Trust Guidelines

University Hospitals Plymouth NHS Trust

Guidance Title: Pulmonary Embolism Clinical Guidelines

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Accountabilities	
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Links to other documents

SOP Investigation and Management of Venous Thromboembolism (VTE)
Deep Vein Thrombosis Clinical Guidelines

Version History

V 1.0	February 2011	Original Guidance
V 1.1	March 2019	Interim review awaiting full review
V 2.0	Jan 2022	Updated post DOAC and NICE guidance

Last Approval	Due for Review
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PULMONARY EMBOLISM

RECOGNITION AND ASSESSMENT

Pulmonary embolism (PE) is a common acute medical presentation that can vary in severity with either few or no symptoms through to a life-threatening emergency with severe hypoxia and haemodynamic collapse. PE is often missed clinically, and the diagnosis should be suspected in patients with vague symptoms, in those not responding to initial therapy, or when there has been an unexplained deterioration. Clinical probability, assessed by a validated prediction rule and/or clinical judgement, is the basis for all diagnostic strategies for PE. Risk stratification tools are available to help determine the most suitable setting for management, the choice of therapeutic agent and long term follow up.

If a patient presents with signs or symptoms of pulmonary embolism (PE), carry out an assessment of their general medical history, a physical examination and a chest X-ray to exclude other causes.

For investigation and treatment of PE in pregnant patients refer to separate UHP guidelines.

A flow chart from the NICE 2020 clinical guidelines 'Suspected PE: diagnosis and initial management' is at the end of this document.

Symptoms

- Dyspnoea - may be of sudden onset
- Pleuritic chest pain
- Haemoptysis
- Syncope
- Symptoms of DVT

Signs

- May be absent
- Tachypnoea
- Tachycardia
- Fever
- Pleural rub
- Hypotension

Major risk factors for PE

- Surgery (where appropriate prophylaxis is used relative risk is much lower)
  - Major abdominal/pelvic surgery
  - Hip/knee replacement
  - Intensive care admission
  - Lower limb problems
  - Fracture leading to immobility

- Malignancy
  - Abdominal/pelvic
  - Advanced/metastatic

- Obstetrics
  - Late pregnancy
  - Puerperium
  - Caesarean section

- Reduced mobility
- Hospitalisation
- Institutional care
- Previous venous thromboembolism
- Recent Covid-19 infection

Minor risk factors for PE

Congenital heart disease

- Congestive cardiac failure
- Hypertension
- Superficial venous thrombosis
- Indwelling central venous catheter
- Oestrogens
- Oral contraceptive: combined pill
- Hormone replacement therapy
- COPD
- Neurological disability
- Thrombotic disorders
- Hyperviscosity syndromes
- Family history of venous thromboembolism (First degree relative)
- Long distance sedentary travel (>4 hrs)
- Immobility
- Age >60
- Active chemotherapy
- Obesity
- Others (Inflammatory bowel disease, myeloproliferative disorder, nephrotic syndrome, chronic dialysis, paroxysmal nocturnal haemoglobinuria, Behcets disease)

Differential diagnosis

- Pulmonary –pneumonia, pneumothorax
- Cardiac – acute MI, angina, pericarditis, aortic aneurysm

- Collapse - vasovagal syncope, seizure, postural hypotension, dysrhythmias, stroke

Exacerbations of dyspnoea in asthma, COPD or heart failure may be due to an acute pulmonary embolism

Pulmonary Embolism Rule Out Criteria (Applies to ED/AAU only)

If clinical suspicion of PE is low based on clinical impression and risk factors (see below) and other diagnoses are possible, consider using the pulmonary embolism rule-out criteria (PERC) to help determine whether further investigations are needed. If all of the following apply: Age <50, HR < 100, SaO2≥94, no prior DVT/PE, no surgery or trauma requiring GA within 4 weeks, no haemoptysis, no use of oestrogen, no unilateral swollen leg, then no further investigation is necessary.

Confirming the diagnosis

- A preliminary assessment identifying haemodynamic instability* or severe hypoxia (FiO2>0.6) must lead to an emergency diagnostic algorithm leading to consideration of thrombolysis – *see below* 'Treatment of Haemodynamically Unstable Pulmonary Emboli'. These patients have a high risk of death and need level 1 or level 2 ward care. An immediate weight adjusted bolus of unfractionated heparin (suggested dose 80 units /kg, max dose 6000 units) should be considered if thrombolysis is under consideration (*see below*) as this has a significantly shorter half-life than LMWH and can be fully reversed if needed. Early mortality in these patients is at least 15%, and the degree of hemodynamic compromise is the most powerful predictor of in-hospital death.

  *haemodynamic instability: cardiac arrest, shock with systolic BP <90 for more than 15 mins not caused by acute arrhythmia, hypovolaemia or sepsis.

- Patients with suspected PE who are haemodynamically stable should still, where reasonably practical, undergo investigation on the day of presentation, ideally within a few hours of arrival. Investigations should confirm the diagnosis and whether there are markers of increased risk. A strategy of interim anticoagulation and outpatient imaging within 24 hours can be considered if patients are deemed low risk (*see below* 'Assessing suitability for OP Management'). In-patients suspected of having a PE should commence anticoagulation whilst awaiting imaging conformation.

- ECG and chest x-ray. These are often normal and should not be used to confirm or refute the diagnosis but are useful for identifying other diseases and to explain symptoms.

ECG may show sinus tachycardia, an S1 Q3 T3 pattern, right bundle branch block, p pulmonale or right axis deviation.

Chest x-rays may show non- specific shadows or a raised hemidiaphragm, pulmonary oligaemia, linear atelectasis or small pleural effusion. A normal chest x-ray is generally required before a VQ scan is performed.

• Determine a pre-test probability using the Wells Score (*see* Table 1)

Table 1 Two level Wells Score

Clinical feature	Points	Patient score
Clinical signs and symptoms of DVT (minimum of leg swelling and pain with palpation of the deep veins)	3	
An alternative diagnosis is less likely than PE	3	
Heart rate > 100 beats per minute	1.5	
Immobilization for more than 3 days or surgery in the previous 4 weeks	1.5	
Previous DVT/PE	1.5	
Haemoptysis	1	
Malignancy (on treatment, treated in the last 6 months, or palliative)	1	
Clinical probability simplified scores		
PE *likely*	More than 4 points	
PE *unlikely*	4 points or less	

• If pre-test probability is '*likely*' commence anticoagulation and offer either a CTPA or V/Q scan*.

