Challenges in the management of acute pulmonary embolism

Case: A pregnant woman presenting with clinical suspicion of acute venous thromboembolism: Appropriate diagnostic and therapeutic strategy in pregnancy.

Steen Husted, MD, DSc
Director of Medical Department
Hospital Unit West, Denmark
Leading causes of deaths in UK

From UK Enquires into Maternal Deaths

Rates per million maternities

- VTE
- Preeclampsia
- Sepsis
- Amniotic embolism
- Haemorrhage
- Ectopic
- Anaesthetic
Norwegian register-based case-control study

- 613,232 pregnancies from 1990-2003
- Incidence of VTE 1 per 1,000 pregnancies

<table>
<thead>
<tr>
<th></th>
<th>Antenatal VTE n/1,000 (95% CI)</th>
<th>Postnatal VTE n/1,000 (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PE</strong></td>
<td>0.06 (0.045-0.075)</td>
<td>0.22 (0.19-0.25)</td>
</tr>
<tr>
<td><strong>DVT</strong></td>
<td>0.43 (0.40-0.46)</td>
<td>0.30 (0.27-0.33)</td>
</tr>
</tbody>
</table>

Incidence of VTE in pregnancy

Distribution of VTE in pregnancy and puerperium

Number of VTEs per week.

Pregnancy induces risk factors for VTE

- Changes of hemostasis:
  - Increased levels of Factors I, V, VII, VIII, IX, X, XII and von Willebrand factor
  - Decreased levels of Protein S
  - Impaired Fibrinolysis

- High venous pressure
  - Increased diameter of major leg veins
  - Reduction in venous blood flow

Increase of D-dimer levels during normal uncomplicated pregnancy

Szecsi, Jørgensen et al. Thromb Haemost 2010
VTE in Pregnancy

Case

30 year old pregnant woman in 25\textsuperscript{th} week admitted to hospital because of sudden onset dyspnoea, chest pain synchronous with respiration and palpitations

- No family or personal history of VTE
- No swelling or other symptoms from her legs
VTE in Pregnancy
Case

- Auscultation without pulmonary abnormality – regular tachycardia 105 beats/min, BP 120/75 mmHg, subfebrile
- ECG: Sinus tachycardia, no signs of ischemia or RV strain
- D-dimer 2.8 mg/L (normal <0.5 mg/L), normal troponin
- echocardiography: Normal
Clinical assessment is problematic

- Symptoms compatible with VTE, but of non-thrombotic origin, are common during pregnancy
- Prevalence of VTE in pregnant patients presenting with a clinical suspicion < 10 %
- Prevalence of VTE in non-pregnant patients presenting with a clinical suspicion ca 25 %
Diagnosis of VTE in Pregnancy

- Clinical assessment

- Visualizing the occluded vein(s)
  - DVT
    - (Color-Doppler) – compression ultrasonography
    - CT or MR
    - Venography
  - PE
    - Perfusion-ventilation scintigraphy (SPECT)
    - Echocardiography
    - Helical CT (multislice)
    - MR

- Biochemical methods
  - D-Dimer (fibrin fragments)
VTE in Pregnancy

Case

Question: Next diagnostic measure:

1. Bilateral lower limb CUS
2. Perfusion lung scan
3. Perfusion and ventilation lung scan
4. CT-angiography
Estimated radiation absorbed by fetus:

- Chest radiography: 0.01 mSv
- Perfusion lung scan: 0.06-0.12 mSv
- Perfusion and ventilation lung scan: 0.2 mSv
- CT pulmonary angiography: (first t.: 0.003-0.02; second t.: 0.008-0.08; third t.: 0.051-0.13)

Upper limit with regard to danger of injury to fetus: 50 mSv

Ginsberg JS et al., Thromb Haemost 1989
Winer-Muran HT et al., Radiology 2002
VTE in Pregnancy

Case

Question: Treatment options in this patient

1. Thrombolysis followed by anticoagulant therapy
2. Warfarin preceded by UFH/LMWH
3. Fondaparinux subcutaneously
4. LMWH subcutaneously
VTE in Pregnancy

Case

Treatment:
- Tinzaparin in therapeutic dosis

Treatment duration:
- LMWH throughout pregnancy and ≥ 3 months postnatal
- LMWH may be replaced by warfarin postnatal
Are Low Molecular Weight Heparins safe and efficient in pregnancy?

