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Venous thromboembolic diseases:
the management of venous thromboembolic diseases and the role of thrombophilia testing

Support for education and learning
Pulmonary embolism:
Clinical case scenarios

June 2012

Clinical Guideline Implementation Tools

NICE clinical guideline 144

These clinical case scenarios accompany the clinical guideline: 'Venous thromboembolic diseases: the management of venous thromboembolic diseases and the role of thrombophilia testing' (available at www.nice.org.uk/guidance/CG144). Issue date: June 2012.

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Introduction

Venous thromboembolism (VTE) is a condition in which a blood clot (a thrombus) forms in a vein, most commonly in the deep veins of the legs or pelvis. This is known as deep vein thrombosis, or DVT. The thrombus can dislodge and travel in the blood, particularly to the pulmonary arteries. This is known as pulmonary embolism, or PE. The term 'VTE' includes both DVT and PE.

Venous thromboembolic diseases cover a spectrum ranging from asymptomatic calf vein thrombosis to symptomatic DVT. They can be fatal if they lead to PE, in which the blood supply to the lungs is badly blocked by the thrombus. Non-fatal VTE can cause serious long-term conditions such as post-thrombotic syndrome.

Thrombophilia is a major risk factor for VTE. It is an inherited or acquired prothrombotic state that predisposes to venous thromboembolism. Other major risk factors for VTE include a history of DVT, age over 60 years, surgery, obesity, prolonged travel, acute medical illness, cancer, immobility and pregnancy.

Failure to diagnose and treat VTE correctly can result in fatal PE. However, diagnosis of VTE is not always straightforward. The NICE clinical guideline on Venous thromboembolic diseases includes advice on the Wells score, D-dimer measurement, ultrasound and radiological imaging. It also offers guidance on the management of VTE, investigations for cancer in patients with VTE and thrombophilia testing. The guideline covers adults with suspected or confirmed DVT or PE. It does not cover children or young people aged under 18, or women who are pregnant.

To ensure comprehensive management and continuity when developing a programme of care for patients who are at risk of or who develop VTE, users of this guideline are encouraged to refer to NICE guidance on

Venous thromboembolism: reducing the risk (NICE clinical guideline 92

Rivaroxaban for the prevention of venous thromboembolism after total hip or total knee replacement in adults (NICE technology appraisal guidance 170)

Dabigatran etexilate for the prevention of venous thromboembolism after hip or knee replacement surgery in adults (NICE technology appraisal guidance 157)

Medicines adherence (NICE clinical guideline 76)

Patient experience in adult NHS services (NICE clinical guideline 138)

(see also section 6 of the VTE diseases NICE clinical guideline).

Key to terms

The following terms are used in these clinical case scenarios and the NICE guideline.

International normalised ratio (INR) A standardised laboratory measure of blood coagulation used to monitor the adequacy of anticoagulation in patients who are having treatment with a vitamin K antagonist (VKA).

Provoked deep vein thrombosis (DVT) or pulmonary embolism (PE) DVT or PE in a patient with an antecedent (within 3 months) and transient major clinical risk factor for VTE – for example surgery, trauma, significant immobility (bedbound, unable to walk unaided or likely to spend a substantial proportion of the day in bed or in a chair), pregnancy or puerperium – or in a patient who is having hormonal therapy (oral contraceptive or hormone replacement therapy).

Proximal DVT DVT in the popliteal vein or above. Proximal DVT is sometimes referred to as 'above-knee DVT'.

Renal impairment Reduced renal function that may be acute or chronic. An estimated glomerular filtration rate of less than 90 ml/minute/1.73 m^2 indicates a degree of renal impairment in chronic kidney disease. (For NICE guidance on the classification of chronic kidney disease see Chronic kidney disease [NICE clinical guideline 73]).

Unprovoked DVT or PE DVT or PE in a patient with:

- no antecedent major clinical risk factor for VTE (see 'Provoked deep vein thrombosis or pulmonary embolism' above) who is not having hormonal therapy (oral contraceptive or hormone replacement therapy) **or**
- active cancer, thrombophilia or a family history of VTE, because these are underlying risks that remain constant in the patient.

