk to the ascending aorta greater than 1.0.

The transverse dimensions of the RV and left ventricle (LV) are measured in the axial plane as the distance between the ventricular endocardium and the interventricular septum, perpendicular to the long axis of the heart. The maximum ventricular dimensions may be found at different levels. RV dilatation is confirmed if an RV/LV diameter ratio is greater than 1. The RV/LV ratio is the most essential measurement required in the assessment of eligibility for interventional treatment.

In addition, endovascular treatment preparation should include assessment of obstructions or anatomical variations of vessels that constitute the access path for catheters, as seen in imaging studies (Figure 2).

Echocardiography

Transthoracic echocardiography (TTE) is used in the diagnostic workup and risk stratification of patients with acute PE and also in the evaluation of treatment efficacy. Signs of RV pressure overload or dysfunction, presence of thrombi in the heart chambers, and other potential causes of hemodynamic instability are of particular importance when deciding on interventional treatment in patients with acute PE.

Indicators of RV dysfunction whose prognostic significance for acute PE was confirmed in numerous studies and which are simple to measure on TTE are as follows: an increased RV/LV ratio greater than 1 (measurement in the apical 4-chamber view) and decreased tricuspid annular plane systolic excursion (TAPSE) of 16 mm or less [5, 23, 24]. The prognostic role of other echocardiographic parameters is currently being investigated [25, 26].

TTE is of great importance in monitoring response to treatment in patients with acute high-risk PE who do not show hemodynamic improvement in after thrombolytic therapy within 2 to 4 hours of observation. TTE should be performed in intermediate-high-risk patients who deteriorate hemodynamically despite anticoagulation or whose condition does not improve despite anticoagulation treatment. In such situations, worsening/no improvement in echocardiographic parameters is an indication to consider invasive treatment, including CDT.

Pulmonary angiography during catheter-directed treatment

Images obtained during CT angiography should be reviewed before the procedure. However, notably, CT angiography of the pulmonary arteries may not reflect the current situation — particularly in patients after ST or after prolonged anticoagulation. Before CDT, selective pulmonary angiography can be performed using an automated injector (usually with 25–30 ml of contrast agent) or manually. The most common projections are AP or RAO 30° (the right lung) and LAO 30° (the left lung). Pulmonary angiography may be omitted in catheter-directed infusion procedures (catheter-directed thrombolysis, CDL).

RISK STRATIFICATION IN PATIENTS WITH ACUTE PULMONARY EMBOLISM

Eligibility for interventional treatment of acute PE requires assessment of the patient's risk of death [5, 27]. Risk stratification includes assessment of clinical presentation and abnormalities in imaging and laboratory findings that

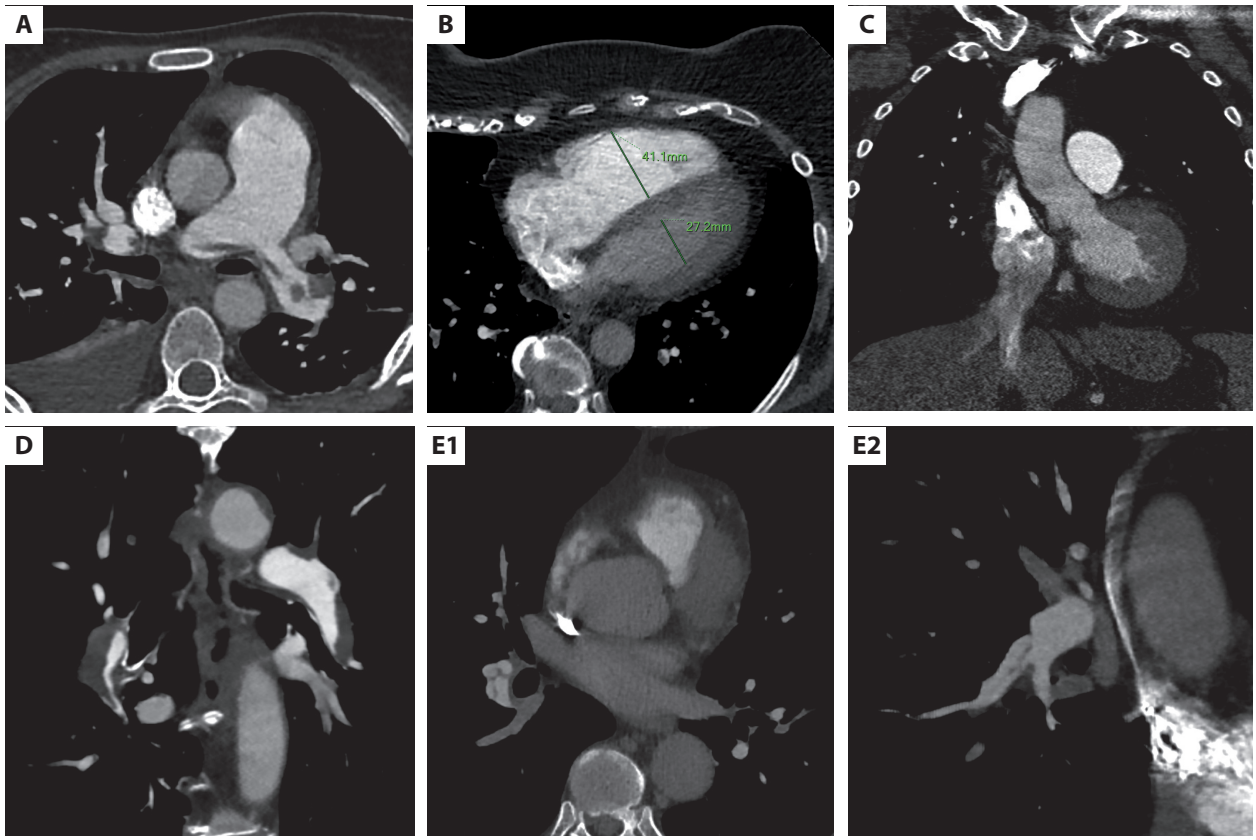

Figure 2. Features of pulmonary embolism (PE) on computed tomography pulmonary angiography. Acute PE: saddle PE, that is, a thrombus at the bifurcation of the dilated pulmonary trunk (**A**); dilatation of the right ventricle with flattening of the interventricular septum, right ventricular to left ventricular diameter ratio, 1.5 (**B**); contrast agent pooling into the inferior vena cava and hepatic veins (**C**). Chronic PE: wall-adherent thrombi within the pulmonary arteries (**D**); **E1** and **E2** — stenosis and slits in the lumen of the arteries of the right lower lobe

Table 3. Classification of pulmonary embolism based on severity and risk of early (in-hospital or 30-day) death