• If pre-test probability is '*unlikely*' and no other justifiable cause for hypoxia, carry out a d-dimer test and if positive commence anticoagulation and offer either a CTPA or V/Q scan*. For patients over 50 years old, use age adjusted d-dimer threshold (ie. patients age in years/100 mcg/ml), as this reduces false positives without substantially increasing false negatives

*Choose between CTPA or V/Q scan taking into account possible contrast allergy, radiation risks, renal function and the presence of pre-existing airway disease or CXR abnormalities. Discuss with the duty radiologist if uncertain.

If imaging investigations cannot be performed within 4 hours, take blood samples (FBC, U+E, LFT, PT, APTT, troponin) and commence interim anticoagulation. Do not wait for the blood results. If possible, choose an interim anticoagulant that can be continued if PE is confirmed. Review within 24 hours. N.B. Admission may not be required while confirmatory investigations are arranged, *see below* 'Assessing suitability for OP investigation and management of PE'.

• If pre-test probability 'unlikely' and either a negative d-dimer or a positive d-dimer and negative radiology investigation, or if pre-test probability 'likely' and both a negative radiology scan and no suspected DVT, advise these patients that it is unlikely they have a PE. Consider alternative diagnoses if symptoms persist. Discuss when and where to seek further medical help if admission not required.

When pulmonary embolism is confirmed:

Depending on co-morbidities, social support and degree of haemodynamic disturbance, patients may be treated via ambulatory care, admitted to a general medical bed or to a higher care area. Specifically, look for markers of increased risk of mortality ie co-morbidities, severe hypoxia, haemodynamic instability, or right heart strain as demonstrated by imaging or biomarkers (eg elevated troponin or BNP). Patients being discharged with a confirmed diagnosis must be supplied with written information about the diagnosis, treatment and follow up plans. (*see appendix 2* Patient Information Leaflet)

Assessing suitability for OP investigation and management of PE

A proportion of patients can be managed safely via an ambulatory care pathway and do not require admission. These patients must satisfy **all** of the following criteria for OP management (based on PESI/sPESI criteria):

- HR < 100
- Systolic BP >100
- O2 saturation >95% on room air
- Troponin negative (obligatory if RV strain on echo/CTPA)
- No co-morbidity requiring hospital admission
- Age <80
- Adequate social situation, able to travel to and from hospital.
- No contra-indication to anticoagulation and no increased bleeding risk (eg CKD 4/5, severe liver disease, recent bleeding or surgery, cancer diagnosed within 1 year or under active management, unexplained anaemia).

If outpatient investigation and management is being considered, this must be subject to review by a senior decision maker prior to discharge. Patients must be provided with an information leaflet (*see* Appendix 2) with specific hospital contact details for further advice and help. A checklist is provided (Appendix 3). It is good practice for patients with a proven PE who are not being admitted to hospital to have a clinical review within 7 days of diagnosis to confirm understanding of their diagnosis and management plan and to ensure no complications are arising. This can be by telephone if preferred by the patient.

See ‘Treating haemodynamically stable patients’, ‘Screening for malignancy’, ‘Screening for thrombophilia’ and ‘Discharge Policy’ for further advice regarding treatment choices, specific issues and general guidance regarding communication with primary care, patient information and follow up.

TREATMENT OF HAEMODYNAMICALLY STABLE PE

General

- Supplemental O_2 to achieve O_2 saturations 94-98% unless clear risk factors for developing hypercapnia are present (eg significant chronic lung disease), in which case the target range is 88-92%.
- Adequate analgesia for pleuritic pain
- Allow right atrial pressure (ie JVP) to remain high if elevated
- **AVOID** diuretics and beta blockers.
- Be aware that patients with either high oxygen requirements (FiO2 > 0.4), or evidence of right ventricular (RV) strain on echo or CTPA, or biomarkers of RV strain (raised BNP) or RV injury (elevated troponin) carry an increased risk of mortality. These patients should be managed in a level 1 area. Referral to respiratory via SALUS is advised.

Specific

- Start anticoagulation. If oxygen saturations 94-98% breathing air, with no biomarkers of RV strain (raised BNP) or RV injury (elevated troponin), treatment may be commenced with either enoxaparin or one of the DOACs (apixaban or rivaroxaban). Long-term anticoagulation choice will depend on patient preference as well as co-morbidities eg renal failure, active malignancy, extremes of weight and thrombophilia. For further information see table 2 and ‘Subsequent management of all PE patients requiring admission’ (below).
- Patients with either high oxygen requirements (FiO2 > 0.4), evidence of right ventricular strain on echo or CTPA, or who have biomarkers of RV strain (raised BNP) or RV injury (elevated troponin) are at increased risk of deterioration therefore we advise sub-cutaneous enoxaparin. Our advice is to use 1.5mg/kg od for uncomplicated patients and 1mg/kg bd for patients with active cancer, obesity, recurrent VTE, proximal thrombosis or if several markers of higher risk are present (see above) until FiO2 <0.4. (*See* table 2). In patients with multiple markers of higher risk it may be prudent to consider alerting the interventional radiology team so that should any further deterioration occur, a rapid transfer for catheter directed thrombolysis can be arranged.
- If enoxaparin is used an accurate patient weight is needed, the dosing chart is shown below. If patients weigh over 120Kg please discuss with a haematologist.
- Mobile clot within the right heart chambers (‘thrombus in transit’), although rare, carries a high mortality (approx. 25%) and such cases need to be closely monitored. While no systematic trials of treatment modalities are available, the existing data suggest that either thrombolysis or surgery offer better chance of survival than anticoagulation alone. Low dose thrombolysis via catheter is probably the safest option but each case needs to be considered on its merits by a multi-disciplinary team.

Table 2.