<table>
<thead>
<tr>
<th>Study</th>
<th>Therapeutic dosis</th>
<th>Prophylactic dosis</th>
<th>LMWH used</th>
<th>Bleeding</th>
<th>VTE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Greer 2005</td>
<td>174</td>
<td>2603</td>
<td>LMWHs</td>
<td>2 %</td>
<td>1.4 %</td>
</tr>
<tr>
<td>Voke 2007</td>
<td>126</td>
<td>0</td>
<td>LMWHs</td>
<td>0 %</td>
<td>5 %</td>
</tr>
<tr>
<td>Bauersachs 2007</td>
<td>116</td>
<td>469</td>
<td>Dalteparin</td>
<td>5.1 %</td>
<td>0.6 %</td>
</tr>
<tr>
<td>Nelson-Piercy 2011</td>
<td>254</td>
<td>1013</td>
<td>Tinzaparvin</td>
<td>2.8 %</td>
<td>1.2 %</td>
</tr>
</tbody>
</table>

LMWHs seem to be safe during pregnancy.
Venous thromboembolism (VTE) in pregnancy

- VTE is still the most common cause of maternal morbidity and mortality
- VTE in pregnancy is often preventable
- Thromboprophylaxis should be used more widely, particularly in high risk patients

OPTIMIZING VTE TREATMENT OR PROPHYLAXIS IN PREGNANCY

- Individual risk assessment of all women in early pregnancy
- Repeat risk assessment if admission or intercurrent problems
- Antenatal thromboprophylaxis as early in pregnancy as practical
- Consider:
  - Indication for LMWH
  - Low, intermediate or high prophylactic dose
  - Duration of full dose in acute VTE
  - Dosis monitoring
Challenges in the management of acute pulmonary embolism

Case: A pregnant woman presenting with clinical suspicion of acute venous thromboembolism: Appropriate diagnostic and therapeutic strategy in pregnancy.

Steen Husted, MD, DSc
Director of Medical Department
Hospital Unit West, Denmark
## Adjusted odds ratios (AOR) for Risk of VTE in pregnancy

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>AOR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Previous VTE</td>
<td>24.8</td>
<td>17.1 - 36</td>
</tr>
<tr>
<td>Postpartum haemorrhage + surgery</td>
<td>12.0</td>
<td>3.9 - 36.9</td>
</tr>
<tr>
<td>Immobility postnatal</td>
<td>10.8</td>
<td>4.0 - 28.8</td>
</tr>
<tr>
<td>Obstetric haemorrhage</td>
<td>9.0</td>
<td>1.1 - 71</td>
</tr>
<tr>
<td>Systemic lupus erythematosus</td>
<td>8.7</td>
<td>5.8 - 13</td>
</tr>
<tr>
<td>Immobility antenatal</td>
<td>7.7</td>
<td>3.2 - 19</td>
</tr>
<tr>
<td>Transfusion</td>
<td>7.6</td>
<td>6.2 - 9.4</td>
</tr>
<tr>
<td>Heart disease</td>
<td>7.1</td>
<td>6.2 - 8.3</td>
</tr>
<tr>
<td>Sickle cell disease</td>
<td>6.7</td>
<td>4.4 - 10.1</td>
</tr>
<tr>
<td>Postpartum infection + caesarean section</td>
<td>6.2</td>
<td>2.4 - 16.2</td>
</tr>
<tr>
<td>Preeclampsia + fetal growth restriction</td>
<td>5.8</td>
<td>2.1 - 16</td>
</tr>
<tr>
<td>Obesity, body mass index &gt; 30</td>
<td>5.3</td>
<td>2.1 - 13.5</td>
</tr>
<tr>
<td>Assisted reproductive therapy</td>
<td>4.3</td>
<td>2.0 - 9.4</td>
</tr>
</tbody>
</table>
A normotensive 75-year-old man with intermediate-risk pulmonary embolism: a candidate for thrombolysis?

Guy Meyer
Hôpital Européen Georges Pompidou
Université Paris Descartes
Paris, France
Case scenario

• 75-year-old man
• No previous medical history
• Shortness of breath of acute onset and syncope one week after a long-haul flight
• Blood pressure: 110/70, heart rate: 120 bpm, respiratory rate: 28 cpm, SaO2: 92%
• No shock, no sign of right ventricular failure
Case scenario

- Large central PE confirmed by MDCT
- Troponin I: 0.6 µg/L (n < 0.40 µg/L)
- BNP: 500 ng/ml (n < 100 ng/ml)
- Right ventricular dilatation
According to ESC guidelines, is this patient considered as a low-risk, intermediate-risk or high-risk patient?

