Pulmonary Embolism ALERT
Think Fast, Act Together!
Common PE Symptoms Include:
- Shortness of breath
- Progressively worsening chest pain
- Cough
- Clammy or discoloured skin
- Excessive sweating
- Rapid or irregular heartbeat
- Lightheadedness or dizziness

Venous thromboembolism (VTE) is a condition in which a blood clot forms – usually in the deep veins of the leg, groin or arm (deep vein thrombosis or DVT). When the clot travels in the circulation and lodges in the lungs, it is known as pulmonary embolism (PE).

79% of patients presenting with PE have evidence of DVT

PE occurs in up to 50% of patients with proximal DVT

VTE is responsible for more deaths in the US each year than highway fatalities, breast cancer and AIDS combined

VTE is responsible for more deaths in certain EU countries each year than breast cancer and AIDS combined

PE causes or contributes to 15% of all hospital deaths

VTE is responsible for more deaths in certain EU countries each year than breast cancer and AIDS combined

About Venous Thromboembolism and Pulmonary Embolism
The Diagnosis and Management of Acute PE

A PE can be immediately fatal. However, if a PE can be diagnosed and the appropriate therapy started, the mortality can be reduced from approximately 30% to less than 10%.

The PE roadmap shown here is adapted from the European Society of Cardiology (ESC) Guidelines.

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Clinical Suspicion of PE

- Yes
  - Shock / Hypotension?
    - Yes: Diagnostic algorithm as for suspected high-risk PE
    - No: Diagnostic algorithm as for suspected NOT high-risk PE

- No
  - PE Confirmed
    - High risk
      - Intermediate-high risk
        - Consider further risk stratification
        - RV function (echo or CT) & laboratory testing
      - Intermediate-low risk
        - A/C; consider early discharge & home treatment, if feasible
    - Intermediate risk
      - A/C; monitoring; consider rescue reperfusion
    - Low risk
      - A/C; hospitalisation

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Measuring RV/LV Ratio

- Apical 4-chamber view
- End diastolic image
- Centre line through interventricular septum
- Obtain tricuspid annular line
- Obtain subannular line 1cm above annular line
- Obtain RV and LV dimensions using endocardial borders

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Sample Pre and Post RV/LV Measurement Leveraging 2-Hour OPTALYSE Protocol

**CTA Pre PE Therapy:** RV/LV ratio: 1.516

- RV: 52.9mm
- LV: 34.9mm

**CTA 48 Hours Post PE Therapy:** RV/LV ratio: 0.798

- RV: 37.8mm
- LV: 47.5mm

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Why Intervene on Intermediate-High-Risk Patients?

Various studies report the presence of right ventricular dysfunction (RVD) as a predictor of poor clinical outcomes:

- The presence of RV hypokinesis on the baseline echo is associated with higher mortality at 2 weeks and 3 months compared to cases with no RV hypokinesis.
- Patients with RVD defined as RV/LV >0.9 have a greater chance of adverse events within 30 days than those with RV/LV ≤0.9.
- Patients with unresolved RVD are 8 times more likely to experience recurrent venous thromboembolism (VTE) than those without RVD.

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† Based on data presented in Grifoni et al., Arch Intern Med, 2006; 166: 2151-6.
Developing a Successful PE Programme

PE Alert Checklist
Pre-hospital identification is a vital initial step in the emergency medical management of PE. A symptoms-based screening tool facilitates rapid, standardised, symptomatic clinical assessment. Based on the assessment, routing the acute PE patient to the most appropriate treatment facility which offers the latest therapies and interventional technologies, including the EKOS™ system, will improve outcomes for patients.

Establishing PE Patient Pathway
In order to facilitate a rapid, robust response to the diagnosis of PE, it is important to establish a multidisciplinary pulmonary embolism response team (PERT) and implement a PE Pathway.

The PERT model is based on existing multidisciplinary teams such as heart teams and rapid response teams. A PERT is composed of clinicians from the range of specialties involved in the treatment of PE, including pulmonology, critical care, interventional radiology, cardiology and cardiothoracic surgery among others.

