

Reporting Standards for Endovascular Treatment of Pulmonary Embolism



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J Vasc Interv Radiol 2010; 21:44–53

Abbreviations: CDT = catheter-directed therapy, DVT = deep venous thrombosis, IVC = inferior vena cava, PE = pulmonary embolism

PULMONARY embolism (PE) is a prevalent disease with significant morbidity and mortality. The estimated annual incidence is 1.45 per 1,000 person-years (1), which translates to 1,350,000 cases per year in the United States (2). The incidence of massive PE approached 11% in a postmortem evaluation of all deaths in one series (3). The 30-day mor-

tality rate for massive PE approached 30% (4), and the presence of shock in these patients defines a three- to seven-fold increase in mortality, with a majority of deaths occurring within 1 hour of presentation (5).

The role of the interventional radiologist in the diagnosis and treatment of PE continues to evolve. Traditionally, pulmonary angiography was performed as a diagnostic modality and for many years was the gold standard in the diagnosis of PE. With the evolution of computed tomographic (CT) angiography and marked improvement in the detection of thromboembolic events, as well as the development of endovascular therapy with thrombectomy devices, the interventional radiologist's role has shifted from diagnosis to treatment of PE. Although the mainstay of treatment remains anticoagulation, more aggressive treatment is now possible in the hemodynamically unstable patient.

In cases of massive PE, interventional radiologists have used catheter-directed thrombolytic therapy, mechanical thrombectomy, or a combination of the two in an effort to rapidly restore pulmonary blood flow in a life-saving effort (6,7). Currently as of 2009, there are no clear evidence-based guidelines that identify those patients who should be treated more aggressively with endovascular therapies, nor are there standard approaches to reporting clinical trial results in this area (8). The American College of Chest Physicians recommends against the use of mechanical approaches for most patients with PE, but

the American College of Chest Physicians guidelines suggest that endovascular treatment of massive PE should be used in selected highly compromised patients who are unable to receive intravenous systemic thrombolytic therapy or whose critical status does not allow sufficient time to infuse thrombolytics (9).

The purpose of the current document is to facilitate improved quality and relevance of clinical trials of endovascular therapies for the treatment of PE by providing a basic standardized framework for reporting results in the literature. Current treatment options, patient population considerations, endpoints, follow-up modalities, clinical trial designs, and statistical plans will be discussed.

CURRENT TREATMENT OPTIONS

Anticoagulation and Systemic Thrombolytic Therapy

Presently, anticoagulation remains the preferred treatment for deep venous thrombosis (DVT) and thromboembolic disease. There has been demonstrated reduction in mortality rates to an estimated 8% in patients who receive anticoagulation for the treatment of PE (10), whereas untreated PE carries a mortality rate of approximately 30% (9,11–13). Intravenous unfractionated heparin is commonly used during initial hospitalization to prevent propagation of existing thrombus, and it has been long established that heparin decreases the recurrence of life-threatening PE (14).

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T.W.I.C. is a paid consultant for, has patent ownership or part ownership in, and has a royalty agreement with Merit Medical Systems Inc. D.K.R. is a paid consultant for CR Bard. None of the other authors have identified a conflict of interest.

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DOI: 10.1016/j.jvir.2009.09.018

Typical regimens use unfractionated heparin and/or low-molecular-weight heparin during hospitalization. These are later replaced by oral anticoagulants (eg, warfarin) for extended periods.

The standard American College of Chest Physicians–recommended medical treatment for patients in extremis from massive PE (eg, failure to maintain blood pressure without supportive measures) is systemic thrombolysis with tissue plasminogen activator (15). Use of this therapy has been considered on a case-by-case basis in the setting of persistent hypotension, severe hypoxemia, large perfusion defects, right ventricular dysfunction, free-floating right ventricular thrombus, and patent foramen ovale (16,17). Systemic thrombolytic therapy compared with heparin was associated with a significant reduction in recurrent PE or death in trials that enrolled patients with major (hemodynamically unstable) PE (18). However, the benefit of systemic thrombolytic therapy has not been established in prospective randomized trials and there is a known increased risk of major hemorrhage (ie, intracranial hemorrhage, retroperitoneal hemorrhage, bleeding leading to death, hospitalization or transfusion) (19). The estimated rate of major hemorrhage from systemic tissue plasminogen activator is approximately 20%, including a 3%–5% rate of intracerebral hemorrhage, when used to treat acute PE (20,21).