<table>
<thead>
<tr>
<th></th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Low-risk (30-day mortality &lt; 1%)</td>
</tr>
<tr>
<td>2.</td>
<td>Intermediate-risk (30-day mortality 3-15%)</td>
</tr>
<tr>
<td>3.</td>
<td>High-risk (30-day mortality &gt; 15%)</td>
</tr>
</tbody>
</table>
PE risk stratification according to guidelines

<table>
<thead>
<tr>
<th>PE-related early MORTALITY RISK</th>
<th>RISK MARKERS</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>CLINICAL (shock or hypotension)</td>
</tr>
<tr>
<td>HIGH &gt;15%</td>
<td>+</td>
</tr>
<tr>
<td>NON HIGH 3–15%</td>
<td>-</td>
</tr>
<tr>
<td>Low &lt;1%</td>
<td>-</td>
</tr>
</tbody>
</table>

Will thrombolytic therapy reduce right ventricular afterload faster than heparin in this patient?

1. Yes
2. No
Haemodynamic improvement

<table>
<thead>
<tr>
<th></th>
<th>Rt PA</th>
<th>Heparin</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Before 2h</td>
<td>Before 2h</td>
</tr>
<tr>
<td>mPAP (mm Hg)</td>
<td>30.2 ± 7.8</td>
<td>21.4 ± 6.7</td>
</tr>
<tr>
<td>CI(L/min/m²)</td>
<td>2.1 ± 0.5</td>
<td>2.4 ± 0.5</td>
</tr>
</tbody>
</table>

Dalla-Volta S. et al. JACC 1992; 20: 520-6
What is the risk of major bleeding with the use of thrombolytic treatment in this patient?

1. < 5%
2. 5-10%
3. >10%
Major bleeding in stable PE patients

<table>
<thead>
<tr>
<th></th>
<th>Thrombolysis</th>
<th>Heparin</th>
<th>Odds Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stable patients</td>
<td>2.4%</td>
<td>3.2%</td>
<td>0.67 (0.24-1.86)</td>
</tr>
</tbody>
</table>

6 randomized trials, 494 patients with PE
- invasive diagnosis (1 study); non-invasive diagnosis (5 studies)
- rtPA 100 mg over 2 hours (5 studies); urokinase (1 study)

Will thrombolytic therapy reduce the risk of death in this patient?

1. Yes
2. No
3. I don’t know
Thrombolysis vs heparin in clinically stable PE

6 studies, 494 patients with low-risk or intermediate-risk PE

<table>
<thead>
<tr>
<th></th>
<th>Thrombolysis (n = 246)</th>
<th>Heparin (n = 248)</th>
<th>Odds Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recurrence</td>
<td>2.0%</td>
<td>2.8%</td>
<td>0.76 (0.28-2.08)</td>
</tr>
<tr>
<td>Death</td>
<td>3.3%</td>
<td>2.4%</td>
<td>1.16 (0.44-3.05)</td>
</tr>
<tr>
<td>Recurrence or death</td>
<td>5.3%</td>
<td>4.8%</td>
<td>1.07 (0.50-2.30)</td>
</tr>
</tbody>
</table>


In selected patients with acute PE not associated with hypotension and with a low bleeding risk whose initial clinical presentation, or clinical course after starting anticoagulant therapy, suggests a high risk of developing hypotension, we suggest administration of thrombolytic therapy (Grade 2C).

Kearon C. et al. Chest 2012; 141: e419S–e494S
Case scenario

- Six hours later, the blood pressure suddenly drops to 80 mm Hg, the heart rate rises to 140 bpm with signs of shock.
In this case, would thrombolytic therapy reduce the risk of death or recurrent PE?

1. Yes
2. No
3. I don’t know
## Thrombolysis vs heparin in « high risk » PE

5 studies; n = 254, including 37 patients with high-risk PE

<table>
<thead>
<tr>
<th></th>
<th>Thrombolysis (n = 128)</th>
<th>Heparin (n = 126)</th>
<th>Odds Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recurrence</td>
<td>3.9%</td>
<td>7.1%</td>
<td>0.61 (0.23-1.62)</td>
</tr>
<tr>
<td>Death</td>
<td>6.2%</td>
<td>12.7%</td>
<td>0.47 (0.20-1.10)</td>
</tr>
<tr>
<td>Recurrence or death</td>
<td>9.4%</td>
<td>19.0%</td>
<td>0.45 (0.22-0.92)</td>
</tr>
</tbody>
</table>

Current guidelines (High-risk PE patients)

Thrombolytic therapy is the first-line treatment in patients with high-risk PE presenting with cardiogenic shock and/or persistent arterial hypotension, with very few absolute contraindications. (Class I, level A)


In patients with acute PE associated with hypotension (eg, systolic BP < 90 mm Hg) who do not have a high bleeding risk, we suggest systemically administered thrombolytic therapy over no such therapy (Grade 2C).