A PERT serves as a 24/7 consult service that is able to provide expert advice on the initial management of PE patients and convene in real time to develop a consensus treatment plan specifically tailored to the needs of a particular patient and consistent with the capabilities of the institution. 

*Treater (EKOS™ User): Clinicians treating with EKOS™ are typically interventional cardiologists, interventional radiologists, cardiothoracic, cardiovascular or vascular surgeons.
Acoustic Pulse Thrombolysis™ treatment is a minimally invasive system for dissolving thrombus. The ultrasonic core generates an acoustic field which greatly accelerates lytic dispersion by driving the drug deeper into the clot and unwinding the fibrin to expose plasminogen receptor sites.

**Acoustic Pulse Thrombolysis™ Treatment:**
- Speeds time to dissolution
- Increases thrombus removal and clinical improvement compared to either standard catheter-directed therapy (CDT) or thrombectomy
- Lowers the risk of bleeding and other complications

**More Effective Drug Delivery:**
- Reduces dosage requirements by as much as 68% compared to standard CDT
- Requires up to 4x less drug dosage than systemic delivery
- 48% greater drug absorption within 1 hour
- 84% greater drug absorption within 2 hours

**EKOS™ System Lower Patient Risk. Higher Procedure Predictability**

The EkoSonic™ Endovascular System includes an ultrasonic core within an infusion catheter, and control unit. At-a-glance operating status, alarms and treatment times are easy to read from a distance.

**Reduced Procedure Time**
EKOS™ requires significantly shorter treatment times, typically only 33%-50% of standard CDT. Unlike more complex surgical solutions, EKOS™ is an efficient, three-step process:

1. **Insert the EKOS™ 5.4 F infusion catheter through the thrombus**
2. **Insert the ultrasonic core until it locks in place**
3. **Activate the lytic infusion and acoustic pulse**

**Targeting the Thrombus, Safely**
The EKOS™ System’s safety and efficacy are supported by Level 1 and Level 2 data.

**Acoustic Pulse + Lytic™**
More drug reaches entire thrombus, accelerating absorption.

**Drug Delivery Lumen**

**Central Coolant Lumen**

**Therapy Optimisation Sensor**

**Therapy Optimisation Sensor**

**Coolant**

**Ultrasound Core Transducer**

**Marker Band**

**Treatment Zone**

**Treatment zones range from 6cm to 50cm with radiopaque marker bands at each end of the treatment zone to enhance visualisation.**
Randomized, Controlled Trial of Ultrasound-Assisted Catheter-Directed Thrombolysis for Acute Intermediate-Risk Pulmonary Embolism

Nils Kucher, MD et al. Circulation 2014; 129: 479-486

**Patients**

Acute PE with RV/LV ratio ≥ 1.0

**Methods**

Infusion Protocol
- IV bolus: 80 IU/kg
- Infusion: 18 IU/kg/hour

Unfractionated Heparin
- IV bolus: 80 IU/kg
- Infusion: 18 IU/kg/hour

Unfractionated heparin administered immediately after randomisation

**Key Results**

- RV/LV ratio significantly improved at 24 hours
- Reduction in RV/LV ratio significantly greater at 24 hours and improved at 90 days
- No deaths or significant bleeding complications
- Systolic RV dysfunction significantly improved

**Conclusion**

ULTIMA confirmed that a fixed-dose, ultrasound-assisted catheter-directed thrombolysis using EKOS™ regimen was superior to anticoagulation alone in improving RV dysfunction at 24 hours without an increase in bleeding complications.
METHODS
Ultrasound-facilitated fibrinolysis using EKOS™

A Prospective, Single-Arm, Multicentre Trial of Ultrasound-Facilitated, Low-Dose Fibrinolysis for Acute Massive and Submassive Pulmonary Embolism

PATIENTS
Acute massive and submassive PE with RV/LV ratio ≥ 0.9 (n = 150; 22 centres)

If unilateral PE:
- tPA 1 mg/hr using one EKOS™ system for 24 hours

If bilateral PE:
- tPA 1 mg/hr/per EKOS™ system (using two simultaneously) for 12 hours