A few nonrandomized clinical trials and meta-analyses failed to demonstrate a mortality benefit with thrombolytic therapy compared to anticoagulation alone (22,23), whereas others have suggested some mortality benefit (18,24). Of note is that most studies were designed to primarily evaluate the thrombolytic effect and were not sufficiently powered to detect differences in mortality. Some have also suggested benefit of thrombolytics on important parameters including pulmonary arterial blood pressure, right ventricular function, pulmonary perfusion, and reduced need for treatment of in-hospital events (25–28). The true benefit of peripherally administered thrombolytic therapy, if any, has to be established in prospective trials as newer thrombolytic agents emerge. Despite the lack of definitive data demonstrating a mortality benefit and the known increased risk of major hemorrhage, many clinicians may consider use of systemic thrombolytics in patients

with hemodynamically unstable PE, who are at low risk for a bleeding event.

Catheter-directed Thrombolysis

Catheter-directed thrombolysis (CDT) is a technique that uses the delivery of the thrombolytic agent directly into the thrombus through an endovascular catheter. CDT has been performed in patients with massive PE who could not tolerate systemic thrombolysis or in patients who failed systemic thrombolysis.

In addition, CDT may be useful for patients with relative contraindications to systemic anticoagulative treatment such as recent abdominal surgery, pregnancy, and severe allergic or idiosyncratic reactions to anticoagulants. CDT has been used in hemodynamically unstable patients with massive PE who are at significant risk for bleeding complications associated with systemic thrombolytic therapy. In addition, CDT has been used to emergently treat massive PE refractory to systemic thrombolysis (29).

Because the main cause of death due to massive PE is attributed to irreversible right ventricular failure (30,31), early revascularization of the pulmonary bed in an effort to decrease right ventricular afterload has been a goal of CDT. There is considerable debate regarding the safety and efficacy of catheter-directed thrombolytic therapy, and there is no evidence that direct infusion into the pulmonary artery confers greater benefit than peripheral venous infusion (32). Nonetheless, some have suggested that results from intrapulmonary thrombolytic infusion (ie, placement of catheter proximally in the pulmonary artery in a position remote from the embolus) may be inadequate and intra-embolus infusion is needed to provide maximal pharmacologic and mechanical lysis (33). Data are limited, and well-controlled clinical trials are necessary to establish the safety and effectiveness profiles of catheter-directed thrombolytic administration.

Mechanical Thrombectomy

There has been increased interest in the use of mechanical thrombectomy devices to treat PE. Many of these mechanical or rheolytic systems were originally developed and/or approved for use in smaller blood vessels or grafts. Each of these devices varies in design, ease of

use, and efficacy in removing thrombus. They are designed to remove the thrombus by suction (aspiration thrombectomy), macerate the thrombus and send it distally (fragmentation), or create vortex forces that break up the thrombus and suction it into the catheter (rheolytic thrombectomy). Although some preliminary data regarding the treatment of PE with the newer device technologies appear promising, they are limited and none of the endovascular techniques have been compared with other forms of therapy in prospective randomized controlled studies.

Clinical data on the following devices have been reported in the literature to date:

Fragmentation devices.—Various techniques have been reported to fragment thrombus in an effort to send particles more distally and to expose a larger aggregate surface area of the thrombus to pharmacologic thrombolytic agents. There have been reports of the use of hand rotation of a standard pigtail catheter (34,35), a rotatable pigtail catheter system (William Cook Europe, Bjaeverskov, Denmark) (36), and a system with an impeller that homogenizes clot (Amplatz Thrombectomy Device; Microvena, White Bear Lake, Minnesota) (37). Adjunctive fragmentation with an angioplasty balloon has also been described (6,29).