Risk of early death		Risk factor			
		Hemodynamic instability	Clinical indices of the severity of acute PE and/ /or comorbidities: PESI class III-IV or sPESI ≥1	RV dysfunction on TTE or CTPA (LV/RV >1 or TAPSE ≤16 mm)	Elevated cardiac troponin levels
High		+	(+)[a]	+	(+)[a]
Intermediate	High	–	+	+	+
	Low	–	+	One or none present	
Low		–	–	–	Optional testing; if assessed – negative

[a]Troponin levels or PESI or sPESI scores are not required for the diagnosis of acute high-risk PE

Abbreviations: CTPA, computed tomography pulmonary angiogram; LV, left ventricle; PESI, Pulmonary Embolism Severity Index; sPESI, simplified Pulmonary Embolism Severity Index; TAPSE, tricuspid annular plane systolic excursion; TTE, transthoracic echocardiography; other — see Table 1

correlate with the severity of acute PE and risk of early death (i.e., within 30 days). Based on this, 3 risk groups are distinguished: high, intermediate (further divided into intermediate-high and intermediate-low), and low (Table 3).

Patients are classified as high risk if any of the following acute PE manifestations are present: cardiac arrest, obstructive shock, or persistent hypotension.

In other patients, the risk is determined based on clinical severity (Pulmonary Embolism Severity Index [PESI]/ Simplified Pulmonary Embolism Severity Index [sPESI]) and evidence of RV overload in imaging and laboratory findings, as shown in Table 3.

At the same time, it is important to remember that risk defined in such a way is dynamic and may change during treatment and follow-up.

Table 4 summarizes the most important risk factors for hemodynamic collapse in patients without initial diagnosis of acute high-risk PE. They are useful for monitoring treatment effects in patients with acute PE. Worsening or no improvement in the above-mentioned abnormalities suggest ineffectiveness of pharmacological treatment of acute PE.

Currently, early warning scores that could identify patients at high risk of hemodynamic deterioration are being explored [28]. The National Early Warning Score 2 (NEWS2)

Table 4. Clinical, imaging, and laboratory indicators of pulmonary embolism severity in patients without hemodynamic instability[a] [2]

Clinical	Imaging	Laboratory
HR >100/min SBP 90–100 mm Hg Respiratory rate >20 breaths/min SaO_2 <90% (without oxygen therapy) Comorbidities: heart failure, active neoplasm	Echocardiography (at least 1 parameter): • RV/LV >1.0 • TAPSE ≤16 mm • No inspiratory collapsibility of the IVC CTPA: • RV/LV >1.0	Elevated troponin levels or NT-proBNP >600 pg/ml or Lactate level ≥2 mmol/l

[a]Adapted from Pruszczyk P, Klok FA, Kucher N, et al. Percutaneous treatment options for acute pulmonary embolism: a clinical consensus statement by the ESC Working Group on Pulmonary Circulation and Right Ventricular Function and the European Association of Percutaneous Cardiovascular Interventions. EuroIntervention. 2022; 18(8): e623–e638

Abbreviations: CTPA, computed tomography pulmonary angiography; SBP, systolic blood pressure; HR, heart rate; IVC, inferior vena cava; LV, left ventricle; NT-proBNP, N-terminal fragment of B-type natriuretic propeptide; SaO_2, arterial blood oxygen saturation; other — see Tables 1 and 3

is an example. It includes 6 physiological parameters: respiratory rate, arterial blood oxygen saturation, body temperature, systolic blood pressure, heart rate, and level of consciousness. The higher the score, the higher the risk of death. A score of 5 or more indicates that the patient's condition needs to be urgently reassessed and treatment escalation should be considered; a score of 7 or greater calls for immediate treatment optimization.

CATHETER-DIRECTED TREATMENT IN THE MANAGEMENT ALGORITHM FOR PATIENTS WITH ACUTE PULMONARY EMBOLISM

The clinical practice guidelines [5] include CDT among reperfusion treatment modalities, along with ST and SPE. The role of these therapies in the management algorithm for patients with acute PE is shown in Figure 3 (Central Figure). Reperfusion therapy aims to restore patency of the pulmonary arteries more effectively than anticoagulation. Its goal is to locally dissolve (CDL) or remove (catheter-directed mechanical thrombectomy [CDMT]) embolic material from the pulmonary arteries, reduce the RV afterload, and improve the efficiency of pulmonary gas exchange [29]. Clinical effects of reperfusion include an increase in systemic pressure, a decrease in tachycardia, an improvement in organ perfusion, and an increase in blood oxygen saturation or a decrease in oxygen demand. Notably, the main goal of CDT is to improve the patient's general condition, not to completely clear thrombi out of the pulmonary arterial bed. Usually, CDT is first performed in the lung with more clots detected. Thrombi located in the main pulmonary arteries, lobar branches, and initial sections of the large segmental arteries are anatomically accessible for CDT treatment. Acute PE limited to the segmental or subsegmental level is rarely an indication for CDT.

According to the ESC guidelines [5], CDT's role varies depending on the severity of acute PE. In acute high-risk PE, the role of CDT is to restore the patency of the pulmonary artery as quickly as possible so that the patient with hypotension or shock can be stabilized. CDT is not the first-line treatment in this patient population and should be considered in patients with contraindications to ST or patients ineligible for SPE. CDT should also be considered in patients in whom ST has not been effective. A recent meta-analysis showed that CDT can reduce the risk of in-hospital death [30] compared with ST.

In acute intermediate-high-risk PE, CDT is a rescue treatment option for patients who become hemodynamically unstable while on anticoagulant therapy. Also, patients who do not improve on anticoagulation may be considered candidates for CDT to prevent RV decompensation. Table 5 summarizes indications for CDT in acute PE, and Table 6 summarizes contraindications to ST.

DEFINITION OF FAILURE OF ANTITHROMBOTIC THERAPY IN ACUTE PULMONARY EMBOLISM

Failure of anticoagulation

We propose the following definition of anticoagulation failure: (1) hemodynamic deterioration in initially hemodynamically stable patients, even if they do not meet the criteria for overt shock; or (2) no improvement after anticoagulation [2].

Hemodynamic deterioration and lack of improvement can be assessed based on the increase or no change, respectively, in the parameters shown in Table 4.

One way to make the diagnosis of clinical deterioration objective is to use the NEWS2 scale described above.

There are no data on the optimal duration of anticoagulation after which failure of treatment can be identified; thus, such duration should be tailored individually for each patient and decided upon with the PERT. The ESC consensus statement [2] indicates a period of 24 to 48 hours of therapeutic anticoagulation. We believe that this period may be subject to change as the experience of the teams performing the procedures and the safety of the technologies increases.