Weight	1.5 mg/kg regimen GFR > 30 mls/min	1mg/kg BD regimen GFR > 30 mls/min	Both dose regimens **GFR < 30 mls/min**
40-49 kg	60mg daily	40mg twice daily	40mg daily
50-59 kg	80mg daily	60mg twice daily	60mg daily
60-74 kg	100mg daily		
75-89 kg	120mg daily	80mg twice daily	80mg daily
90-109 kg	150mg daily	100mg twice daily	100mg daily
110-120 kg	180mg daily	120mg twice daily	120mg daily
> 120 kg	Contact haematologist regarding dose and monitoring requirements		

TREATMENT OF HAEMODYNAMICALLY UNSTABLE PULMONARY EMBOLI

- Patients with major risk factors for PE presenting with severe dyspnoea, central chest pain, syncope or cardiovascular collapse with evidence of right heart strain and shock (SBP <90mmHg) have an increased mortality (10%-30%) and need to be treated as an emergency.
- An echocardiogram without markers of right ventricular overload or dysfunction excludes PE as the cause of haemodynamic instability. Conversely, in a haemodynamically unstable patient with major risk factors for PE, unequivocal echo signs of RV pressure overload justify emergency reperfusion treatment if immediate radiographic confirmation is not feasible and there are no other causes of RV overload.
- Thrombolysis should be considered for patients who are haemodynamically unstable due to pulmonary emboli. The greatest benefit comes when thrombolysis is administered within 48 hours of symptom onset. It can be

administered systemically by peripheral cannula, or centrally via a radiologically inserted catheter. When cardiac arrest is imminent, and there is a high suspicion of pulmonary emboli, systemic thrombolysis with 50 mg alteplase given as a bolus over 1 - 2 minutes is recommended, even if the diagnosis has not been confirmed with imaging. Where PE is confirmed and patients are acutely unstable with haemodynamic compromise, it is safer to give prompt systemic thrombolysis rather than delaying to arrange catheter directed treatment. However, it is likely that catheter directed therapy has a lower risk of bleeding than systemic thrombolysis and in selected patients it may be appropriate to consider this modality. eg in patients whose initial response to anticoagulation does not lead to improvement, or who show signs of deteriorating over the first 24-48 hours of treatment. Catheter directed thrombolysis may also be favoured over systemic thrombolysis when systemic treatment is contra-indicated eg recent surgery or elevated bleeding risk. Where there is no haemodynamic compromise, it is likely that the risks of thrombolysis, however administered, outweigh the potential benefit, as such patients generally have a good outcome with mortality <5%.

- Absolute contra-indications to thrombolysis are a history of haemorrhagic stroke, ischaemic stroke within 6 months, CNS cancer, major surgery, trauma or head injury within 3 weeks, bleeding diathesis or active bleeding, severe allergy to thrombolytic agents.
- Relative contraindications include TIA within 6 months, anticoagulation, pregnancy or within 1 week of delivery, non-compressible puncture sites, age >75, advanced liver disease, endocarditis, bleeding episode within 2-4 weeks. When weighing up the risk associated with these relative contraindications, the risk of death from not offering thrombolysis also needs to be considered. Discussion with a senior physician or intensivist is encouraged.
- Trial data for systemic thrombolysis show a 10% rate of severe bleeding and 2% risk of intra-cranial haemorrhage. It is probable that 'real-world' outcomes are worse than this, particularly in the elderly or those with other co-morbidities. Trials of catheter directed therapy suggest a lower risk. Patients should, where possible, give written consent for this treatment.

How to give systemic thrombolysis with alteplase (rTPA) in confirmed PE

While making arrangements to commence systemic thrombolysis give a weight adjusted loading dose of unfractionated heparin (suggested dose 80units/kg intravenously, max dose 6000 units), followed by a continuous infusion of 18 units/kg/hour aiming to keep a target APTTR of 1.5-2.5. This is preferred to LMWH or other anticoagulants, but if already administered, LMWH does not preclude the use of thrombolysis.

Table 3

Dosing regimen of alteplase for the treatment of massive PE

Weight	IV bolus dose (over 1-2 minutes)	Subsequent IV infusion dose (over 2 hours)	Strengths of vial required to make up bolus	Strengths of vials to use to make up infusion and bolus
40kg	10mg	50mg	1 x 10mg	1 x 50mg
45kg	10mg	55mg	1 x 10mg	1 x 50mg and 1 x 10mg
50kg	10mg	65mg	2 x 50mg – take bolus & infusion from same vials	
55kg	10mg	70mg	2 x 50mg – take bolus & infusion from same vials	
60kg	10mg	80mg	2 x 50mg – take bolus & infusion from same vials	
≥65kg	10mg	90mg	2 x 50mg – take bolus & infusion from same vials	

- Unfractionated heparin is usually administered by infusion for 24-48 hours after thrombolysis while monitoring for signs of late bleeding. 4 hours after completing thrombolysis check the APTTR. If less than 2.0, resume heparin infusion aiming to keep APTTR in range 1.5-2.5. If APTTR post thrombolysis >2, re-check every 4 hours and resume heparin once value values below 2.0. If stable after 24-48 hours, transition to LMWH and then an oral agent. *See* 'Subsequent management of all PE patients requiring admission'.

Catheter directed thrombolysis (CDT):

- There is emerging evidence from small trials and case series that delivering an infusion of thrombolytic agent via a centrally placed catheter may allow clot resolution using lower doses of thrombolytic agent with lower risk of bleeding. This requires the involvement of an interventional radiologist and availability of a level 2 bed in HDU or CCU. Discuss this modality of treatment with a senior

physician and the consultant interventional radiologist on call if all of the following criteria are present:

- Cardiac arrest not imminent (these patients require systemic thrombolysis)
- No absolute contraindications to thrombolysis (see above)
- Patient requires FiO2 60% or a non-rebreathe mask to maintain SaO2 >94%
- Patient has systolic BP ≤90 (where other potential causes eg arrhythmia, hypovolaemia or sepsis excluded).
- Elevated troponin or BNP.
- RV:LV diameter on echo or CT >1
- Evidence of large volume of acute clot on imaging or clot seen in RV on CT or echo.
- Patient able to lie flat (2-3 pillows) and remain still during procedure.

If considering CDT, please refer to the attached operational protocol. (*See* Appendix 1)

N.B. Patients who fail to respond to systemic thrombolysis or who have relative contraindications to thrombolysis may be suitable for low dose CDT with suitable discussion at senior level.