Aspiration thrombectomy devices.—Various sheaths and guiding catheters have been used in conjunction with fragmentation devices in an attempt to aspirate PE following clot fragmentation. (29,38). The Aspirex device (Straub Medical, Wangs, Switzerland), a mechanical thrombectomy catheter, consists of a high-speed rotational coil that aspirates, macerates, and removes thrombus through an L-shaped aspiration port at the catheter tip. In vitro and in vivo animal experiments demonstrated reversal of cardiogenic shock in the setting of massive PE (39).

Rheolytic devices.—The Hydrolyser thrombectomy catheter (Cordis, Miami, Florida) (40–42) and Oasis thrombectomy catheter (40) (Boston Scientific, Natick, Massachusetts) create a vortex to draw thrombus into the catheter. The AngioJet catheter (Possis Medical, Minneapolis, Minnesota) (43,44) is a conceptually similar over-the-wire system. Several complications have been reported with the AngioJet device, and it is unclear if its use for PE lysis should con-

Table 1
Definitions of Terminology

PE	Intravascular migration of a venous thrombus to the pulmonary arterial circulation
Proved PE	PE proved by a positive pulmonary angiogram, an unequivocally positive helical CT scan, a high-probability ventilation-perfusion scan, or autopsy; imaging method and the extent of PE must be reported
Symptomatic PE	Clinical PE symptoms and/or signs such as chest pain, dyspnea, hemoptysis, palpitations, or tachycardia
Asymptomatic PE	PE detected on an imaging study in a patient without clinical symptoms
Suspected PE	PE suspected based on clinical symptoms and/or signs but for which definitive diagnosis has not been made by imaging or autopsy
Venous thromboembolism	Single common disease entity with two principal manifestations: DVT and PE
DVT	Presence of thrombus within a deep vein of the body as proved by diagnostic imaging; imaging method and the extent of PE must be reported
Major bleeding complication	Intracranial, intraocular, or retroperitoneal hemorrhage or any hemorrhage requiring transfusion and/or resulting in a hematocrit decrease $\geq 15\%$ or hemoglobin decrease ≥ 5 g/dL
Major vascular complication	Any of the following related to the index procedure: hematoma at access site >5 cm, vascular surgical repair or US compression, false aneurysm, arteriovenous fistula, peripheral ischemia/nerve injury, retroperitoneal bleed, or procedure-related transfusion
Acute technical success	Successful delivery of device to the site, operation of the device, and removal of the device
Acute procedural success	Acute technical success with achievement of intended therapeutic goal

tinue. These complications include chest pain, hemolysis, hemoglobinuria, bradyarrhythmia, heart block, hypotension, and fatal hemoptysis (45–50).

Although evaluation of the safety and effectiveness of endovascular mechanical thrombectomy is ongoing, a recent systematic review and meta-analysis of catheter-based treatment for massive PE showed a pooled clinical success rate of 86.5% among 594 patients treated with modern CDT, and the pooled rate of major procedural complications was 2.4% (51).

Surgical Embolectomy

Traditionally, massive PE was treated by surgical embolectomy, with or without thrombolytic therapy. Surgical embolectomy is performed as a last resort in some institutions (52,53). In addition to the aforementioned clinical scenarios that may prompt more aggressive thrombolytic or catheter-based therapies, surgical embolectomy has been prompted by echocardiographic evidence of right atrial or right ventricular clot as well as clot trapped in a patent foramen ovale (54). Surgical embolectomy has not been compared to catheter-directed embolectomy or primary thrombolytic therapy. However, outcomes data after surgical embolectomy are few. Actuarial survival after surgical embolectomy at 1-year follow-up was 86% at one center (55).

Placement of Inferior Vena Cava (IVC) Filters

IVC filters have been used to prevent large venous thrombi from embolizing to the lung by capturing the clot in the IVC. IVC filters have been approved by the U.S. Food and Drug Administration for use in the management of acute PE in patients with an absolute contraindication to anticoagulation or failure of anticoagulation. IVC filters are also used in emergency treatment during massive PE as well as chronic, recurrent PE where anticoagulation has failed or is contraindicated. In clinical practice, IVC filters have also been placed in patients with poor cardiopulmonary reserve, patients who have undergone embolectomy, and as prophylaxis in select patients (eg, malignancy, trauma) (56). Available data suggest that IVC filters decrease recurrent PE and increase recurrent DVT (57) without an effect on mortality (58). However, in a subgroup of patients with persistent hypotension due to PE, a mortality benefit is suggested (16). To address the long-term complications with IVC filter placement, removable filters have been developed; however, data on their use are limited and preliminary.