Unsuccessful systemic thrombolysis

The goal of ST in patients with acute PE is to rapidly achieve hemodynamic stability, and failure to do so should be considered unsuccessful ST [2]. Although hemodynamic instability persisting 36 hours after the end of intravenous thrombolysis has been described in 8% of patients [4], there is no accepted definition of ST failure in the treatment of patients with acute PE. In our opinion, the occurrence of a complete hemodynamic collapse during or after infusion

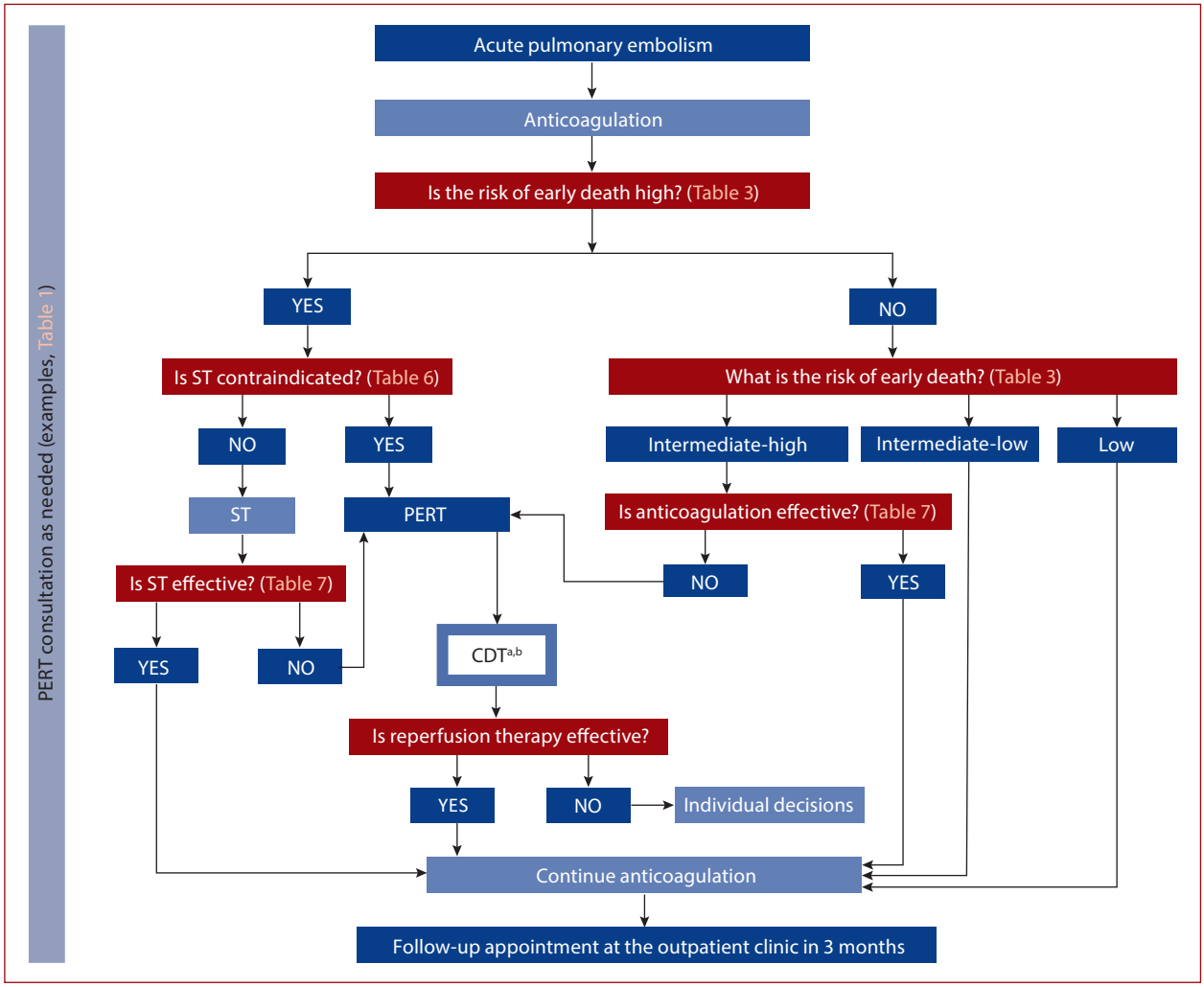

Figure 3. Central figure. Role of catheter-directed therapies in acute pulmonary embolism (PE)
Red boxes include essential questions to be answered when determining the best therapeutic strategy for a patient with acute PE. Blue boxes indicate treatment methods used in specific clinical situations
[a]In patients with acute high-risk PE and contraindications to systemic thrombolysis (ST), surgical pulmonary embolectomy (ESC class I recommendation) or percutaneous treatment (ESC class IIa recommendation) is recommended. In patients with acute high-risk PE in whom percutaneous or cardiac surgery cannot be performed, relative contraindications to thrombolysis should not preclude the use of ST as a life-saving treatment;
[b]In intermediate-high-risk patients who deteriorate hemodynamically on anticoagulant therapy, rescue thrombolytic therapy (ESC class IB recommendation) is advised; alternatively, surgical embolectomy (ESC class IIa recommendation) or transcatheter therapy (ESC class IIa recommendation) should be considered. In our opinion, in patients who do not improve with anticoagulation as well as in patients with increased risk of bleeding who deteriorate clinically/hemodynamically, catheter-directed therapies should be considered as a safer and equally effective modality compared with ST or surgical pulmonary embolectomy

Abbreviations: PERT, pulmonary embolism response team; other — see Table 1 and Figure 1

Table 5. Indications for catheter-directed therapies in acute pulmonary embolism

Risk of death	Indications[a]	Comment
High	• Contraindications to ST (Table 6) • Ineffective ST (Table 7)	Systemic thrombolysis is the first-line treatment in patients with acute high-risk PE and no contraindications[b]
Intermediate-high	• Failure of anticoagulation defined as hemodynamic deterioration or lack of improvement (Table 7)	CDT appears to have a more favorable safety profile compared with ST

[a]Catheter-directed treatment is an alternative to surgical embolectomy. The decision on using one of these methods should be consulted by the PERT and should be based on individual characteristics of pulmonary embolism episode, the patient's condition, and availability of experienced interventional or surgical teams; [b]In our opinion, in patients with acute high-risk PE in whom percutaneous intervention or cardiac surgery cannot be performed, relative contraindications to thrombolysis should not preclude the use of ST as a life-saving treatment

Abbreviations: see Table 1 and Figure 1

Table 6. Absolute and relative contraindications to fibrinolytic treatment based on Konstantinides et al. [5]