An alternative regime to CDT (when for instance CDT is unavailable) is to administer 'half dose' thrombolysis via a peripheral cannula (ie for a 70kg patient - 10mg tPA bolus over 2 mins and 40 mg infusion over 2 hours). This might be considered in a haemodynamically unstable patient with relative contra-indications to full dose systemic thrombolysis. Nb this is an unlicensed dose with limited supporting evidence.

Failure to respond to thrombolysis

Exceptional cases may not respond to thrombolysis. Senior expert review is advised, with consideration of echocardiography and repeat imaging to confirm residual acute thrombus (and exclude organised/chronic thrombotic disease) and re-assess RV function. Options where acute thrombi remain include CDT/surgical embolectomy.

Surgical Embolectomy

- Surgical embolectomy should be considered in cases of haemodynamically unstable PE, usually when thrombolysis is contraindicated or has failed. It may also be considered when there is mobile clot within the right side of the heart and further embolization is a concern. Discussion with a senior physician or intensivist and the duty cardiothoracic surgeon is advised.

SUBSEQUENT MANAGEMENT OF ALL PE PATIENTS REQUIRING ADMISSION

- Daily clinical examination for signs of further embolization, right heart failure, and secondary infection of a pulmonary infarct. Echocardiography is probably unnecessary unless patients have evidence of ongoing right heart compromise or persistent requirement for supplemental oxygen.
- Once the diagnosis is confirmed enoxaparin is generally used for initial management of inpatients for 48-72 hours until FiO2 $\leq$ 0.28 by Venturi mask or $\leq$ 2litres/min by nasal cannulae and other observations (temp/RR/HR/BP) are stable. See table 2 for recommended doses.
- For patients with active cancer, the choice of long term agent requires consideration of the tumour site, interactions with other drugs used and bleeding risk. Edoxaban apixaban and rivaroxaban can be used in active malignancy although should be avoided if there is an increased risk of mucosal bleeding eg active GU or GIT tumours. If a DOAC is unsuitable, consider LMWH alone or with warfarin after LMWH loading
- For patients with 'triple positive' antiphospholipid syndrome warfarin (target INR 2.5) is the recommended treatment option, these patients should be referred to haematology for out patient follow up.
- Table 4 provides further details to inform decision making for long term therapy.

Table 4. Some guidance on the other medications for PE treatment.

Drug/ Brand Name	Rivaroxaban (Xarelto)	Dabigatran (Pradaxa)	Apixaban (Eliquis)	Edoxaban (Lixiana)	Warfarin (Coumadin)	Clexane (Enoxaparin)
Dosage Adults > 50kg	15mg BD 3/52 followedby 20mg OD	150mg BD following at least 5/7 treatment with LMWH	10mg BD 7 days then 5mg BD	60mg OD following at least 5/7 treatment with LMWH *reduce dose to 30mg ODif weight <61kg*	Variable dependent upon INR once daily following initial treatment with LMWH	Weight related dose
Dosage Adults < 50kg	SPC advisesno dose adjustment needed. **SeeNICE guidance below**	No dose adjustment is necessary , but close clinical surveillance recommended in patients with a body weight < 50 kg **See NICE guidance below**	Low body weight (< 60 kg) may increase hemorrhagic risk **See NICE guidance below**	Patients <60kg reduce dose to 30mg OD after at least 5/7 treatment LMWH	Variable dependent upon INR once daily following initial treatment with LMWH	Weight related dose

Dosage Adults > 130kg	SPC advises no dose adjustment needed. **See NICE guidance below**	No dose adjustment is necessary, but close clinical surveillance is recommended in patients with a body weight < 50 kg **See NICE guidance below**	Compared to apixaban exposure in subjects with body weight of 65 to 85 kg, body weight > 120 kg was associated with approximately 30% lower exposure **See NICE guidance below**	SPC advises no dose adjustment needed. **See NICE guidance below**	Variable dependent upon INR once daily following initial treatment with LMWH	Weight related dose
Further dose change	6/12 Rx equipoise patients can reduce to 10mg OD	No routine change	After 6/12 Rx reduce to 2.5mg BD	No routine change	No routine change	No routine change
Renal Function	If creatinine clearance 30-49ml/minute reduce to 15mg OD if bleeding risk outweighs risk of recurrent VTE. Limited data for CrCl 15-30, use with caution or consider alternative eg apixaban	If creatinine clearance 30-50ml/minute reduce to 110mg BD or consider alternative treatment	Use with caution if creatinine clearance 15-29ml/minute	Reduce dose to 30mg OD in moderate to severe impairment	In severe renal failure monitor INR more often	CC <15ml/ minute avoid use
Food	Must be taken with Food	Not needed	Not needed	Not needed	Foods with Vit K will affect INR	Not needed
Reversal Agents	Not currently	Yes idarucizumab	Yes Andexanet Alfa (GI bleed only, discuss with haematology first).	Not Currently	Yes	Partial
Routine Lab Monitoring	Annual FBC U&E	Annual FBC U&E	Annual FBC U&E	Annual FBC U&E	Routine INR Monitoring	Anti Xa levels may be required in obese patients, pregnant or severe renal impairment

NICE guidance on extremes in body weight: *Consider anticoagulation treatment with regular monitoring of therapeutic levels for people with confirmed proximal DVT or PE who weigh less than 50 kg or more than 120 kg, to ensure effective anticoagulation*

Monitoring treatment

- If Warfarin is to be used then an INR should be taken every day for the first 4 days of warfarin treatment and then initially monitored very frequently (less than a weekly basis). There is guidance on starting patients on warfarin on page 10 of the Trust drug chart/ePMA

- If patient is still on unfractionated heparin, check platelet count every 2-3 days from day 4 until day 14 to ensure that heparin-induced thrombocytopenia has not developed.

- For patients on enoxaparin no further monitoring of APTTR is required but some patients may require monitoring with Anti Xa levels: morbidly obese (BMI > 35), renal failure, pregnancy. See appendix 3 for further advice.

- For patients taking either rivaroxaban or apixaban no further monitoring is generally required but there is a need to ensure the dose is changed as per the licence after either 3/52 or 1/52 respectively.

