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Catheter-directed thrombolysis in patients with acute pulmonary embolism

Submission date
30/01/2022

Recruitment status
No longer recruiting

Registration date
31/01/2022

Overall study status
Completed

Last Edited
08/06/2022

Condition category
Circulatory System

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[X] Results
[ ] Individual participant data

Plain English summary of protocol

Background and study aims
Acute pulmonary embolism (PE) is a common and life-threatening disease. It occurs when a blood clot gets lodged in an artery in the lung, blocking blood flow to part of the lung. Patients with intermediate- to high-risk acute PE have an increased risk of early death. Based on the current treatment recommendations, systemic thrombolysis (treatment to dissolve blood clots) is not recommended in these patients because of the increased risk of severe bleeding complications (including bleeding in the brain), so anticoagulation treatment (medicines that help prevent blood clots) have been the mainstay of treatment over the last decades. The aim of this study is to compare catheter-directed local thrombolysis to standard anticoagulation treatment in patients with intermediate to high-risk acute PE. Catheter-directed thrombolysis uses x-ray imaging to help guide medication to the site of a blood clot and dissolve it.

Who can participate?
Patients aged over 18 years with acute pulmonary embolism.

What does the study involve?
Participants are randomly allocated to undergo catheter-directed treatment or standard anticoagulation treatment. All participants will undergo CT scans, first as a standard diagnostic procedure and a second at 48 hours after random allocation.

What are the possible benefits and risks of participating?
The study will provide information about the effectiveness and safety of catheter-directed local thrombolysis in patients with intermediate to high-risk acute PE. There is a small risk of bleeding complications taking into account invasive procedures and the use of a small dose of antithrombotic drugs.

Where is the study run from?
University Hospital Kralovske Vinohrady, Prague (Czech Republic)

When is the study starting and how long is it expected to run for?
September 2019 to May 2021

Who is funding the study?
1. University Hospital Kralovske Vinohrady (Czech Republic)
2. Charles University in Prague (Czech Republic)

Who is the main contact?
Josef Kroupa
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Contact information

Type(s)
Public

Contact name
Mr Josef Kroupa

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
EK-VP/49/0/2019

Study information

Scientific Title
Catheter-directed thrombolysis in patients with intermediate-high risk acute pulmonary embolism: a randomized pilot study

Study objectives

Catheter-directed local thrombolysis in patients with intermediate-high risk acute pulmonary embolism improves right ventricle function more effectively in comparison to standard anticoagulation therapy without an increased risk of severe bleeding complications.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 04/09/2019, University Hospital Kralovske Vinohrady Ethics Committee (Srobarova 1150/50, 100 34 Prague, Czech Republic; +420 (0)267 16 2272; eticka.komise@fnkv.cz), ref: EK-VP /49/0/2019

Study design
Single tertiary care centre investigator-initiated randomized interventional study

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details to request a participant information sheet

Health condition(s) or problem(s) studied
Acute pulmonary embolism

Interventions
Study participants with CT angiographically (CTA) verified acute pulmonary embolism are randomized using the envelope method into two groups - catheter-directed local thrombolysis (CDT group - interventional) and standard anticoagulation therapy (standard care group). Patients randomized into the CDT group will undergo the interventional procedure catheter-directed local thrombolysis using two thrombolytic catheters placed in each of the right and left interlobar pulmonary arteries with a short overlap in the main pulmonary artery. Subsequent continuous infusion of alteplase at 1 mg/h/catheter will be initiated for 10 h (total dose 20 mg). After the end of local thrombolysis, the catheters will be removed and standard anticoagulation therapy will be continued. Patients randomized into the standard care group will continue standard anticoagulation therapy. All patients will undergo a second CTA at 48 h after randomization. Follow-up periods in-hospital, discharge, 30 days.

