A Prospective, Multicenter Study of the Indigo* Aspiration System Seeking to Evaluate the Long-Term Safety and Outcomes of Treating Pulmonary Embolism

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The objective of this study is to evaluate real world long-term functional outcomes, safety and performance of the Indigo Aspiration System for the treatment of pulmonary embolism (PE)

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Embolism and thrombosis
Study type	Observational non invasive

Summary

ID

NL-OMON53658

Source
ToetsingOnline

Brief title
STRIKE-PE

Condition

- Embolism and thrombosis

Synonym
clot in the lungs, Pulmonary Embolism

Research involving
Human

Sponsors and support

Primary sponsor: Penumbra Europe GmbH
Source(s) of monetary or material Support: Penumbra Inc

Intervention

Keyword: Clot, Pulmonary Embolism

Outcome measures

Primary outcome

Safety: A composite of device-related death, major bleeding, device-related clinical deterioration, device-related pulmonary vascular injury and device-related cardiac injury (Major Adverse Events) at 48 hrs

Performance: Change in RV/LV Ratio (matched imaging pairs CTA or echocardiogram, as available) at 48hrs post-procedure

Secondary outcome

1. Quality of Life and functional outcome at 90 days post-procedure

2. Incidence of device related SAE(s)

3. Any-cause mortality within 30 days

4. Symptomatic PE recurrence within 30 days

Study description

Background summary

Acute massive pulmonary embolism (PE), defined as hemodynamic instability from acute PE, and acute submassive PE, defined by right ventricular strain without hypotension, are common life-threatening conditions that represent the serious manifestations of venous thromboembolic disease. In the United States, an estimated 530,000 cases of symptomatic PE occur annually;1 and approximately 300,000 people die every year from acute PE.2 The mortality rate can exceed 58% in patients with acute massive PE presenting with hemodynamic shock,3 and most

of these deaths occur within 1 hour of presentation.2-4 Acute massive PE is believed to be the third most common cause of death among hospitalized patients.5

The physiologic effect of massive PE is right ventricular failure, which reduces left ventricular preload and can lead to systemic hypotension and sudden death. While submassive PE has a lower mortality than massive PE, it is associated with a higher mortality and higher rate of clinical deterioration than low-risk PE. Therapeutic anticoagulation is the standard of care (SOC) first-line treatment; the 2016 American College of Chest Physicians (ACCP), 2019 European Society of Cardiology (ESC) and 2011 American Heart Association (AHA) guidelines all recommend the prompt use of anticoagulant therapy (Grade 1b, Class Ia and Class 1a respectively).6-8

Treatment escalation beyond therapeutic anticoagulation is also common practice. Current approved medical therapy for acute massive PE consists of systemic thrombolysis with 100 mg of tPA (Alteplase; Genentech, South San Francisco, California) infused intravenously (IV) over a period of 2 hours.9 Escalating therapy with systemic thrombolytics, while it improves short-term and potentially long-term PE related adverse outcomes, is associated with high incidence of major bleeding.

A meta-analysis of 15 trials involving a total of 2057 massive and submassive PE patients found that major hemorrhage (OR: 2.91; 95% CI: 1.95 to 4.36) and fatal or intracranial hemorrhage (OR: 3.18; 95% CI: 1.25 to 8.11) was significantly more frequent among patients receiving thrombolysis.10 An international registry on massive PE patients who received fibrinolytics and/or inferior vena cava filter placement reported a 90-day mortality rate of 52.4% (95% CI, 43.3% to 62.1%).11 The study also concluded that thrombolytics did not reduce the 90-day mortality rate.11 In another meta-analysis of 8 randomized trials investigating submassive PE, major bleeding including intracranial hemorrhage was significantly more common with systemic thrombolytics compared to anticoagulants alone.12

The optimal treatment strategy for patients with submassive PE is not as clear. Experts agree that further research is needed to tailor treatment protocols and to evaluate long-term outcomes. Several studies have shown higher rates of in-hospital adverse events as well as pulmonary hypertension and poor functional status at follow-up in high risk submassive PE patients given anticoagulants alone.12-14