REPORTING RECOMMENDATIONS

As new device technologies and pharmaceuticals emerge, standardized

approaches to clinical evaluation will prove useful to facilitate comparability of results. Suggested standards of practice for reporting those results are included below.

Definitions

Widely accepted definitions applicable to the current topic have been outlined in the, “Reporting Standards for Endovascular Treatment of Lower Extremity Deep Vein Thrombosis” (59). Relevant definitions from this document as well as additional definitions are included in **Table 1**.

Patient Population

For clinical trials designed to assess the use of endovascular therapies for the treatment of PE, a thorough description of the patient population is critical to allow for reasonable data interpretation. Standardized use of definitions as well as customary approaches to patient selection including consideration of patient risk factors, co-morbidities, and baseline studies are important. A thorough discussion of the patient selection criteria is important to define the patient population in consideration of known and presumed independent risk factors for poor outcome, predisposing risk factors for the development of PE, medical co-morbidities that may affect outcome, and baseline diagnostic studies. Basic demographic data must be provided.

Table 2
Risk Factors for Poor Outcome

Arterial hypotension <90 mm Hg
Circulatory collapse with need for cardiopulmonary resuscitation
Shock with peripheral hypoperfusion and hypoxia
Right heart strain at echocardiography suggestive of pulmonary hypertension
Significant PE on clinical basis and/or imaging in a patient with contraindication to anticoagulation or thrombolytic therapy
Widened arterial-alveolar O ₂ gradient (>50 mm Hg)
Contraindication to anticoagulation

Study inclusion and exclusion criteria must be specifically stated and the method of assigning treatment to patients must be described.

Risk factors for poor outcome.—Anticoagulation has been shown to be effective in reducing mortality associated with PE so the use of more aggressive endovascular therapies is currently considered indicated only for “high-risk” patients. Therefore, risk stratification is critical in deciding which patients should undergo thrombolytic therapy or CDT. There are no definitive guidelines to this effect; however, some investigators have proposed criteria for endovascular treatment (7). **Table 2** includes known and presumed risk factors for poor outcome from an acute PE. Consideration of this information, including the age and the functional status of the patient, may prove useful in the development of relevant patient inclusion criteria and in the reporting of relevant baseline characteristics. Furthermore, one may consider use of standardized measures that have been used in prior studies to assess the severity of illness. These include angiographic assessment scores (Miller index [60]), CT evaluation of the right ventricular dysfunction (61), the Urokinase Pulmonary Embolism Trial index (62), and the Shock index (63).

Risk factors for the development of venous thromboembolism.—Consideration of predisposing risk factors for the development of venous thromboembolism may also prove useful in secondary analyses of outcome. Known and presumed predisposing risk factors for the development of venous thrombosis

Table 3
Risk Factors for the Development of Venous Thromboembolism

Chronic heart disease
Fracture of long bone
Heavy cigarette smoking (>25 cigarettes per day)
History of thromboembolism
Hypercoagulable state (primary and acquired)
Hypertension
Immobilization
Increased age
Indwelling venous catheters
Malignancy
Obesity (body mass index ≥ 29 kg/m ²)
Oral contraceptive use
Preexisting respiratory disease
Pregnancy and postpartum state
Stroke
Surgery
Varicose veins

have been reported in the literature and are included in **Table 3** (64–67).

Baseline evaluation.—Complete characterization of the baseline pretreatment condition is important to allow for clinical interpretation of study results, particularly given that patients to be treated with endovascular techniques will likely be a “high-risk” subset of PE patients. Baseline evaluation of the DVT distribution and thrombus load and assessment of PE location and severity should be included in the baseline evaluation.

Diagnosis and extent of DVT.—Ultrasonographic (US) examination of the lower extremities with localization of the thrombus and overall thrombus burden should be performed and reported according to previously reported standards (59). Briefly, the baseline anatomic extent of thrombosis and the imaging methods of diagnosis must be specified. The proportion of patients with calf vein DVT, femoropopliteal DVT, iliofemoral DVT, infrarenal IVC involvement, and suprarenal IVC involvement must be reported (59).