Wells scores Clinical prediction rules for estimating the probability of DVT and PE. There are a number of versions of Wells scores available. This guideline recommends the two-level DVT Wells score and the two-level PE Wells score.

Clinical case scenarios: pulmonary embolism

Clinical case scenarios are an educational resource that can be used for individual or group learning. They are also available in slide set format to support group learning. Each question should be considered by the individual or group before referring to the answers.

These clinical case scenarios are an essential component of the workshop set out in the Pulmonary Embolism training plan. They have been put together to improve your knowledge of 'Venous thromboembolic diseases: the management of venous thromboembolic diseases and the role of thrombophilia testing' (NICE clinical guideline 144) and its application in practice. They illustrate how the PE-related recommendations from the NICE guideline can be applied to the care of adults presenting to the acute care setting. These cases assume that you are the lead clinician throughout the patient's acute phase. Although it is acknowledged that in reality this is not likely, they have been developed in this way to facilitate learning and understanding of the whole diagnosis and management pathway. They may also be informative for those in primary care who may be the initial point of contact for a person with signs and symptoms of VTE diseases and who may be involved in the care of their VTE disease after discharge from the acute setting.

You will need to refer to the NICE guideline to help you decide what steps you would need to follow to diagnose and manage each case, so make sure that users have access to a copy (either online at www.nice.org.uk/guidance/CG144 or as a printout). You may also want to refer to the VTE NICE pathway (http://pathways.nice.org.uk/pathways/venous-thromboembolism) and the topic page on NHS Evidence (www.evidence.nhs.uk/topic/venous-thromboembolism).

Each case scenario includes details of the patient's initial presentation. The clinical decisions about recognition, referral, diagnosis and management are then examined using a question and answer approach. Relevant recommendations from the NICE guideline are quoted in the text (after the answer), with corresponding recommendation numbers.

This resource has been developed to illustrate the application of the recommendations in ‘Venous thromboembolic diseases’ (NICE clinical guideline 144) in practice and should only be used to support learning. The recommendations and these cases only cover the scope of the NICE guideline. It is acknowledged that when a patient presents with suspected VTE there are multiple considerations including those beyond the scope of the NICE guideline. These cases do not reflect treatment plans for actual patients and should not be used as such. If an individual clinician has any queries or concerns about the relationship between NICE guidance and this educational resource they should always refer to the original guidance published by NICE, and this should in all cases be regarded as the only definitive statement of the guidance. The NICE clinical guideline may be found at http://www.nice.org.uk/CG144

Case scenario 1: Helen

Presentation

Helen is a 78-year-old woman who smokes cigarettes and has a history of angina. She presents to your accident and emergency (A&E) department with chest pain worse on inspiration and shortness of breath.

You note that her hospital records show that because of her religious beliefs she does not want to have any treatments of porcine origin.

1.1 Question

You believe Helen has symptoms of a suspected pulmonary embolism: what would you do next?

1.1 Answer

Carry out an assessment of her general medical history, a physical examination and a chest X-ray to exclude other causes.

Relevant recommendation

- If a patient presents with signs or symptoms of PE, carry out an assessment of their general medical history, a physical examination and a chest X-ray to exclude other causes. **[1.1.7]**

On admission Helen's blood pressure is 132/86 mmHg, SpO_2 95% in air, respiratory rate 16 breaths per minute, heart rate is 72 beats per minute temperature 36.2^0c. There are no clinical signs of a DVT. Upon further questioning you identify that she sprained her ankle 5 days ago and has 'been keeping her feet up' since.

1.2 Question

You still suspect pulmonary embolism: what would you do next?

1.2 Answer

Use the two-level PE Wells score to estimate the clinical probability of PE[1].

Relevant recommendation

If PE is suspected, use the two-level PE Wells score (appendix 2) to estimate the clinical probability of PE. **[1.1.8]**

- Feet up for 5 days, so she has been immobile = 1.5

You calculate the two-level PE Wells score as 1.5 (PE unlikely).