- For patients who are to be treated with dabigatran or edoxaban, these drugs should only be initiated after a minimum of 5 days of enoxaparin.

Investigating for malignancy

- For patients with an unprovoked PE who are not known to have cancer, a history and examination looking for relevant clinical symptoms or signs of malignancy is required together with a review of medical history and baseline blood tests (FBC, renal and liver function, PT & APTT). Do not offer further investigations eg CT scanning unless there are specific findings indicative of possible malignancy.

Investigating for thrombophilia

- For patients with a provoked PE, there is no role for thrombophilia testing.
- For patients with an unprovoked PE who are continuing anticoagulation, there is no role for thrombophilia testing.
- For patients with an unprovoked PE who are discontinuing anticoagulation, refer to haematology to consider testing for antiphospholipid syndrome and hereditary thrombophilias.
- Do not routinely offer thrombophilia testing to first degree relatives of patients with a history of PE and thrombophilia.

Inferior Vena Cava (IVC) Filters

- Do not offer an IVC filter unless either patient enrolled in a clinical trial, anticoagulation is contra-indicated, or the PE has occurred during anticoagulation (where adherence to treatment is confirmed, hypercoagulability has been considered and other treatment options eg alternative anticoagulant drug or dose considered).
- If inserted, there must be documentation whether the filter is intended to be temporary or permanent. Temporary filters should have a retrieval date booked at the time of insertion and this must be checked pre-discharge.

DISCHARGE POLICY

- All patients being discharged from hospital with a confirmed diagnosis of pulmonary embolus must have written information, in addition to the discharge summary, describing the anticoagulation regime being prescribed, necessary monitoring and potential side-effects or interactions to be aware of. Contact details for information and support must be made available. Patients should be given an anticoagulation alert card and advised to carry it at all times. Women of childbearing age must be warned of the teratogenic effects of warfarin and DOAC medication and that if they become pregnant whilst taking any of these drugs they must inform their doctor immediately. A suitable patient information leaflet is available: *see* Appendix 2.

  The discharge summary or a letter to the GP must explain the likely cause of the PE (provoked or unprovoked) and the management plan including plans for further investigations and follow up as well as the intended duration of anticoagulation.

- If the patient is being treated with warfarin they must be stabilized on warfarin with the INR in the appropriate range before discharge to GP care. A telephone call to the surgery must handover that this drug has been started and when the next INR is required.

- The patient should be warned that many drugs (including alcohol) interact with warfarin and to remind their GP that they are taking warfarin if additional medication is added.

- Advice about when the dose of the DOAC should be reduced, if applicable, and whether it needs to be taken with food, should be given on discharge

- Duration of treatment and any follow up should be advised and a haematology follow up arranged (via SALUS) for recurrent or unprovoked thrombosis to look at need for long term anticoagulation.

- Some guidance on length of anticoagulation is given in table 5.