Intervention Type
Procedure/Surgery

Primary outcome measure
1. Effectiveness of CDT, defined as improved right ventricle function (at least two of the following criteria are met):
1.1. Reduction of the RV/LV ratio by 25% between admission and 48 h post-randomization, as revealed by CTA
1.2. Reduction of the systolic pulmonary artery pressure (sPAP) by 30% from baseline or attainment of normotension (≤35 mmHg sPAP), as revealed by echocardiography at 24 h post-randomization
1.3. Reduction of the Qanadli score by 30% between admission and 48 h post-randomisation, as revealed by CTA
2. Safety of CDT, defined as the absence of intracranial or life-threatening bleeding according to the Bleeding Academic Research Consortium (BARC) classification (i.e., type 5 or 3c bleeding) within 72 h post-randomisation

Secondary outcome measures
1. Technical success of catheter-directed treatment, defined as successful catheter placement followed by continuous infusion of alteplase at the time of the procedure
2. All bleeding complications scored by Bleeding Academic Research Consortium classification during hospitalization
3. Hemodynamic instability, defined as cardiac arrest or persistent hypotension (systolic blood pressure <90 mmHg or blood pressure drop ≥40 mmHg, either lasting >15 minutes, not caused by hypovolaemia, sepsis, or arrhythmia), recorded during hospitalization
4. Length of hospitalization collected from medical records during hospitalization
5. In-hospital mortality collected from medical records during hospitalization

Overall study start date
04/09/2019

Completion date
31/05/2021

Eligibility

Key inclusion criteria
1. Aged >18 years
2. Computed tomography angiography (CTA)-verified proximal* PE and symptom onset <14 days prior
3. Intermediate-high risk PE with a SPESI score ≥1 and RV dysfunction** and an elevated biomarker *** (hs-troponin or NT-proBNP) level

* A perfusion defect in at least one main or one lobar pulmonary artery evident on CTA
** RV/LV ratio ≥0.9 on transthoracic echocardiography or CTA
*** hs-troponin I (TnI) >53 ng/l (men) or >34 ng/l (women); NT-proBNP level >600 pg/ml

Participant type(s)
Patient

Age group
Adult

Lower age limit

18 Years

Sex
Both

Target number of participants
45

Total final enrolment
28

Key exclusion criteria
1. Active clinically significant bleeding
2. Any hemorrhagic stroke OR a recent (< 6 months) ischaemic stroke/transient ischaemic attack
3. Recent (<3 months) cranial trauma OR another active intracranial/intraspinal process
4. Major surgery within 7 days prior
5. RV/LV ratio <0.7 on transthoracic echocardiography or CTA
6. Active malignancy or other severe illness with expected survival <2 years
7. Haemoglobin level <80 g/l; international normalised ratio >2.0, platelet count ≤100 x 10e9; creatinine level >200 µmol/l
8. Pregnant or breastfeeding, fertility without previous exclusion of gravidity
9. Allergic to thrombolytics or heparin or low-molecular-weight heparin (LMWH), contrast allergy, a history of heparin-induced thrombocytopenia
10. Participation in another clinical trial

Date of first enrolment
01/11/2019

Date of final enrolment
30/04/2021

Locations

Countries of recruitment
Czech Republic

Study participating centre
University Hospital Kralovske Vinohrady
Srobarova 1150/50
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Sponsor information

Organisation
Fakultní nemocnice Královské Vinohrady

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Sponsor type
Hospital/treatment centre

Website
http://www.fnkv.cz/

ROR
https://ror.org/04sg4ka71

Funder(s)

Funder type
University/education

Funder Name
Univerzita Karlova v Praze

Alternative Name(s)
Charles University, Charles University in Prague, Univerzita Karlova, Karls-Universität zu Prag, UK

Funding Body Type
Government organisation

Funding Body Subtype
Universities (academic only)

Location
Czech Republic

Results and Publications

Publication and dissemination plan
Planned publication in a peer-reviewed journal. Additional documents are not available.

Intention to publish date
01/02/2022

Individual participant data (IPD) sharing plan
Participant level data will be available upon request to principal investigator Josef Kroupa (mudr.kroupa@gmail.com). Data are already available, will be available for 5 years, and are anonymized. Participant consent was not obtained for sharing other data.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		27/05/2022	08/06/2022	Yes	No