Absolute contraindications	Relative contraindications
• History of hemorrhagic stroke or stroke of unknown origin • Ischemic stroke in previous 6 months • Major trauma, surgery, or head injury in previous 3 weeks • Central nervous system neoplasm • Hemorrhagic diathesis • Active bleeding	• Transient ischemic attack in previous 6 months • Oral anticoagulation • Pregnancy or first post-partum week • Non-compressible puncture sites • Traumatic resuscitation • Refractory hypertension (systolic blood pressure >180 mm Hg) • Advanced liver disease • Infective endocarditis • Active peptic ulcer disease • Use of extracorporeal membrane oxygenation

(after excluding massive bleeding) should be considered the primary criterion for ST failure. In addition, no hemodynamic improvement several hours after full-dose ST also warrants the diagnosis of treatment failure. Although there are no data to specify this time frame, we believe that lack of improvement within 2 to 4 hours after the end of intravenous thrombolysis warrants the diagnosis of treatment failure and, in justified cases, the initiation of CDT.

Making the decision to perform urgent interventional treatment in the case of complete hemodynamic destabilization or sudden cardiac arrest during thrombolysis poses a major challenge. In such situations, the decision to escalate therapy and immediately perform an intervention should be made on a case-by-case basis taking into account the capabilities and experience of the local PERT. It is worth noting that tissue plasminogen activator is rapidly metabolized, and its plasma half-life is about 4 to 5 minutes. Thus, after 20 minutes, less than 10% of the initial concentration remains in plasma. Table 7 summarizes the currently accepted definitions of anticoagulation failure and ST failure in acute PE.

TIME TO CATHETER-DIRECTED TREATMENT

The time from the PERT's decision to the start of CDT depends on the patient's condition. However, reliable data on the optimal time for treatment are lacking. We believe that once the decision is made, interventional treatment should be implemented as soon as possible. Notably, a major reason for prolongation of time to CDT can be the need to transport a patient from a center that does not have CDT capabilities.

VASCULAR ACCESS DURING CATHETER-DIRECTED TREATMENT

Femoral access is the preferred type of vascular access for CDT. Before establishing vascular access, ultrasound evaluation of the external femoral and iliac veins is recommended to rule out the presence of thrombi. In some cases, angiography of the iliac veins and IVC is also performed. Ultrasound-guided puncture is recommended, especially for procedures with anticipated thrombolysis or in patients recently treated with thrombolysis. If the thrombosis is present in the femoral or iliac veins unilaterally, the procedure should be performed using access established on the contralateral limb. If there are anatomical obstacles in the IVC or bilateral anatomical obstacles in the external iliac veins or common femoral vein such as thrombi, abdominal tumors, vascular anomalies, or filter thrombosis, the procedure should be performed with access through one of the jugular veins.

After the procedure is completed, the vascular access sheath is removed. The access site can be secured with a hemostatic "Z"-stitch (for >8 F devices) or a compression dressing usually for 4 to 6 hours.

PERIOPERATIVE ANTICOAGULATION

The ESC recommends that patients with acute high-risk PE should be treated with unfractionated heparin (UFH), including a weight-adjusted bolus. UFH should also be the preferred option in patients at risk of hemodynamic instability who may require rescue reperfusion treatment. If there are no absolute contraindications, for example, active bleeding, then parenteral anticoagulation with UFH should be used during CDT. Given that there are no conclusive data in the literature, anticoagulation intensity and monitoring remain to be considered on a case-by-case basis. With CDMT, we suggest using a standard UFH dose in accordance with the guidelines for the treatment of acute PE. In CDL-treated patients who receive UFH as the initial treatment, we suggest continuing UFH during the procedure and up to a maximum of 4 hours after its completion at a flow rate of 300 to 600 U/h (subtherapeutic dose: activated partial thromboplastin time [APTT] <60 seconds, or activated clotting time [ACT] <200 seconds), and then continue at full dose. In patients treated with low-molecular-weight heparins (LMWHs) at a therapeutic weight-adjusted dose,

Table 7. Definition of pharmacological treatment failure in acute pulmonary embolism

Clinical setting	No improvement[a]	Hemodynamic deterioration[b]
Ineffective ST in patients with acute high-risk PE	No hemodynamic improvement 2–4 hours after completing full-dose ST	Overt cardiorespiratory instability necessitating cardiopulmonary resuscitation, mechanical ventilation, catecholamines, or ECMO or Worsening of the parameters shown in Table 4
Ineffective anticoagulation in intermediate-high--risk patients	No improvement in parameters shown in Table 4 despite therapeutic anticoagulation	

[a]Despite full-dose anticoagulation/fibrinolysis; [b]After starting anticoagulation/fibrinolysis

Abbreviations: see Table 1

we suggest a continuous infusion of UFH for the duration of the procedure and up to 4 hours afterward at a flow rate of 300 to 600 U/h (subtherapeutic dose: APTT <60 seconds, or ACT up to 200 seconds) without pre-bolus administration. In patients treated with oral anticoagulants, caution is advised during the procedure and lower doses of UFH should be used with ACT not exceeding 200 seconds. In most patients, after the intervention is completed and clinical stability is reached, the vascular access sheaths are removed, and it is possible to switch UFH to subcutaneous LMWH and then to NOACs/vitamin K antagonists or UFH directly to NOACs.

CATHETER-DIRECTED THROMBOLYSIS

CDL is one of the strategies of reperfusion therapy. It involves infusing a fibrinolytic agent directly into the affected pulmonary artery (local thrombolysis) using a percutaneous endovascular catheter. The principles of the procedure are shown in Figure 4 [31, 32].

A distinctive feature of currently available infusion catheters such as EkoSonic (Boston Scientific), UniFuse (Angiodynamics), Cragg-McNamara (Medtronic), Fountain infusion system (Merit Medical), or pigtail catheter, is the so-called treatment zone at the distal end of the catheter with small holes in the catheter wall used for the administration of a thrombolytic drug. Catheter length and treatment zones are selected individually for each patient. The catheters of the EkoSonic system are additionally equipped with an ultrasound core mounted within the catheter, which allows the delivery of acoustic waves into the thrombi to separate fibrin strands and enhance the fibrinolysis process [33, 34].

The insertion of infusion catheters into the pulmonary arteries is done under fluoroscopic guidance and should be preceded by: (1) a detailed analysis of CT angiography with regard to thrombus distribution in the pulmonary arteries to assess indications for unilateral or bilateral local thrombolysis and determine target catheter placement in the pulmonary bed; and (2) ultrasound evaluation of vascular access. The treatment zone of infusion catheters is typically placed within the main and lobar arteries. The diameter of the vascular sheath should take into account the planned number and total diameter of infusion catheters to be inserted. Two-channel cannulas are a practical solution.