Kearon C. et al. Chest 2012; 141: e419S–e494S
Home treatment in patients with acute pulmonary embolism

Menno Huisman, MD PhD
Department of Thrombosis and Hemostasis
LUMC Leiden, the Netherlands
Case 3

• A 55-year-old man with **acute pulmonary embolism** and **low clinical risk**:
  
  • Blood pressure 140-80 mm Hg, pulse rate 20/-, SO2 94%
  • No history of venous thromboembolism

• Admission to the hospital or immediate discharge and home treatment?
How is a ‘low risk PE patient’ defined?

- ESC criteria (Torbicki et al Eur Heart J 2008):
  - Low risk < 1% mortality if: no clinical signs of shock, no RV dysfunction, no sign of myocardial damage

<table>
<thead>
<tr>
<th>PE-related early MORTALITY RISK</th>
<th>RISK MARKERS</th>
<th>Potential treatment implications</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>HIGH</strong> &gt;15%</td>
<td>+</td>
<td>Thrombolysis or embolectomy</td>
</tr>
<tr>
<td><strong>Intermediate</strong> 3–15%</td>
<td>–</td>
<td>Hospital admission</td>
</tr>
<tr>
<td><strong>Low</strong> &lt;1%</td>
<td>–</td>
<td>Early discharge or home treatment</td>
</tr>
</tbody>
</table>
• “In patients with low-risk PE and whose home circumstances are adequate, we suggest early discharge over standard discharge (eg, after the first 5 days of treatment) (Grade 2 B)”

• Suggested criteria for the selection of outpatients:
  • (1) Clinically stable with good cardiopulmonary reserve
  • (2) good social support with readily access to medical care, and
  • (3) expected to be compliant with follow-up
  • Patients also need to feel well enough to be treated at home (eg, absence of severe symptoms or co morbidity)
**Question 1**

- Do you send some patients with acute PE directly/early at home for out of hospital initiation of anticoagulant treatment?
  
  - A. Yes
  
  - B. No
Question 2

If you send patient home, what triage are you following?

A. own clinical estimation of risk
B. clinical decision rule: (s)PESI score, Hestia score
C. troponin
D. echocardiography/CT assessment for RV dysfunction
E. combination
F. other
Risk stratification - tools

Clinical decision rules / Prognostic models

- Pulmonary Embolism Severity Index (PESI) (Aujesky et al.)
- Simplified PESI (Jiménez et al.)
- Hestia criteria (Zondag et al.)
- Geneva risk score (Wicki et al.)

Laboratory parameters
- BNP/ NT-proBNP
- Troponin
- D-dimer

Imaging findings
- CT / echocardiography: RV/LV ratio
- CT: embolus load (Qanadli score)
- CT: highest level of thrombus (central/segmental/subsegmental)
Question 3

• What is your cut-off level for 30 day risk of mortality in low risk patients to send them home initially?

  • A. < 1 %
  • B. < 2 %
  • C. < 5 %
Question 4

• What is your cut-off level for 90 day risk of recurrent PE in low risk patients to send them home?

• A. < 3 %
• B. < 5 %
• C. < 10 %
Pulmonary Embolism Severity Index: PESI score

- Consists of 11 items from clinical history and physical examination
- Stratifies patients into 5 groups according to their 30-day all-cause mortality risk
- It is *suggested* that patients who fall in class I or II could be safely managed as outpatients

**OTPE Trial**

- First RCT that compared outpatient treatment (mean hospital stay 0.5 days) versus hospitalization (3.9 days)

- Patients with PE and PESI class I or II eligible

- 334 patients included (> 1300 patients screened)

- **Conclusion**: Risk of recurrent VTE comparable for patients treated as outpatients (0.6%) and inpatients (0%)

- No difference in the bleeding and mortality risk

Simplified PESI score

• The original PESI includes 11 items to which different scores are assigned: difficult for use in busy clinical practice

• Therefore, a simplified score has been proposed, including 5 items; awarding 1 point to each item