Follow up at 48 +/- 6 hours
- CT measurement of RV/LV ratio
- Echocardiogram to estimate PA systolic pressure

KEY RESULTS
25% decrease in RV/LV ratio over 48 hours
Minimised risk of intracranial haemorrhage
Rapidly relieved pulmonary artery obstruction
Reduced pulmonary hypertension

CONCLUSION
Ultrasound-facilitated, catheter-directed, low-dose fibrinolysis for acute PE improves RV function and decreases pulmonary hypertension and angiographic obstruction. By minimising the risk of intracranial bleed, it represents a potential “game-changer” in the treatment of high-risk PE patients.

EKOS™ PE Clinical Studies
SEATTLE II Trial

A Prospective, Single-Arm, Multicentre Trial of Ultrasound-Facilitated, Low-Dose Fibrinolysis for Acute Massive and Submassive Pulmonary Embolism

25% decrease in RV/LV ratio over 48 hours

Minimised risk of intracranial haemorrhage

Rapidly relieved pulmonary artery obstruction

Reduced pulmonary hypertension

Study | Intracranial Haemorrhage (Fibrinolysis Group)
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ICOPER (Goldhaber SZ, et al. 1999) | 9/304 (3%)
PEITHO (Meyer G, et al. 2014) | 10/506 (2%)
SEATTLE II (Piazza G, et al. 2014) | 0/150 (0%)
EKOS™ PE Clinical Studies

**OPTALYSE PE Study**

**Optimum Duration and Dose of tPA with the Acoustic Pulse Thrombolysis Procedure for Submassive Pulmonary Embolism: OPTALYSE PE**


**PATIENTS**

Acute PE with RV/LV ratio ≥0.9 (n = 101; 17 centres)

<table>
<thead>
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<th>Cohort 2</th>
<th>Cohort 3</th>
<th>Cohort 4</th>
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<td>4/8mg tPA*</td>
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<td>12/24mg tPA*</td>
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**METHOD**

- Anticoagulation therapy using heparin
- Acoustic Pulse Thrombolysis™ treatment using EKOS™ – following duration and dosage of randomly assigned study cohort
- Follow up at 48hrs post treatment start with CTA

**KEY RESULTS**

RV/LV ratio continued to reduce after 48h. P value <0.0001 @ 365d

Long-term OPTALYSE safety & efficacy at 365d

- **PEmB-QoL score decreased for all cohorts**
- **PROMIS-PF score increased for all cohorts**

**CONCLUSION**

The EKOS™ System’s very low dose and short duration regimens, in the OPTALYSE PE Trial, resulted in rapidly improved measures of right-heart function that were maintained for one year. Additionally, the favourable mortality rates, recurrent PE rates, and quality-of-life results demonstrate long-term benefits of EKOS™ therapy. This data further proves the PE clinical efficacy and safety of the OPTALYSE PE treatment protocols.

Safety and Efficacy of Ultrasound-Accelerated Catheter-Directed Lytic Therapy in Acute Pulmonary Embolism With and Without Haemodynamic Instability

**METHODS**

Insertion of the Catheter System
In cardiac catheterisation lab
- Venous access – common femoral vein under US guidance:
  - 0.035” guidewire and angiographic catheter to cross occlusion
  - With guidewire tip within large lower-lobe segmental branch, angiographic catheter exchanged for EKOS™ Infusion Catheter
  - Guidewire removed and EKOS™ ultrasonic core inserted
  - Infusions started then ultrasound turned on

Infusion Protocol
- Average of 30.5mg tPA infused at 1mg/h
- Saline coolant 35mL/h during infusion
- After four hours tPA reduced to 0.5mg/h
- Average thrombolytic time was 14.2 hours
- EKOS™ devices removed bedside
- After procedure, standard anticoagulation was administered