Diagnosis of extent and severity of PE.—Currently, CT angiography has become the clinically preferred modality to diagnose PE and has largely replaced pulmonary angiography at most institutions (68,69). CT angiography offers good specificity for the detection of PE in main, lobar, and segmental arteries and also facilitates the diagnosis of other disease entities (17,70–72). The sensitivity and specificity of CT angiog-

raphy is expected to improve with improved CT technology (eg, higher contrast resolution with better peripheral visualization, less motion artifact) and greater experience with scan interpretation. CT angiography may also be used to evaluate the extent and location of clot and may, in some cases, give information regarding the severity of PE. For example, CT angiography may offer information regarding noncontroversial indicators of severity (eg, right ventricular/left ventricular diameter ratio, IVC diameter, and azygos diameter) as well as controversial indicators of severity (eg, pulmonary artery clot load, pulmonary artery diameter, septal bowing, IVC contrast reflux) (73). While information regarding the predictors of severity increases, it may prove useful to report known and potential imaging predictors for future analysis.

Other baseline testing.—Advances are also being made with the use of magnetic resonance (MR) angiography and diffusion imaging with hyperpolarized helium 3 in the diagnosis of PE. As technical problems (eg, respiratory/cardiac artifact, suboptimal resolution, susceptibility artifact from adjacent lung) and logistical problems (eg, MR scheduling, study time, screening issues) are addressed, MR angiography may have an increased role in the diagnosis of PE in the future (74).

Each patient being considered for endovascular therapy should undergo baseline imaging to diagnose PE (ie, CT angiography, ventilation-perfusion scanning, pulmonary angiography, and/or MR angiography), and the diagnostic modality should be justified. Given current clinical practice, it is expected that CT angiography will be the preferred method to diagnose and characterize massive PE.

Patients who present with symptoms and signs of PE (ie, dyspnea, pleuritic chest pain, tachypnea, tachycardia) will often get a preliminary work-up to include vital signs, basic blood work (complete blood count, chemistries), electrocardiography, arterial blood gases, and chest radiography. These tests are nonspecific and further evaluation is required for diagnosis. Additional tests that may have diagnostic and/or prognostic roles in the detection and treatment of PE are included in **Table 4**.

Table 4
Diagnostic Tests

Duplex US	Duplex US has largely replaced diagnostic venography for the detection and characterization of DVT. Regarding the current topic, the presence of massive PE should not be a diagnostic dilemma; therefore, evaluation for DVT is not intended to facilitate diagnosis, rather to define vessel patency prior to intervention and to serve as a potential covariant regarding outcome.
BNP	BNP may be elevated in acute PE presumed secondary to increased right ventricular wall stress. Although the magnitude of BNP elevation is nonspecific, some have suggested that BNP levels may provide prognostic information regarding benign versus complicated clinical course (77).
Troponin	Similar to BNP, serum troponin I and troponin T are elevated in some patients with PE (78). Similar to BNP, elevated troponin is nonspecific but may also offer some prognostic information in patients with PE (eg, mortality risk) (79). Recently, some have proposed biomarker risk stratification models that include a combination of BNP and troponin values (80).
D-dimer	D-dimer assays for the diagnosis of PE have good sensitivity and negative predictive value, but poor specificity (81). Attempts have been made to correlate D-dimer values with extent of disease and prognosis, but this approach is not widely accepted.
Echocardiography	Echocardiographic evidence of right ventricular dysfunction (ie, increased right ventricular volume, decreased right ventricular function, tricuspid regurgitation) in patients is estimated to be only 30%–40% (82). Right ventricular dysfunction has been shown to be associated with a two-fold increase in PE-related mortality (83).

Note.—BNP = brain natriuretic peptide.

TREATMENT DESCRIPTION

Device Description and Procedure Description

Information regarding the device(s) selected for treatment should be provided, including a description of the device (name, model, manufacturer), its mechanism of action, and the reason why it was chosen. If multiple devices are included in a single study, clarification should be provided regarding the method by which devices were selected for use. Details regarding the procedure should be provided, including technique, procedure length, need for sedation, venous access, and procedural medications. In particular, details must be provided regarding thrombolytic drug type and dose and the method of transluminal removal of thrombus from the pulmonary arterial system.