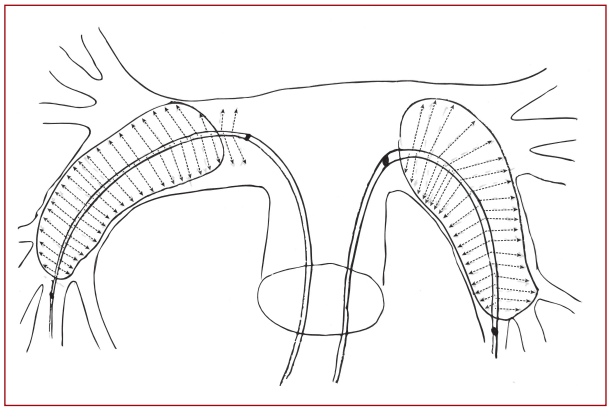

Figure 4. Catheter-directed thrombolysis. The treatment zones on the catheters used for fibrinolytic drug delivery (marker bands/black markers) are placed in the thrombus filling the right and left pulmonary arteries. The thrombolytic drug penetrates the thrombus through numerous small holes in the catheter walls in the treatment zones. This mode of administration allows for significantly smaller doses while maintaining high efficacy and a better safety profile compared with systemic thrombolysis [22]

A J-tip 0.035-inch guidewire is the optimal choice for the insertion of an infusion catheter. A Swan-Ganz, pigtail, or multipurpose catheter can be used to place the guidewire in the distal branch of the target artery. It also enables assessment of the hemodynamic parameters of the pulmonary circulation.

Catheters should be secured for the duration of the fibrinolytic drug infusion to prevent accidental dislodgement or ejection. Catheter removal does not require fluoroscopy.

In practice, alteplase (recombinant tissue plasminogen activator [r-tPA]) is most commonly used in CDL. The most commonly used dose regimen is an infusion of 1 mg/h/catheter (0.5–2 mg/h/catheter). Treatment time and total dose vary from center to center and range from 5 to 24 hours and 12 to 24 mg of tPA, respectively. Recent studies indicate that the optimal treatment time is 5 to 10 hours, with a total dose of 10 to 20 mg [35, 36]. In our opinion, it may be good practice to conduct a 5-hour infusion of tPA at a dose of 1 mg/h/catheter with a subsequent decision to terminate or extend treatment depending on the effects and safety of the therapy. A 1- to 2-mg tPA catheter-directed bolus is used at some centers to initiate the infusion. Available data show that local thrombolysis in patients at increased hemorrhagic risk and with relative contraindications to thrombolysis is safe. Some case reports have shown successful and safe use of low-dose CDL in patients after recent (<3 weeks since major trauma) surgery or stroke [37]. In our opinion, relative contraindications to ST usually do not constitute a contraindication to local thrombolysis. In addition, in patients with acute non-high-risk PE, CDL should be preferred to ST in those at increased risk of bleeding, which includes the following factors: age greater than 75 years, history of bleeding, renal disease, liver damage, malignancy, anemia, thrombocytopenia, diabetes, antiplatelet therapy, recent trauma, or minor surgery. In patients with absolute contraindications to thrombolysis not eligible for surgical treatment, CDMT is preferred.

Continuous infusion of UFH is the standard anticoagulation used during local thrombolysis and in the early postoperative period.

Safety monitoring during thrombolytic therapy necessitates regular clinical evaluation as well as evaluation of red blood cell parameters and coagulation parameters. Although scientific data is limited, some centers monitor the above-mentioned parameters at 3- to 6-hour intervals, and

the decision to discontinue therapy or reduce the dose is made depending on the dynamics of their changes. The occurrence of life-threatening bleeding is an absolute indication to discontinue fibrinolytic therapy.

The results of the ongoing Hi-Peitho study (Ultrasound-facilitated, Catheter-directed, Thrombolysis in Intermediate-high Risk Pulmonary Embolism; NCT04790370) will be important for further development of catheter-directed thrombolysis techniques. This is a phase 4, multicenter, randomized trial comparing ultrasound-facilitated catheter-directed thrombolysis with heparin in a population of patients with PE of intermediate-high-risk.

CATHETER-DIRECTED MECHANICAL THROMBECTOMY

The main goal of CDMT is to remove embolic material quickly and directly from the pulmonary arteries, restore patency, and improve blood flow [38]. Usually, the removal of about 50% of the volume of the thrombus is sufficient to achieve a significant improvement in hemodynamic and clinical parameters in a patient with acute intermediate-high- or high-risk PE [39]. Figure 5 shows the idea of CDMT.

There is a growing body of evidence from observational studies indicating that CDMT in patients with acute high- and intermediate-high-risk PE is safe and effective and is associated with a low rate of serious complications, especially hemorrhagic complications, significant and rapid improvement in hemodynamic and clinical parameters, and shortened hospitalization [40]. However, to date, no randomized clinical trials have shown improved prognosis compared with pharmacological treatment or SPE.

In some patients without absolute contraindications to thrombolysis, a combination (hybrid) pharmacomechanical treatment is possible, namely, thrombectomy supplemented with low-dose thrombolysis administered before, during, or after the catheter-directed procedure, especially if thrombectomy is not effective enough [40, 41].

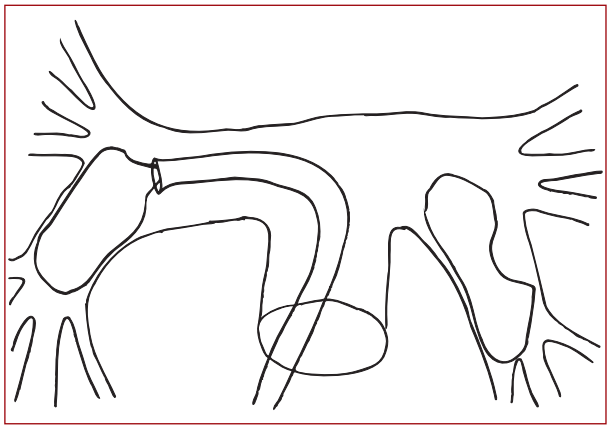

Figure 5. Catheter-directed mechanical thrombectomy. The catheter used to remove the thrombus is placed in the right pulmonary artery

Complications of catheter-directed mechanical thrombectomy

CDMT can be technically difficult and requires operators to have the experience and knowledge of passing and manipulating large-diameter catheters within the RV and pulmonary arteries. Potential complications of CDMT, besides complications at the vascular access site (hematomas, aneurysms, retroperitoneal bleeding), include cardiac tamponade, guidewire- or catheter-related pulmonary artery injury, distal embolization, alveolar hemorrhage, excessive blood loss due to aspiration, and bradycardia/atrioventricular block/asystole (resulting from a transient increase in bradykinin, adenosine, or potassium levels secondary to hemolysis or the catheter compressing the atrioventricular node or right bundle branch), hemolysis, and hemoglobinuria (rheolytic thrombectomy). In addition, acute kidney injury after administration of a contrast agent (contrast-induced nephropathy) may occur.