**KEY RESULTS**

Acute PE patients treated with EKOS™ therapy showed:
- Complete resolution of cardiac dysfunction in 64% of patients immediately post procedure
- Direct pulmonary artery pressure showed an average reduction of 40.2%
- No deaths through 90 days of follow-up and no major periprocedural bleeding events
- Fewer adverse events at 2-year follow-up compared to patients treated with anticoagulation only
- Shorter average length of stay: EKOS™ treated = 3.2 days vs. AC = 6.7 days

**CONCLUSION**

EKOS™ therapy is an effective PE treatment for reducing pulmonary artery pressures and resolving haemodynamic abnormalities, with excellent mortality and complication rates.
Ultrasound-Assisted Catheter-Directed Thrombolysis of Acute Pulmonary Embolism: A Review of Current Literature

Cureus 9(7): e1492. DOI 10.7759/cureus.1492

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Objective:
Review to elaborate current evidence and research on risk stratification of PE and safety, efficacy, limitations and complications of ultrasound-assisted catheter-directed thrombolysis (UACDT).

Results:
• 14 retrospective (n=524) and 6 prospective (n=383) studies published efficacy and safety data for UACDT. 13 Studies included patients with massive PE (n=180)
• Overall, UACDT was found to offer greater benefits with fewer major bleeding events and mortality events, suggesting better safety:
  - The pooled incidence of in-hospital, 30-day and 90-day mortality was 2.3%, 0.4% and 0.8% respectively
  - The pooled incidence of major and other bleeding episodes was 2.8% and 7.2%, respectively
  - The pooled incidence of recurrent PE was 0.4%
  - One intracranial haemorrhage (ICH) reported in Ozcinar et al prospective observational study. The authors could not identify any further ICH in any other study

Conclusion:
• Ultrasound-assisted catheter-directed thrombolysis (UACDT) is emerging as an alternative revascularisation procedure to systemic thrombolysis and surgical embolectomy for PE
• UACDT is superior in improving RV/LV ratio, pulmonary artery pressure (PAP), thrombotic burden and cardiac index with a lower risk of bleeding and other complications
• Further prospective randomised studies are warranted to compare the efficacy and safety of UACDT with catheter-directed thrombolysis without ultrasound and systemic thrombolysis

EKOS Corporation, a BTG International group company, pioneered the development and clinical application of ultrasound infusion technologies in medicine, introducing its first system for the treatment of vascular thrombosis in 2005.

Today, interventional radiologists, cardiologists, and cardiothoracic and vascular surgeons at leading institutions around the world use the EKOS™ system to provide faster, safer and more complete dissolution of thrombus.

BTG is committed to raising awareness of pulmonary embolism and to working with healthcare professionals to improve standards in its diagnosis and treatment. In order to do this, we support a number of development and training initiatives.
REFERENCES


ABBREVIATIONS

A/C: Anticoagulation
CDT: Catheter-directed therapy/thrombolysis
CT: Computed tomography
CTA: Computed tomographic angiogram
DVT: Deep vein thrombosis
GP: General Practitioner
ICHI: Intracranial haemorrhage
ICU: Intensive care unit
IV: Intravenous
IVR: Intra venous
LV: Left ventricle/ventricular
PA: Pulmonary artery/arterial
RAP: Pulmonary artery pressure
PE: Pulmonary embolism
PERT: Pulmonary embolism response team
PEIS: Pulmonary embolism severity index
PROMIS: Patient Reported Outcomes Measurement Information System
(RF): (physical function)
QoL: Quality of life
RV: Right ventricle/ventricular
RVD: Right ventricular dysfunction
sPESI: Simplified pulmonary embolism severity index
TPA: Tissue plasminogen activator
UA: Ultrasound-assisted
UACDT: Ultrasound-assisted catheter-directed thrombolysis
VTE: Venous thromboembolism

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Share and discuss PE and DVT cases in the EKOS Clinical Discussion Group on MedShr
https://medshr.it/ekos

MedShr
The App for Doctors

Note: MedShr is not intended for reporting adverse patient outcomes and/or product-related issues.

Please contact the EKOS Help Line at +1 888-356-7435 or +1 425-415-5100 to report adverse patient outcomes and/or product-related issues.