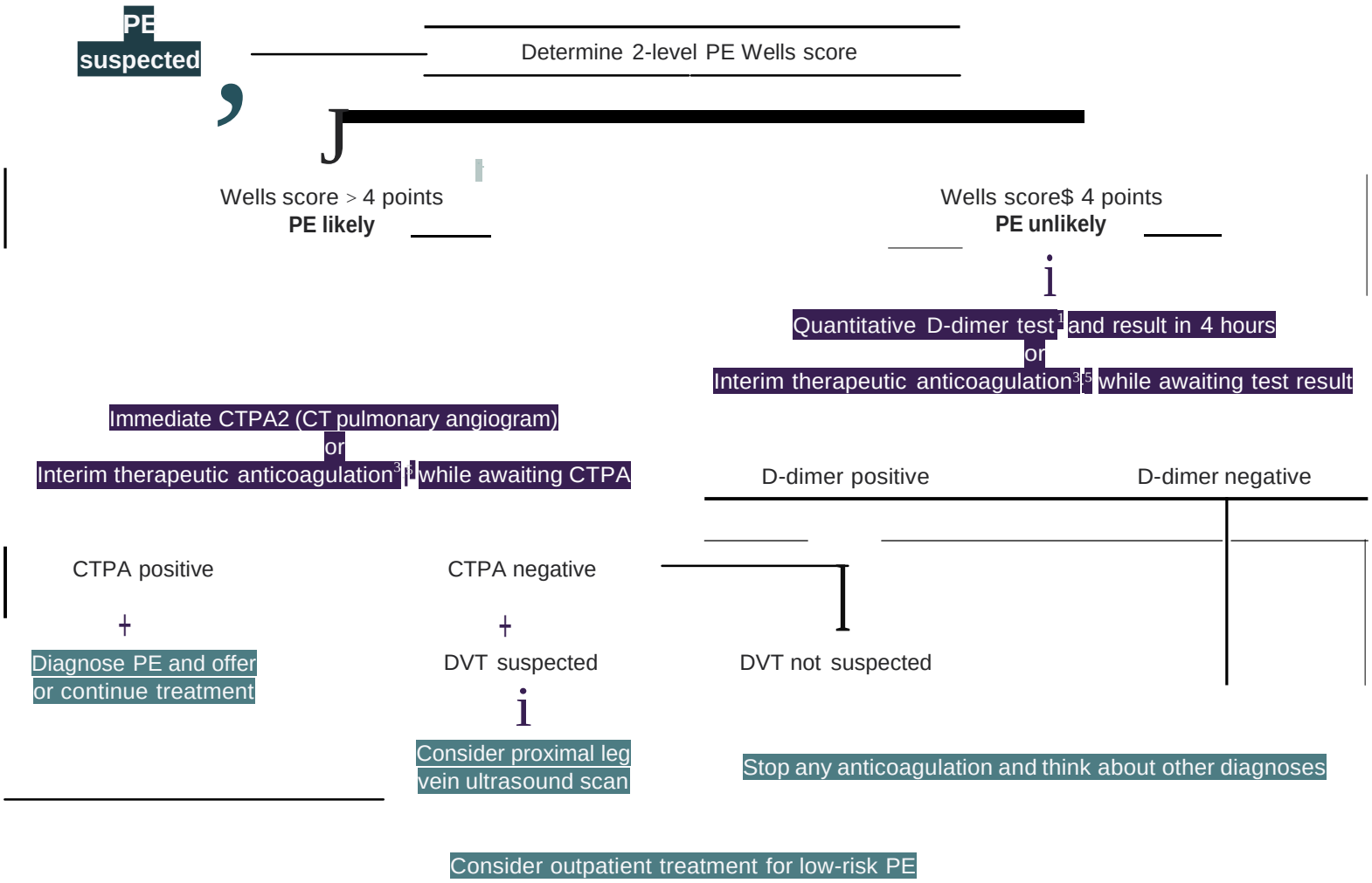
Table 5

Indication	**Circumstances**	Duration
PE	Provoked and first thromboembolic event	3 months (6 months for patients with active cancer) if provoking factor resolved
PE	Idiopathic 'unprovoked' and first thromboembolic event	Consider life-long treatment if low bleeding risk (HAS-BLED <4)
PE	Major ongoing risk factors eg active cancer	Consider continuing until risk resolved
Recurrent PE	On therapeutic anticoagulation	Use warfarin with target INR 3.5 for 6 months and consider long term treatment and/or referral to haematology
Recurrent PE	Two spontaneous events	Consider life-long treatment

Outpatient Follow up

- All patients with an unprovoked PE, a PE occurring on therapy (if compliance was good) and those with a strong family history should be referred to the thrombosis clinic. An internal referral via SALUS should be sent. Advise patients that they will be contacted approximately 3 months after discharge.
- Persistent breathlessness is reported by 20-50% of patients post PE. In the majority of these cases deconditioning is the cause, particularly if raised BMI or other cardiorespiratory conditions co-exist. Patients should be advised to gradually increase their exercise levels after discharge, aiming to return to pre-PE levels of activity within 2 months. Patients should be advised to contact their GP if persistently breathless so that simple causes can be excluded by checking FBC, BNP and CXR. More detailed investigations eg. echocardiography to assess right ventricular function and a V/Q or CTPA should be considered together with referral to the Chest Clinic for specialist advice.

Suspected PE: diagnosis and initial management



2-level PE Wells score

Clinical feature	tffll
Clinical signs and symptoms of DVT (minimum of leg swelling and pain with palpation of the deep veins)	3
An alternative diagnosis is less likely than PE	3
Heart rate more than 100 beats per minute	15
Immobilisation for more than 3 days or surgery in previous 4 weeks	15
Previous DVT/PE	15
Haemoptysis	1
Malignancy (on treatment, treated in the last 6 months, or palliative)	1

PE likely: More than 4 points
PE unlikely: 4 points or less

Adapted with permission from Wells et al. (2000)

'Laboratory or point-of-care test Consider age-adjusted threshold for people over 50

[2]CT pulmonary angiogram. Assess suitability of V/Q SPECT or V/Q planar scan for allergy, severe renal impairment (CrCl <30 ml/min estimated using the Cockcroft and Gault formula; see the BNF) or high irradiation risk

[3]Measure baseline blood count, renal and hepatic function, PT and APTT but start anticoagulation before results are available and review within 24 hours

[4]If possible, choose an anticoagulant that can be continued if PE is confirmed

[5]Direct-acting anticoagulants and some LMWHs are off label for use in suspected PE. Follow GMC guidance on prescribing unlicensed medicines

Appendix 1

Operational Protocol for Catheter Directed Thrombolysis (CDT)

Rationale

Delivery of low dose thrombolysis via a centrally placed catheter is though to be as effective in reducing acute thrombus burden and reducing RV afterload as administering a larger dose by peripheral cannula. The lower dose is thought to carry a lower risk of major bleeding complications, although necessitates a more invasive strategy that requires a longer period of intensive monitoring as well as the specific skills of an interventional radiologist.

Patient Selection

CDT can be justified in cases where there is significant haemodynamic instability with impending or definite clinical deterioration when the delay to commence treatment is deemed not to be excessive (ie <120 minutes). Where patients are either very unstable, peri-arrest or deteriorating quickly, systemic thrombolysis is the correct treatment modality.

Indications and contra-indications for CDT are described in detail in the UHP Pulmonary Embolism Guidelines (*see* Treatment of Haemodynamically Unstable PE). As bleeding risks are lower, relative contra-indications to thrombolysis may be 'down graded' if CDT is being administered, subject to senior agreement and with the patients explicit consent. Note also that allergy to iodinated contrast agents or severe renal dysfunction may preclude this treatment modality.

Pathway for Arranging CDT delivery

Confirm with senior physician that PE explains/most likely explains haemodynamic instability and that thrombolysis is indicated. Review inclusion/exclusion criteria and agree that patient does not need immediate systemic thrombolysis. Discuss treatment plan with patient and obtain consent to proceed.

Contact Bed Manager to inform that a bed will be needed on either Torcross or Penrose within 120 minutes. At the time of production of this guideline, both areas are clinically suitable for post procedure care of thrombolysis, whether delivered systemically or via catheter. Choice of ward will depend on bed availability. Lengthy discussion is not appropriate. Alert the SpR responsible for the ward selected.

Contact duty interventional radiologist. If likely delay of >120 minutes, then a transfer to either Torcross or Penrose for systemic thrombolysis at full or reduced dose may be more appropriate. The respiratory level 1 bays on 09 are also suitable locations for systemic thrombolysis.

Arrange transfer to IR theatre as per IR team availability.

Post procedure, the patient should be managed on either Torcross or Penrose. Refer to respiratory via SALUS if outside Penrose/Pencarrow.

Post procedure Care

- One-to-two nursing.
- Monitor pulse, BP, O2 saturations at 15 minute intervals for two hours, then hourly thereafter.
- Neurological observations at 15 minute intervals for the first hour, hourly thereafter.
- Monitor access sites for bleeding complications.
- Monitor for general bleeding eg haematuria.
- The patient would typically be nursed inclined up to 30 degrees.
- Patient can eat and drink normally if position allows.
- Ensure all infusions continue as prescribed.
- No intramuscular injections should be prescribed or given during thrombolysis (except adrenaline for anaphylaxis or cardiac arrest).
- Avoid non-steroidal anti-inflammatory drugs (NSAIDs).
- Check coagulation screen, fibrinogen, tpa-antigen, d-dimer every three hours during thrombolysis and at the end of thrombolysis
- The patient may eat and drink normally.