Contraindications to catheter-directed mechanical thrombectomy

Contraindications to CDMT, in addition to lack of patient consent, include disseminated pulmonary metastases (risk of perforation and bleeding), foci of tuberculosis, hemorrhagic diathesis, severe anemia, an IVC filter (in the case of femoral access), thrombus in the RV and right atrium, especially crossing the patent foramen ovale (PFO) (relative contraindication).

Procedure

Typically, the procedure begins by inserting a pigtail catheter into the pulmonary artery and performing pulmonary artery angiography to localize thrombi and determine the anatomy of the pulmonary arteries. In some centers, the pigtail catheter is left in place for the duration of the procedure for monitoring purposes, while the therapeutic catheter is inserted from another access site. Angiography is not necessary if a current CT pulmonary angiogram of good quality is available. The next stage of the procedure is the insertion of a guidewire into the pulmonary artery (through the vena cava, right atrium, and RV), followed by an appropriate therapeutic catheter, depending on the device. During the procedure, the patient should be continuously monitored (ECG, systemic blood pressure, oxygen saturation). It may be necessary to administer oxygen. The procedure should be terminated if: no more thrombi can be removed (distal thrombus, organized thrombus, thrombus diameter larger than the diameter of the catheter), hemodynamic improvement is noted (improvement or stabilization of systemic pressure, reduction of pulmonary artery pressure, improvement of arterial oxygen saturation, reduction of heart rate), or clinical improvement is reached (reduction of dyspnea, cough). If blood loss is excessive (e.g., exceeds 300–400 ml), the benefit-risk balance should be evaluated before the procedure is continued.

Catheter-directed mechanical thrombectomy devices

Rapid progress in the field of CDMT devices has been noted in recent years. Two types of such devices can be distinguished—for thrombus fragmentation (maceration) and various types for thrombus aspiration. The most used techniques are discussed below.

Thrombus fragmentation

A technique that had been available for many years was thrombus fragmentation using a rotational movement of a pigtail catheter in the pulmonary arteries. The technique had a relatively low success rate although some small-sample observational studies showed its clinical utility [42]. However, simplicity, widespread availability in hemodynamic laboratories, and low cost were the definite advantages of this technique. CLEANER XT (Rex Medical, Conshohocken, PA, US) is another system available for thrombus fragmentation. It is inserted through a catheter into the thrombus, then a drive system that rotates an atraumatic sinuous wire is activated to break up the clot. A few case reports have shown the effectiveness of the device in patients with acute PE [43–45]. At present, however, due to the availability of more modern and effective mechanical thrombectomy devices, thrombus fragmentation techniques are becoming obsolete.

AspirexS (Straub Medical, Wangs, Switzerland)

The device is inserted through an 8 F catheter and uses a rotating Archimedes screw which provides fragmentation and aspiration of the thrombus, followed by thrombus transportation throughout the catheter. The drive system allows for a rotation rate of 40 000 rounds per minute. Some observational studies have been published on the use of this method in patients with acute PE [46].

Rheolytic thrombectomy

The AngioJet PE device (Boston Scientific, Minneapolis, MN, US) provides fragmentation and aspiration of intravascular thrombi using a saline jet based on the Bernoulli phenomenon. The device's Power Pulse mode also allows preinjection of a low-dose thrombolytic into the thrombus. Case series, including some from Poland, show the relatively high effectiveness of the AngioJet system in patients with acute PE [14, 47, 48]. However, significant hemolysis can occur during the procedure, which can result in serious adverse events, for example, hypotension, dyspnea, bradycardia, (release of bradykinin and adenosine from erythrocytes and platelets), or worsening renal failure (hemoglobinuria) [49]. This led the Food and Drug Administration (FDA) to issue a warning about the use of the AngioJet system in the treatment of patients with acute PE. For this reason, the device should be used with caution, observing a limit of about 20 seconds per application; moreover, the total use time in one session should not exceed 120 seconds. However, when used by experienced teams, AngioJet appears to be effective and relatively safe. In a recent observational study, rheolytic thrombectomy was administered to 56 patients with acute intermediate-high- to high-risk PE with relative or absolute contraindications to thrombolysis. The treatment resulted in a significant hemodynamic and clinical improvement. During hospitalization, major bleeding occurred in 7.1% of patients, and death occurred in 8.9%. Perioperative deterioration of renal function occurred in as many as 39.3% of patients, but only 1 patient (1.8%) required dialysis. The role of the AngioJet system in the treatment of patients with acute PE requires further investigation [50].

Indigo 8 F/ Lightning 12 (Penumbra Inc, Alameda, CA, US)

The Indigo 8 F system enables direct thrombus aspiration from the pulmonary bed using an 8 F catheter (CAT8TRQ) connected to an aspiration pump. The advantage of this system is the almost immediate hemodynamic and clinical improvement but at the expense of perioperative blood loss and sometimes the need for blood transfusion after surgery (average blood loss per operation is about 200–400 ml) [49, 51, 52]. It should also be noted that the diameter of the catheter (8 F) precludes complete aspiration of large thrombi. In some cases, thrombus fragmentation is necessary. The EXTRACT PE study included 119 patients older than 18 years with acute intermediate-high-risk PE with fewer than 14 days without prior thrombolytic treatment. There was a significant reduction in the RV/LV ratio (from 1.47 before to 1.04 at 48 hours after the procedure, a reduction of 0.43 points or 27.3%) and a reduction in systolic pulmonary artery pressure (from 49.0 to 44.5 mm Hg, a mean reduction of 4.7 mm Hg). Severe perioperative complications occurred in 2 patients (1.7%): both patients experienced access site bleeding, and one patient experienced hemoptysis due to pulmonary artery perforation and died. In addition, minor bleeding complications occurred in 3 patients. Two patients died during 30-day follow-up due to progression of pre-existing comorbidities [53]. Recently, the next generation of the device, Lightning 12, has been released. It has a distinctive design that reduces the risk of catheter deformation while maintaining flexibility and a larger diameter of 12 F. The aspiration pump has a computer-controlled pressure valve that responds to overly rapid blood flow to reduce blood loss. The first experiences with the device, including from Polish centers, seem encouraging [54].