Systemic thrombolysis refers to a form of pharmacologic thrombolysis where the infusion of the agent is administered through an intravenous line that is distant from the pulmonary system.

Flow-directed thrombolysis refers to a form of pharmacologic thrombolysis where the infusion is administered through a catheter that is positioned in the pulmonary artery proximal to the location of pulmonary artery thrombus.

Catheter directed intrathrombus thrombolysis refers to the delivery of the thrombolytic agent into the pulmonary

artery thrombus through an infusion catheter, such as a multi-side-hole catheter, that is positioned into the thrombus. In appropriate situations, a lacing dose or a bolus can be given into the thrombus—usually at the initiation of therapy.

Mechanical thrombectomy refers to a method of thrombus removal through a catheter system that removes the thrombus by aspiration, fragmentation or maceration or combination of these.

Pharmacomechanical thrombectomy refers to thrombus removal using a combination of pharmacologic thrombolytic agents and a mechanical catheter-based device.

Concomitant Medical Therapies and Procedures and Intention to Treat Analysis

Concomitant medical therapies (eg, pharmacologic lysis for residual thrombus) and procedures (eg, IVC filter placement) will likely play a significant role in the endovascular treatment of PE; therefore, effort should be made to develop prospective medical therapy regimens and/or algorithmic approaches to treatment such that their role as confounding variables is limited. Data should be collected and reported regarding the type of medications, dose, method of administration, and rationale for use. Parenteral agents that may be used include anticoagulants or platelet inhibitors. Drug doses and appropriate

laboratory values must be reported. The authors must state what treatment was intended and what was actually administered. Any use of adjunctive therapies not included in the original protocol should be reported as deviations and considered intent-to-treat failures. For example, if the protocol for the endovascular procedure includes mechanical thrombectomy alone, any use of additional pharmacologic lysis would be considered a treatment failure. Conversely, if the endovascular treatment includes planned adjunctive pharmacologic treatment (local or systemic) then these cases would not be treatment failures. Nonetheless, the control group or criteria to which the combined pharmacomechanical thrombectomy procedure is compared should be established to elucidate a difference (ie, benefit) with the addition of the endovascular device compared to thrombolysis alone. Furthermore, the protocol should include specific directions regarding the use of IVC filters.

Control Group

Detailed information should be provided regarding the control treatment against which the endovascular treatment is compared. For example, comparison to a thrombolytic agent should include details regarding the agent, dose (ie, bolus, infusion rate, infusion time) and method of administration.

Table 5
Endpoints

Safety	Death Major bleeding and major vascular complications Other major adverse events may be prospectively listed (eg, stroke, myocardial infarction) or established retrospectively. If events are retrospectively adjudicated and categorized as "major" or "minor," it is preferred that each event undergo independent review (ie, Clinical Events Committee).
Effectiveness	Acute technical success Acute procedural success

FOLLOW-UP MODALITIES AND SCHEDULES

Currently, the vast majority of reports of interventional procedures conducted for the purpose of treating PE include retrospective analyses of cases conducted at one or a few institutions. For this reason, reports of outcome often relate to the index procedure or to a subsequent review of the medical record to draw conclusions regarding complications and overall medical condition. Ideally, trials should be conducted with prospective follow-up, with the frequency and type of follow-up depending on the specific research question. Nonetheless, there are standard patient assessments that should be conducted and reported for all trials. Baseline evaluation should include physical examination, basic laboratory tests (eg, chemistries including coagulation), CT angiography (or other modality used to diagnose PE), and assessment of the severity of cardiopulmonary compromise. Follow-up evaluation should include at least a physical examination, monitoring laboratory studies (eg, prothrombin time, partial thromboplastin time, international normalized ratio), assessment of residual PE, and assessment of overall medical condition. Follow-up should continue to evaluate for recurrence of PE, long-term effects of therapy (eg, unintended vascular damage secondary to mechanical thrombolysis), and stability of acute outcomes. The protocol must specify the nature and timing of clinical and imaging follow-up, and results of this follow-up must be reported. Prospectively developed Case Report Forms should be used to record all relevant follow-up information and explanations should be provided regarding any patients who missed a follow-up examination. The

outcomes such as of treatment can be evaluated with follow-up intervals graded as short-term (<30 days), mid-term (30 days to 1 year), or long-term (>1 year).