If excessive bleeding occurs:

- Contact SpR on-call immediately and inform IR consultant.
- Localised compression should be applied if applicable.
- If persistent bleeding; stop the alteplase infusion rate and check FBC, coagulation profile and fibrinogen levels. Discuss with haematology.
- If catastrophic bleeding
    - ♦ Stop CDT alteplase infusion
    - ♦ Administer tranexamic acid 1g iv stat
    - ♦ Give 5g fibrinogen concentrate (available from haematology) – check fibrinogen level 20 mins after end of administration

Clinical assessment:

- Reduction in HR, improved blood pressure, reduced breathlessness / pain should be apparent.

Echocardiogram should be performed DAY 1 post commencement of treatment.

Objective measures of improved right heart function would include

- Echocardiogram - >20% reduction in RV/LV ratio
- Echocardiogram – estimated mean systolic PA pressure >25% reduction

- Direct pulmonary artery pressure measurement >25% reduction

Infusion catheters can be removed on the ward once thrombolysis stopped. Venous sheaths can be removed 1 hour after thrombolysis stopped, followed by a period of manual compression (>5 minutes), followed by Femstop x 2 hours.

Following sheath removal bed rest for 4 hours, then encourage mobilisation as appropriate.

15 minute observations for 2 hours, then 30 minute intervals for 2 hours, then 2 hourly for 4 hours, then 4 hourly.

Restart therapeutic anticoagulation with enoxaparin at a dose of 1mg/kg BD. Give no earlier than 1 hour after removal of the sheath. First post procedure dose should not be given less than 12 hrs after last pre-procedure dose. Fibrinogen should be checked at the end of thrombolysis and supplemented with concentrate if less than 1.5 g/L. Fibrinogen level should be re-checked 20 mins after end of administration of fibrinogen concentrate and give further concentrate if not greater than 1.5 g/L. DO NOT wait for result before administering enoxaparin.

Appendix 2

University Hospitals Plymouth NHS Trust

University Hospital Plymouth

Pulmonary Embolism Patient Information Leaflet

What is a pulmonary embolism?

A pulmonary embolism (or "PE") is a blockage in 1 or more of the blood vessels that supply blood to the lungs. These blockages are usually caused by blood clots that form elsewhere and then travel to the lungs.

A PE can be in an artery in the centre of the lung or one near the edge of the lung. The clot can be large or small and there can be more than one clot.

What are the symptoms of PE?

Common symptoms include:

- Panting, shortness of breath, or trouble breathing
- Sharp, knife-like chest pain when you breathe in or strain
- Coughing or coughing up blood
- A rapid heartbeat or feeling faint

If you get these symptoms, especially if they happen over a short period of time and progress quickly, or if you feel faint or collapse - call 999 for an ambulance.

Why is a PE dangerous?

If a blood clot forms or gets stuck inside a blood vessel, it can block the vessel and prevent blood from getting where it needs to go. When that happens in the lungs, the lungs can be damaged. Having blocked arteries in the lung can make it hard to breath and can be life-threatening if left untreated.

What causes a PE?

A PE usually happens when a blood clot forms in the leg or pelvis (a deep vein thrombosis), and travels to the lung. Sometimes a reason cannot be found as to why the blood clot has formed, but risk factors for blood clots include:

- previous blood clots or a family history of blood clots,
- pregnancy,
- oral contraceptive pill,
- surgery or immobility,
- long haul flights (and other travel if more than four hours in duration),
- smoking,
- being overweight,
- increasing age,
- cancer,
- an underlying condition of ‘sticky blood’.

Doctors call a PE with no associated risk factors ‘unprovoked’.

How is a PE treated?

Blood clots in the lungs are treated with medicines that keep clots from getting bigger and help your body to dissolve them. These medicines are called "**anticoagulants**" or "blood thinners," (although they do not actually thin the blood). Anticoagulants are available as injections or tablets. Patients usually PE begin their PE treatment in hospital.

Duration of use:

Most people start treatment with injections and then move onto tablets after a few days. If for some reason you can't take tablets you may remain on an injectable anticoagulant. You will need to take the medicine for at least 3 months. Many patients will be advised to take anticoagulant treatment for the rest of their lives to prevent a recurrence. This is usually because the risks from another episode of PE are considered greater than the risks of bleeding from prolonged use of anticoagulants. For example, with an ‘unprovoked’ PE, there is a 20-30% risk of recurrence after 5 years if anticoagulation is stopped. A small proportion of these recurrences (2-3%) will be fatal. There is a 10-15% chance of a major bleeding episode (ie bad enough to require hospital admission) with anticoagulation over this period of time. It is widely recommended that patients who have suffered an unprovoked PE, or have previously had a PE, should remain on treatment indefinitely. The risks and benefits should be reviewed by you and your doctors every year and if your health changes for any reason. We aim to offer all patients who have had an unprovoked PE an appointment with a blood-clotting specialist about 3 months after discharge from hospital. For patients experiencing their first PE where there has been an obvious temporary ‘provoking’ factor (eg a long journey or an operation), 3 months treatment is sufficient.

How they work:

The medicines do not dissolve existing blood clots, but they do keep them from getting bigger. They also help keep new blood clots from forming. Taking the

medicine for at least 3 months is important because it gives your body time to dissolve the old clot.

You will need to mention that you take anticoagulants ‘blood thinners’ to any other doctors or surgeons you might see, to your dentist and to your pharmacist. If you become pregnant or are planning to start a family you should mention this to your GP as soon as possible.

There are several different drugs (tablets) used to prevent and treat blood clots. They include apixaban, dabigatran, edoxaban, rivaroxaban, and warfarin. Each medicine is different in terms of the dose, monitoring required and how often you take it. Some choices interact with alcohol and other prescribed medicines or natural therapies. Your doctor will talk to you about your options and preferences. You should avoid taking aspirin or ibuprofen while you receive anticoagulant therapy, unless a doctor has confirmed this is appropriate for you. Paracetamol is safe to use as a painkiller.