Given the incomplete efficacy of anticoagulation alone and high bleeding complications of full dose systemic thrombolysis, endovascular catheter-directed therapy has garnered significant interest. Expert guidelines differ in exact treatment recommendations for acute PE, but do suggest catheter-directed therapy - which includes the Indigo Aspiration System - in certain circumstances.6-8,15

For acute PE, the 2019 ESC guideline states that endovascular treatment should be considered for patients with high-risk PE and failed or contraindicated thrombolysis and for patients with intermediate- or low-risk PE who experience hemodynamic deterioration on anticoagulants (class IIa).8 Percutaneous mechanical thrombectomy (e.g. aspiration thrombectomy, fragmentation

thrombectomy and rheolytic thrombectomy) procedures were graded in the 2011 AHA guidelines as class IIa and in the 2016 ACCP guidelines as class II.6,7 The 2019 AHA scientific statement noted that interventional therapies should be strongly considered in patients with PE and hemodynamic instability, and that catheter-based embolectomy is an option for intermediate risk patients with elevated risk for decompensation and bleeding.15 Thus, catheter-directed therapy should be considered for acute massive PE patients who are not candidates for or who fail systemic thrombolysis, and for the more unstable subset of all other acute PE patients.6-8
Catheter-directed therapy encompasses catheter-directed mechanical fragmentation, aspiration of emboli, and intraclot thrombolytic agent direct local infusion. Therefore, a variety of devices may be used to treat PE. Depending on anticipated bleeding risk, catheter-directed therapy may be performed with no or low-dose local tPA injection. The goal of these techniques is to rapidly debulk central thrombus to relieve life-threatening heart strain, immediately improve pulmonary perfusion and reduce the risk of mortality and clinical deterioration.
Catheter intervention is important not only for creating an immediate flow channel through the obstruction, but also for exposing a greater surface area of thrombus to the locally infused thrombolytic drug. In a meta-analysis of 594 patients with acute massive PE treated with catheter-directed therapy, clinical success was achieved in 86.5% of the cases, with success defined as hemodynamic stabilization, resolution of hypoxia and survival to hospital discharge.16 In the same study, 33% of cases were initiated with mechanical treatment alone without local thrombolytic infusion.16 When injected locally, the required dose of tPA is lower compared with full-dose systemic infusion, potentially reducing the bleeding risk.

Study objective

The objective of this study is to evaluate real world long-term functional outcomes, safety and performance of the Indigo Aspiration System for the treatment of pulmonary embolism (PE)

Study design

Post-market, real world, prospective, multi-center study that will enroll approximately 1500 subjects at up to 80 sites globally

Study burden and risks

not applicable

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

1. Clinical signs and symptoms consistent with acute PE with duration of 14 days or less
2. RV/LV ratio >= 0.9 assessed by diagnostic computed tomographic angiography (CTA) or echocardiogram
3. Frontline endovascular treatment with the Indigo Aspiration System per IFU
4. Patient is >= 18 years of age
5. Informed consent obtained per Institutional Review Board/Ethics Committee requirements

Exclusion criteria

1. Contraindication to systemic or therapeutic doses of anticoagulants (e.g. heparin)
2. Stage IV (metastatic) cancer, active lung cancer or previous history of surgery in the affected lung(s) or chest radiation
3. Known serious, uncontrolled sensitivity to radiographic agents
4. Life expectancy < 180 days
5. Patients on ECMO
6. Pregnant patients
7. Current participation in another investigational drug or device study that may confound the results of this study. Studies requiring extended follow-up for products that were investigational but have since become commercially available are not considered investigational studies
8. Other medical, social, or psychological conditions that, in the opinion of the Investigator, precludes the patient from appropriate consent, could limit the patient's ability to participate in the study, including compliance with follow-up requirements, or that could impact the scientific integrity of the study

Study design

Design

Study phase:	4
Study type:	Observational non invasive
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	25-06-2021
Enrollment:	50
Type:	Actual

Medical products/devices used

Generic name:	Indigo aspiration system
Registration:	Yes - CE intended use

Ethics review

Approved WMO Date:	09-03-2023
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	07-09-2023
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	12-08-2024
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
ClinicalTrials.gov	NCT04798261

Register	ID
CCMO	NL81070.058.22