PRIMARY AND SECONDARY OUTCOMES MEASURES

Treatment decisions regarding endovascular therapies for the treatment of PE will likely be based on the concept that the increased risk to the patient associated with a more invasive treatment may be justified if the benefit to the patient outweighs the risk. Therefore, rigorous collection of both safety and efficacy outcome measures is essential. **Table 5** includes a list of basic clinically relevant endpoints that should be reported for all devices.

In developing primary and secondary safety endpoints, one may consider the potential adverse events listed in **Table 6**. Additional relevant efficacy endpoints may also be considered (eg, length of hospitalization).

Details regarding hemodynamic and physiologic parameters of a procedure should include baseline and posttreatment pulmonary artery pressures and oxygen saturations. Pulmonary angiography performed during the procedure should include arterial, parenchymal, and venous phases. The contrast agent and the volume used during angiography should be reported.

When reporting clinical trial results, the measures that are primary and those that are secondary should be clear and prospectively established. Attempts should be made to choose primary endpoints that have the most direct clinical relevance and would be the most meaningful to consider in future treatment decisions (eg, reduction in mortality,

Table 6
Potential and Observed Adverse Events

Aneurysm
Angina
Arrhythmias
Arteriovenous fistula
Cardiac tamponade
Cardiogenic shock
Dissection
Drug reactions to contrast, thrombolytics, or anticoagulation
Foreign body embolization
Fistulization
Hemoglobinuria
Hemolysis
Hemoptysis
Hypo/hypertension
Infection
Myocardial infarction
Perforation or rupture
Pericardial effusion
Pseudoaneurysm
Renal failure
Respiratory failure
Stroke/transient ischemic attack
Valvular injury/insufficiency

Table 7
SIR Classification of Complications by Outcome

Minor complications
No therapy, no consequence
Nominal therapy, no consequence; includes overnight admission for observation only
Major complications
Require therapy, minor hospitalization (<48 h)
Require major therapy, unplanned increase in level of care, prolonged hospitalization (>48 h)
Permanent adverse sequelae
Death

acute clinical success). Surrogate primary efficacy endpoints should be avoided where possible (eg, improvement in right ventricular dysfunction, reduction in clot burden). All complications should be reported on a per-patient basis and categorized according to the SIR classification of Complications by Outcome shown in **Table 7** (75).

CLINICAL TRIAL DESIGN AND STATISTICAL PLAN

In general, the randomized controlled trial is the preferred trial design

to evaluate new treatments because of inherent benefits to (a) minimize bias, (b) increase the likelihood that comparable groups will actually be compared by balancing known and unknown covariates, (c) allow for comparability of treatments in the current situation where there is the lack of a clear control group, and (d) provide the best evidence so as to avoid providing unnecessary treatment to some patients with all of its attendant costs and risks. Unfortunately, it is recognized that randomized trials are difficult to conduct in the evaluation of all new medical treatments and particularly difficult to employ in the evaluation of treatments of “last resort.” This is the case for endovascular treatment of PE, because patients with nonmassive PE are treated safely and effectively pharmacologically and the anticipated increased risk with invasive treatment is not expected to confer significant offsetting incremental benefit. Initially, it is expected that the evaluation of the feasibility of endovascular treatment of PE will be reserved for patients with massive PE; therefore, comparison may be made with modalities that constitute current standard of care given severity of illness as defined by the patient selection criteria. For some trials, comparison to the expected natural course of the disease may be appropriate. For non-randomized trial designs, every effort should be made to maximize methodologic rigor—especially when evaluating new devices.

Reports should indicate the overall trial design and identify the number of patients and the number of investigational sites. The rationale for choosing a particular trial design should be stated, and any limitations of the chosen design should be discussed. The process by which patients have been screened, enrolled, and assigned to a particular treatment should be described.