• Patients are either classified as low (0 points) or high (≥1 point) risk

• This simplification did not impact the prognostic accuracy of the PESI

<table>
<thead>
<tr>
<th>Variable</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age &gt; 80 y</td>
<td>1</td>
</tr>
<tr>
<td>History of cancer</td>
<td>1</td>
</tr>
<tr>
<td>History of chronic cardiopulmonary disease</td>
<td>1</td>
</tr>
<tr>
<td>Pulse ≥ 110 beats/min</td>
<td>1</td>
</tr>
<tr>
<td>Systolic BP &lt; 100 mm Hg</td>
<td>1</td>
</tr>
<tr>
<td>(\text{SaO}_2) &lt; 90%</td>
<td>1</td>
</tr>
</tbody>
</table>

\(\text{SaO}_2\) = arterial oxyhemoglobin saturation.

* A total point score for a given patient is obtained by summing the points. The score corresponds with the following risk classes: 0, low risk; ≥ 1, high risk.
How is a ‘low risk PE patient’ defined?

- ESC criteria (Torbicki et al Eur Heart J 2008):
  - Low risk < 1 % mortality if: no clinical signs of shock, no RV dysfunction, no signs of myocardial damage
Comparison of the ESC model and the sPESI

- In a cohort of 526 patients, the accuracy of the ESC model and the sPESI in predicting 30-day mortality were compared.

- None of the patients classified as low-risk by sPESI (0 points) died, compared to 3.4% of the low-risk patients by the ESC model (no shock, no RV dysfunction, no myocardial damage).

- Prediction of adverse clinical outcome does not appear to require routine imaging procedures or laboratory biomarker testing.

**Prediction scores: summary**

- The (s)PESI have been extensively validated and repeatedly shown to accurately predict all-cause mortality.

- However: These prediction have not been developed to directly select patients for outpatients. Additional practical criteria have to be added for this purpose.

- Whether 30-day all-cause mortality is the preferable outcome of interest when considering outpatient treatment, is the topic of debate.

- The HESTIA criteria have been introduced to serve as a direct tool for selecting patients eligible for outpatient treatment.
Hestia criteria Zondag et al JTH 2011

- Patient hemodynamically unstable?
- Thrombolysis/embolectomy necessary?
- Need for i.v. pain medication?
- Oxygen needed to keep O2 saturation > 90%?
- PE diagnosed during therapeutic anticoagulation?
- Active bleeding or high risk for bleeding?
- Pregnancy?
- Documented history of HIT?
- Creatinine clearance < 30 ml/min?
- Severe liver impairment?
- Medical/social reason for treatment in the hospital?

If ≥ 1 item is answered with YES, the patient can NOT be treated at home
### Results Hestia Study in 297 patients

<table>
<thead>
<tr>
<th>Clinical outcome</th>
<th>Number</th>
<th>Percentage (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total VTE recurrences</strong></td>
<td>6</td>
<td>2.0 (0.8-4.3)</td>
</tr>
<tr>
<td>Day 3, 8, 10, 28, 48, 60</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fatal recurrent PE</td>
<td>0</td>
<td>0 (0-1.2)</td>
</tr>
<tr>
<td>Non-fatal recurrent PE</td>
<td>5</td>
<td>1.7 (0.6-3.9)</td>
</tr>
<tr>
<td>Recurrent DVT</td>
<td>1</td>
<td>0.34 (0.01-1.9)</td>
</tr>
<tr>
<td><strong>Major bleeding complications</strong></td>
<td>2</td>
<td>0.67 (0.08-2.4)</td>
</tr>
<tr>
<td>Fatal bleeding (day 7)</td>
<td>1</td>
<td>0.34 (0.01-1.9)</td>
</tr>
<tr>
<td>Non-fatal major bleeding (day 14)</td>
<td>1</td>
<td>0.34 (0.01-1.9)</td>
</tr>
<tr>
<td><strong>Clinically relevant non-major bleeding</strong></td>
<td>15</td>
<td>5.1 (2.9-8.2)</td>
</tr>
<tr>
<td>Mortality</td>
<td>3</td>
<td>1.0 (0.2-2.9)</td>
</tr>
<tr>
<td>End-stage malignancy: day 29, 59</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fatal bleeding: day 7</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### Hestia criteria in case 3 patient

- **Patient hemodynamically unstable?** NO
- **Thrombolysis/embolectomy necessary?** NO
- **Need for i.v. pain medication?** NO
- **Oxygen needed to keep O2 saturation > 90%?** NO
- **PE diagnosed during therapeutic anticoagulation?** NO
- **Active bleeding or high risk for bleeding?** NO
- **Pregnancy?** NO
- **Documented history of HIT?** NO
- **Creatinine clearance < 30 ml/min?** NO
- **Severe liver impairment?** NO
- **Medical/social reason for treatment in the hospital?** NO
Follow-up