Be aware that some injectable anticoagulants are of animal origin and that some tablet anticoagulants contain lactose from cow’s milk. Your doctor can discuss this with you if required.

Watch for signs of bleeding – Abnormal bleeding is a risk with all the medicines used to prevent and treat blood clots. That's because while these medicines help prevent dangerous blood clots, they also make it harder for your body to control bleeding after an injury. So it's important to try to avoid getting injured, and to tell your doctor right away if you do have signs of bleeding. This might mean that certain activities, such as contact sports, need to be stopped while you take this treatment.

Other treatments:

In some cases, a person has a clot that is severe enough to cause dangerously low blood pressure. If this happens, doctors can give medicine to dissolve the clot. This is sometimes called "clot-busting" medicine, and is given through a vein. There is a greater risk of bleeding with this treatment.

In exceptional cases, doctors operate to remove the PE. This is reserved for very unwell patients.

People who cannot take medicines to prevent and treat clots, or who do not get enough benefit from the medicines, may receive an "inferior vena cava filter" .

Supportive treatment- is often given in the early stages to help the body cope with the effects of the PE. This may include oxygen, intravenous fluid and painkillers.

For outpatients: Why are we not admitting you to the hospital?

The risks from a PE depend on a number of factors and can be estimated using a scoring system. Low risk patients can be safely managed as an outpatient.

How long will I feel breathless?

It's common to feel breathless for a few weeks or months after a pulmonary embolism. It is safe to start resuming exercise after 1-2 weeks of starting treatment. Initially you should avoid any heavy lifting or exercise that leaves you gasping for breath. Gradually build up the time and intensity of your exercise, aiming to return to your normal level by approximately 8 weeks from starting treatment.

There are lots of conditions that can make you feel short of breath after a pulmonary embolism. If you still feel breathless on exertion after 8 weeks, talk to your GP. Your health care professional will want to check that it is not caused by other problems with your heart or lungs, or that the anticoagulant medication has been ineffective.

What happens when my treatment ends?

We aim to offer all patients with an unprovoked or recurrent PE an appointment with a blood specialist 3 months after discharge. This will be an opportunity to consider further investigations to see if there was a reason for the clot. We will also discuss the potential harms and benefits of continuing long term anticoagulant therapy.

What is the outlook for a PE?

If a PE is treated promptly, the outlook (prognosis) is excellent, and most people will make a full recovery. The outlook is less good if there is a pre- existing serious illness that helped to cause the embolism - for example, advanced cancer.
A PE is a serious condition but the risks are greatly reduced by early treatment.
There is a high risk of another PE occurring within six weeks of the first one. This is why treatment is needed immediately and is continued for at least three months.

What can I do to avoid pulmonary embolism?

Keep active:
After surgery, move around or do leg exercises as soon as you can.
On long-haul flights and other long journeys, do leg stretching exercises: bend and straighten your legs, feet and toes every 30 minutes when you're sitting. Stand up and walk around when you can. Do some deep breathing. It also helps if you drink water regularly. Wear flight socks.
If you're at risk of developing blood clots, consult your health care professional before travelling long distances.

Change habits:

We can all reduce our risk of having a pulmonary embolism by changing our habits.For example:

- stop smoking – your GP can support you with this.
- take regular exercise – at least 150 minutes a week.
- avoid sitting still for a long time – such as when watching TV or using a computer. Take an active break every 30 minutes or so.
- eat a healthy balanced diet, with plenty of fruit and vegetables and maintain a healthy weight

Important contact numbers:

You may wish to discuss further details with one of the following:

- Your General Practitioner for advice regarding your recovery and any further tests.
- Your local pharmacist regarding your new treatment and any other medicines you take, including herbal or natural medicines.
- Your consultant regarding details of your admission, the tests you received and any plans for follow up. Your consultant's contact details should be available on the discharge letter. Please contact the Patient Advice and Liaison Service if you need help with this (tel: 01752 439884 or email: plh-tr.PALS@nhs.net)

This leaflet is available in large print and other formats and languages

Please contact PALS service 01752 439884 for help with this.

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Appendix 3

CHECK LIST FOR OP PULMONARY EMBOLISM MANAGEMENT

	Statements	Yes	No
1	If diagnosis not yet confirmed, has CTPA/VQ been requested and will the patient be able to return for this investigation?		
2	PESI/sPESI completed? (see below)		
3	If low or very low risk on PESI or 0 score on sPESI, have the Exclusion Criteria been applied? **Exclusion criteria :** • Haemodynamic instability? • BP<100, HR >110 • On full dose anticoagulation when developed PE? • Severe pain requiring opiates? • Other medical co-morbidities requiring admission? • eGFR<30ml/min or severe liver disease? • Social reasons for admission? • Evidence of Right heart strain (raised troponin/BNP/Evidence on CT or echo) Admit if 'YES' to any of the exclusion criteria		

4	Reviewed by senior clinician if discharging the patient for OP management?		
5	Verbal information given to patient?		
6	Written information given to patient?		
7	If PE already confirmed, has 7 day follow-up been arranged?		
8	If PE already confirmed, has 3-6 months follow-up been arranged?		

sPESI Score	
Variable	**Points**
Age >80y	1
History of cancer	1
History of cardiopulmonary disease	1
Pulse ≥ 110 beats/min	1
Systolic BP <100mm Hg	1
Arterial oxyhaemoglobin saturation <90%	1
Total point score is obtained by summing the points. Score corresponds with the following risk classes: 0, low risk; ≥ 1, high risk.	

PESI Score	
Variable	**Points**
Age	Age in years
Male sex	+10
Cancer	+30
Chronic heart failure	+10
Chronic pulmonary disease	+10
Pulse rate >110	+20
Systolic BP <100	+30
Respiratory rate >30/min	+20
Temp <36	+20
Altered mental status	+60
O2 sats <90%	+20

Class 1 : ≤65 points- very low 30 day mortality (0-1.6%)
Class 2: 66-85 points - low mortality risk (1.7-3.5%)
Class 3: 86-105 points - moderate mortality risk (3.2-7.1%)
Class 4: 106-125 points- high mortality risk (4-11.4%)
Class 5: >125 points- very high mortality risk (10-24.5%)