FlowTriever (Inari Medical, Irvine, CA, US)

It is a catheter with 3 nitinol disks that open when slid out of a 20 F sheath, which enables complete clot aspiration when inserted into the thrombus. In the FLARE study [55] (104 patients undergoing percutaneous embolectomy with the FlowTriever system), there was a significant reduction in the RV/LV ratio at 48 hours after the procedure (1.56 vs. 1.15; P <0.0001; a reduction of 0.38). Mean hospi-

talization time was 4.1 days (and in 41.3% of patients, the mean was 1.5 days), with a relatively low rate of serious adverse events in 4 patients (3.8%): one patient experienced massive hemoptysis probably due to reperfusion injury requiring lower lobectomy; 2 patients experienced respiratory deterioration requiring intubation; and the last patient experienced ST-segment elevation myocardial infarction treated with coronary angioplasty. There is also some concern about the diameter of the vascular sheath (20–24 F) and the risk of hematoma at the vascular access site with the use of such a large device [55]. Currently, large prospective observational studies and randomized clinical trials are underway to confirm the efficacy of the FlowTriver device in the treatment of acute PE (the PEERLESS Study; a prospective, multicenter, randomized controlled trial of the FlowTriever System compared to Catheter-Directed Thrombolysis for use in the treatment of acute pulmonary embolism, NCT05111613).

Angiovac (AngioDynamics, Inc)

A venovenous extracorporeal bypass circuit is created for the aspiration of large thrombi from the right heart, mainly the right atrium, possibly also the RV. The 26 F drainage (suction) cannula has a funneled tip and drains blood to an extracorporeal circulation pump with an attached reservoir with a filter in which embolic material (thrombi, vegetations, neoplasms, etc.) is collected. The blood is then reinfused back into the vein (femoral or possibly jugular) through a 16- to 20-F inflow cannula. The device is used for the nonsurgical catheter-directed vegetation removal in the course of cardiac device-related infective endocarditis, catheter-related thrombi in cancer patients, as well as in-transit thrombi passing through the heart in patients at risk of acute PE [56].

INFERIOR VENA CAVA FILTERS IN THE TREATMENT OF ACUTE PULMONARY EMBOLISM

Indications for implantation of an IVC filter are limited to 2 clinical scenarios: when a patient with acute PE has absolute contraindications to anticoagulant therapy and in the case of recurrent PE despite adequate anticoagulant therapy [5]. The routine use of filters in patients with PE is not recommended. Most current filters are devices inserted percutaneously into the IVC from femoral or jugular access that can be safely removed after a few weeks or months or left in place long term (if necessary). The device should be implanted during catheter-directed intervention, using the same vascular access. The implantation procedure is preceded by angiography of the IVC to rule out thrombi, and the filter is most often placed in the infrarenal portion of the IVC. After the procedure (up to 24 hours), the correct position of the filter should be checked with an abdominal X-ray. IVC filters are effective in protecting against recurrence of acute PE; however, they may increase the risk of deep vein thrombosis [57]. In a review of the literature including 9002 procedures, the most commonly described complication was venous wall penetration in 19% of patients. Penetration with involvement of adjacent structures was observed in 3.6% of the study population. Major intervention was required in 0.9% of cases (e.g., surgical removal of the filter, placement of an endovascular stent graft, nephrostomy). Other rare complications include filter fracture or displacement; deaths were found very rarely (2 cases) [58].

SURGICAL PULMONARY EMBOLECTOMY

Indications

In practice, SPE is usually used in patients with acute PE in whom other treatment options are ineffective or contraindicated.

The advantage of surgical treatment of patients with acute PE is the ability to safely remove accompanying thrombus "in transit" in the right heart, especially thrombus trapped in the PFO [59]. ST or interventional treatment of PE carries the risk of thrombus traveling from the right heart into the pulmonary circulation, which, together with concomitant RV overload, can lead to cardiovascular collapse. In the case of a thrombus straddling PFO, ST and percutaneous treatment can result in the release of a fragment of the thrombus located in the left atrium, and subsequently, lead to an embolus in the systemic circulation [60]. In patients with acute PE and concomitant chronic lesions in the pulmonary circulation with indications for reperfusion therapy, successful lesion removal can only be achieved surgically [61, 62]. Due to the complexity of the procedure and the required extensive experience, it is advisable to perform such procedures in centers experienced in pulmonary endarterectomy.

Treatment results

Currently, no randomized clinical trials are evaluating or comparing surgical treatment with other treatment options. The population of patients with acute PE is very heterogeneous and includes hemodynamically unstable patients, those in cardiogenic shock, often with multiple organ failure as well as extreme cases after cardiac arrest—surgical treatment is the treatment of last resort in such patients. Hence, surgical outcomes depend on the patient's initial condition, and the mortality rates in the literature vary considerably. In a registry-based study, in-hospital mortality was 15.9% (in patients without shock, 7.9%; those in shock, 23.7%; and those after cardiac arrest, 44.4%) [63]. In addition, the results depended on the experience of the center. In centers with extensive experience in performing surgical embolectomy, the total mortality rate was 4.2% to 6.6% (in patients without shock, 0%–3.6%; those in shock, 10.2%–12%; and those after cardiac arrest, 22%) [59, 64–66].

A limitation of SPE is the number and availability of cardiac surgery departments, which is often associated with the need to transport the patient to a distant facility, whereas

Table 8. Effects of vasopressors and inotropes on selected hemodynamic parameters

Drug/dose	Hemodynamic effects	Drug/dose	Hemodynamic effects
Dopamine 0.5–20 µg/kg/min	↑CO ↑PVR ↑SVR	Dobutamine 2.5–20 µg/kg/min	↑↑CO ↓PVR ↓SVR
Adrenaline 0.01–0.5 µg/kg/min	↑↑CO ↑PVR ↑↑SVR	Milrinone 0.125–0.75 µg/kg/min	↑CO ↓PVR ↓SVR
Norepinephrine 0.05–0.4 µg/kg/min	↑CO ↑PVR ↑↑SVR	Enoximone 2–10 µg/kg/min	↑CO ↓PVR ↓SVR
Vasopressin 0.02–0.04 U/min	↔ PVR ↑↑SVR	Levosimendan 0.05–0.2 µg/kg/min	↑CO ↓PVR ↓SVR

Abbreviations: ↑, increase; ↓ decrease; CO, cardiac output; PVR, pulmonary vascular resistance; SVR, systemic vascular resistance

percutaneous interventions can be implemented in most hospitals with access to a hemodynamic laboratory. Notably, the percutaneous procedure does not preclude SPE.