- LMWH given as nadroparin (fraxodi) once daily 0.8 ml and patient was sent home on the second day after presentation
- Vitamin K antagonists started first day – INR 2-3
- Rivaroxaban from day one at out of hospital basis may be attractive alternative in near future
- No complications occurred in this patient
Take home messages

- Out of hospital treatment appears safe in selected low-risk PE patients; only one randomised study performed – level 1B evidence

- PESI is the best validated clinical prediction score, but does not allow direct selection of outpatient treatment candidates

- Hestia rule allows direct selection of patients who can be safely treated at home, but needs validation

- (additive) value of biomarkers (eg NT-pro BNP) is under investigation
Definition of “low-risk PE patients”

• Accumulating evidence suggests that selected patients with acute PE can safely be treated at home

• The crucial step is to select those patients, who are at low risk of adverse clinical outcome

• For this purpose, several clinical prognostic scores and decision rules have been developed and validated

• In addition, laboratory biomarkers and radiological findings may aid in the selection of low risk patients
Objective: To evaluate the efficacy and safety of outpatient treatment according in patients with acute PE, selected solely on a clinical basis, by the predefined Hestia criteria

Design: multicentre cohort study

Patients: objectively proven acute pulmonary embolism

Intervention: Selected patients, eligible for outpatient treatment, were sent home either immediately or within 24 hours after PE was objectively diagnosed
Results

581 patients screened

338 eligible patients

297 patients treated at home (51%)

Hospital admission:  N=243
- Hemodynamically unstable  30
- Thrombolysis  5
- High bleeding risk  14
- Oxygen supply  73
- i.v. pain medication  15
- PE during OAC therapy  9
- Concomitant illness  63
- Social reason  24
- Unknown  10

Excluded for study reasons:  N=41
- Life expectancy < 3 months  2
- No informed consent  26
- No follow-up possible  9
- Previous participation  4
Conclusion Hestia study

Out of hospital treatment of patients with PE selected by the Hestia criteria could be effective and safe

- Low 3-month (non-fatal) VTE recurrence rate: 2%
  - Non-inferior to historical inpatient cohort
  - Comparable to recurrence rates in outpatients (0%-6.2%)

- Low major bleeding rate 0.7%
  - Comparable to literature (0%-1.2%)
Vesta study

Objectives

• To externally validate the Hestia clinical decision rule
• To assess the safety of outpatient treatment of selected patients with high NT-proBNP

Purpose

To investigate whether a selection strategy for outpatient management of PE based on the Hestia rule alone is as safe as a strategy based on the Hestia rule and the NT-proBNP biomarker
Vesta study

Randomization

[Diagram showing flowchart of study inclusion criteria and randomization process]

Hestia exclusion criteria

Exclusion criteria present

Exclusion criteria absent

A: NT pro BNP

B: Outpatient

Inpatient

High

Low

Outpatient

NT pro BNP

High

Low
### Table 5 Risk stratification according to expected pulmonary embolism-related early mortality rate

<table>
<thead>
<tr>
<th>PE-related early MORTALITY RISK</th>
<th>RISK MARKERS</th>
<th>Potential treatment implications</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>CLINICAL (shock or hypotension)</td>
<td>RV dysfunction</td>
</tr>
<tr>
<td>HIGH &gt;15%</td>
<td>+</td>
<td>(+)(^a)</td>
</tr>
<tr>
<td>NON HIGH</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Intermediate 3–15%</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Low &lt;1%</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>
HOME study

- **Outpatient treatment** in 152 PE patients with low proBNP (<500):
  - Mortality: 0%
  - Recurrent PE: 0%
  - Major bleeding: 0%

- **Inpatient treatment** in 80 PE patients with high proBNP (>500):
  - 1x thrombolysis (day 1)
  - 1x embolectomy (day 2, following collaps)
  - 1x death (day 32 related to heart failure)

**Conclusion:** outpatient treatment of selected PE patients with proBNP < 500 pg/mL appears safe

Agterof, J Thromb Haemost 2010, 8(6): 1235-4
For optimal risk stratification, the following signs are useful:

- Evaluation of the hemodynamic status
- Signs of right ventricular dysfunction
- Signs of myocardial injury

Home treatment or early discharge could be considered in the absence of these signs.