All prospective trials should be designed with sufficiently powered sample sizes calculated from estimated event rates based on the primary endpoint. Randomized trials should also be performed in accordance with Consolidated Standards of Reporting Trials (CONSORT) guidelines (76). Inclusion of the hypothesis in mathematical terms is helpful in focusing the reader on the specific research question around which

Table 8**Recommendations for Research Reporting Standards**

Data	Required	Recommended
Population description		
Inclusion/exclusion criteria	X	
Demographic information	X	
Method of treatment assignment	X	
Imaging method of PE diagnosis	X	
Chronicity (acute vs chronic)		X
Detailed risk factor description	X	
Description of co-morbidities		X
Baseline anatomic extent of embolus	X	
Baseline DVT distribution and extent	X	
Treatment description		
Venous access site	X	
Use of concomitant anticoagulation, dose	X	
Route of delivery (systemic vs intrathrombus)	X	
Thrombolytic agent, dose, duration	X	
Device used, manufacturer, model	X	
Duration of device activation time	X	
Mechanical maceration used?	X	
Aspiration thrombectomy used?	X	
Concomitant IVC filter used?	X	
Standardized measures of severity of illness	X	
Adjunctive surgical procedures	X	
Outcomes assessment		
Technical success	X	
Clinical success and failure	X	
Time to symptom improvement	X	
Degree of thrombolysis by angiography		X
Complications classified by SIR outcome scale	X	
Description of adverse events	X	
Analysis		
Description of study design	X	
Institutional review board approval	X	
Description of statistical methods	X	

the trial is designed. If more novel statistical methods are used (eg, Bayesian, sequential designs), a brief discussion of the statistical method should be included. Primary statistical analyses should be reported on an intent-to-treat basis. A per-protocol analysis may also be reported.

If more than one primary endpoint is stated, the estimated sample size should have sufficient power to detect differences between groups for all primary endpoints. Results for secondary endpoints may be reported; however, caution should be used when making statements regarding the significance of those results. Discussion of significant findings should be restricted to those for which prospective statistical analyses were planned.

If more than one device is used, an explanation should be provided regarding how the data were stratified and

how this issue was addressed during the prospective statistical plan.

CONCLUSIONS

With the promise and excitement of new innovative technologies, rigorous clinical trials are necessary to demonstrate the safety and effectiveness of each new device for its specific intended use in the treatment of PE. A standardized approach to reporting clinical experience with these devices will facilitate understanding, communication, and clinical comparability of clinical trial results. **Table 8** summarizes the data elements that are required or recommended in research on endovascular treatment of pulmonary embolism. Well-designed randomized trials, comparing different treatment modalities conducted early in the device's clinical use, are important to expedite clinical agreement regarding preferred treatment

based on reasoned assessments of device safety and effectiveness and will ultimately allow more patients to receive the best established treatment.

Acknowledgments: Filip Banovac authored the first draft of this document and served as topic leader during the subsequent revisions of the draft. Steven F. Millward is Chair of the Technology Assessment Committee. John F. Cardella is Councilor of the SIR Standards Division. Other members of the Technology Committee within SIR who participated in the development of this Reporting Standard are (listed alphabetically): Mark Baerlocher, MD, John Dean Barr, MD, Gary J. Becker, MD, Carl M. Black, MD, John J. Borsari, MD, Matthew R. Callstrom, MD, Drew M. Caplin, MD, Thomas M. Carr, MD, William B. Crenshaw, MD, Michael D. Dake, MD, Aron Michael Devane, MD, B. Janne D'Othee, MD, Salomao Faintuch, MD, Ron C. Gaba, MD, Joseph Gemmete, MD, Debra Ann Gervais, MD, Craig B. Glaiberman, MD, S. Nahum Goldberg, MD, Neil J. Halin, DO, Thomas B. Kinney, MD, Michael D. Kuo, MD, John A. Lippert, MD, Llewellyn V. Lee, MD, Philip M. Meyers, MD, David A. Phillips, MD, Stefanie M. Rosenberg, PA, David A. Rosenthal, PA, James E. Silberzweig, MD, Richard Towbin, MD, Michael J. Wallace, MD, and John York, MD.

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