MONITORING AND INTENSIVE CARE OF A PATIENT WITH ACUTE PULMONARY EMBOLISM

Pharmacological support of the circulation

Some patients with acute PE require treatment with inotropes or vasopressors. Symptoms of low cardiac output and cardiogenic shock are the most common indications for these drugs. Their dosage and effects on selected hemodynamic parameters are shown in Table 8 [68–70]. Of the inotropic drugs, dobutamine is the most commonly used in acute PE. Low doses (2–5 µg/kg/min) increase cardiac output and reduce pulmonary vascular resistance, while higher doses can cause tachycardia and increase oxygen consumption [71, 72]. In patients with low blood pressure, the most commonly recommended drug is norepinephrine [69–71].

Mechanical circulatory support

Veno-arterial extracorporeal membrane oxygenation (VA-ECMO) can be used in severely hemodynamically compromised patients [73] with refractory cardiac arrest [74], as a bridge to recovery, and a bridge to CDT, SPE, or ST [74–77] and, according to the recommendations from the United States, also during those therapies [78]. VA-ECMO can be used as a bridge to CDT or SPE in patients after unsuccessful ST [79]. The ECMO-first strategy supplemented with percutaneous mechanical thrombectomy can be used for acute, life-threatening PE [80]. The duration of VA-ECMO in patients with acute PE should depend on their hemodynamic status, symptoms of cardiogenic shock, and risk of multiple organ failure. Based on the ESC guidelines, ECMO is only to be considered in patients with refractory shock or cardiac arrest only in combination with SPE or CDT (class IIb recommendation) [5]. We believe that the decision to start ECMO in an individual patient should be made by the PERT and should be based on the patient's characteristics, previous treatment, and the center's experience. There are emerging reports on the use of new devices for RV support in acute PE such as the Impella RP microaxial flow pump [77].

Monitoring

ECG, blood pressure, and blood loss should be monitored during CDT. Hemodynamic monitoring during CDT should be kept to a minimum. Measurements of right atrial pressure, pulmonary artery pressure, and mixed venous oxygen saturation seem to be a minimal and sufficient set of parameters to assess before and after the procedure.

The patient should be monitored for at least 24 hours after the intervention due to the risk of potential complications associated with the procedure. Continuous monitoring of ECG, arterial blood oxygen saturation, and respiratory rate is recommended. Monitoring of central venous pressure and mixed venous oxygen saturation may be considered for high-risk patients. Systematic evaluation of pulse oximetry parameters is advisable on the first day, during and after the procedure. On the next day, a repeat arterial blood gas test should be performed and the concentrations of BNP/NT-proBNP, troponin, and eGFR levels should be measured. Additionally, echocardiography should be performed immediately after the procedure and at 24 and 48 hours [5, 78, 81–83].

Mechanical ventilation

Mechanical ventilation — either non-invasive or invasive — is unnecessary in most cases of acute PE, and hypoxemia can usually be easily managed with conventional oxygen therapy. Arterial blood oxygen saturation of less than 90% requires initiation of oxygen therapy; however, greater values do not rule out respiratory failure [84]. If conventional oxygen therapy is insufficient, high-flow nasal oxygen therapy (HFNOT) can be considered as it provides flow rates of up to 60 l/min and is more comfortable for the patient than oxygen masks [85, 86].

When using invasive ventilatory support, it is important to keep in mind that positive chest pressure can reduce venous return and exacerbate RV failure and hypotension [87]. Hence, positive end-expiratory pressure (PEEP) should be used with caution [88]. Acute PE reduces the cross-sectional pulmonary vascular area, which results in increased pulmonary vascular resistance. Mechanically ventilated patients with poor cardiopulmonary reserve

who have increasing pulmonary vascular resistance may experience deterioration of RV function and consequent severe hemodynamic impairment [89]. Therefore, small tidal volumes (6 ml/kg) should be used to maintain end-inspiratory pressure of less than 30 cm H_2O. A lung-protective ventilation strategy (ARDSnet strategy), that is, reducing plateau pressures, is the treatment of choice [5, 90].

Non-invasive ventilation is associated with reduced hospitalization time, fewer complications, and lower mortality compared with invasive ventilation [91]. If a patient on noninvasive ventilation requires increasingly higher tidal volumes, it can be assumed that intubation will be needed in the near future.

OPERATOR QUALIFICATIONS AND CHARACTERISTICS OF TERTIARY CENTERS FOR INTERVENTIONAL TREATMENT OF ACUTE PULMONARY EMBOLISM

Interventional treatment of acute PE should be performed by experienced operators at tertiary centers. In emergency and immediate life-threatening situations and in situations in which patient transport is not possible, the procedure can also be performed by an experienced interventional cardiologist outside the tertiary center after consultation with the PERT.

The tertiary center should: have a PERT that sees patients in 24/7 mode, provide access to interventional treatment of acute PE (24/7), collaborate with a cardiac surgery center that can ensure pulmonary embolectomy (24/7), and optionally, offer post-discharge outpatient care. The tertiary center should have its own registry/database of acute PE interventions. Participation in clinical trials, observational studies, or multicenter registries is also advisable for such centers.

The center's experience measured as the number of performed procedures influences the results of interventional treatment of acute PE. A recent study reported lower in-hospital mortality in centers performing >12 procedures per year compared with centers performing 1 to 3 procedures per year [92]. Another study found that in-hospital mortality was lower in hospitals performing at least 8 procedures per year compared with lower-volume facilities (6% vs. 11.3%) [93]. We agree that acute PE interventions should be performed on a regular basis at a tertiary center; however, it is not possible to make a clear recommendation on the number of interventions that should be performed due to the lack of data from well-designed clinical trials.

Interventional treatment should be tailored to the individual patient's profile. The equipment of the tertiary center should allow for performing at least one method based on CDMT and at least one based on CDL, both with proven efficacy.

Interventional treatment of acute PE requires the ability to perform diagnostic and therapeutic procedures in the pulmonary circulation and experience in the universal techniques used in interventional cardiology. It is also necessary for operators to acquire skills in using specific devices designed for CDMT, thrombus fragmentation, and CDL.

The requirements to be met by an independent invasive cardiology operator and a right heart catheterization specialist have been defined, respectively, by the Association of Cardiovascular Interventions and the Pulmonary Circulation Section of the Polish Cardiac Society.

There are insufficient scientific data to formulate clear eligibility criteria for interventional treatment of acute PE; however, we suggest that it should be a specialist who holds at least one of the above-mentioned certifications (or other corresponding certifications from medical societies) and who systematically performs interventional procedures in the pulmonary bed. An independent operator in the field of acute PE is expected to participate in conferences including in their scope interventional treatment of acute PE and publish his/her results.

Article information

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