You consider that an alternative diagnosis of ischemic heart disease is likely.

1.3 Question

What would you do next?

[1] Recommendations 1.1.7 and 1.1.8 are likely to happen simultaneously. For example, it is not likely that in reality the clinician would wait for the chest X-ray result before commencing a Wells score. The cases have been presented in this manner in order to illustrate the application of each of the recommendations.

1.3 Answer

Offer an immediate D-dimer test.

Relevant recommendation

- Offer patients in whom PE is suspected and with an **unlikely** two-level PE Wells score a D-dimer test and if the result is positive offer **either**:
  - an immediate CT pulmonary angiogram (CTPA) **or**
  - immediate interim parenteral anticoagulant therapy followed by a CTPA, if a CTPA cannot be carried out immediately. **[KPI 1.1.10]**

1.4 Question

The D-dimer test is positive. Her hospital records show that she had an allergic reaction to contrast media in the past, therefore you cannot offer CTPA. What other investigations could you offer?

1.4 Answer

Assess Helen's suitability for V/Q SPECT or, if it this not available, a V/Q planar scan as an alternative to CTPA.

Helen is suitable for V/Q SPECT and a scan is immediately available.

Relevant recommendation

- For patients who have an allergy to contrast media, or who have renal impairment, or whose risk from irradiation is high:
  - Assess the suitability of a ventilation/perfusion single photon emission computed tomography (V/Q SPECT) scan or, if a V/Q SPECT scan is not available, a V/Q planar scan, as an alternative to CTPA.
  - If offering a V/Q SPECT or planar scan that will not be available immediately, offer interim parenteral anticoagulant therapy. **[1.1.11]**

1.5 Question

PE is identified on Helen's V/Q SPECT scan. What would you do next?

1.5 Answer

Diagnose PE and treat.

Because of Helen's religious beliefs, offer fondaparinux. Start the fondaparinux as soon as possible and continue it for 5 days or until the INR is 2 or above for at least 24 hours (whichever is longer). Start a vitamin K antagonist (VKA) within 24 hours of diagnosis of the PE. This should be continued for 3 months. Ensure an outpatient appointment is booked for her in 3 months' time to assess the benefits and risk of continuing the VKA.

Relevant recommendations

- Diagnose PE and treat (see section 1.2 of the NICE clinical guideline) patients with a positive CTPA or in whom PE is identified with a V/Q SPECT or planar scan. **[1.1.12]**
- Offer a choice of low molecular weight heparin (LMWH) or fondaparinux to patients with confirmed proximal DVT or PE, taking into account comorbidities, contraindications and drug costs, with the following exceptions:
  - For patients with severe renal impairment (estimated glomerular filtration rate [eGFR] < 30 ml/minute/1.73 m^2) offer unfractionated heparin (UFH) with dose adjustments based on the APTT (activated partial thromboplastin time) or LMWH with dose adjustments based on an anti-Xa assay.
  - For patients with an increased risk of bleeding consider UFH.
  - For patients with PE and haemodynamic instability, offer UFH and consider thrombolytic therapy (see recommendations 1.2.7 and 1.2.8 in the NICE clinical guideline).

  Start the LMWH, fondaparinux or UFH as soon as possible and continue it for at least 5 days or until the international normalised ratio (INR) (adjusted by a vitamin K antagonist [VKA]; see recommendation 1.2.3) is 2 or above for at least 24 hours, whichever is longer. **[KPI 1.2.1]**

- Offer a VKA to patients with confirmed proximal DVT or PE within 24 hours of diagnosis and continue the VKA for 3 months. At 3 months, assess the risks

and benefits of continuing VKA treatment (see recommendations □ and □). **[1.2.3]**

Related recommendations

- Offer a VKA beyond 3 months to patients with an unprovoked PE, taking into account the patient's risk of VTE recurrence and whether they are at increased risk of bleeding. Discuss with the patient the benefits and risks of extending their VKA treatment. **[KPI 1.2.4]**
- Consider extending the VKA beyond 3 months for patients with unprovoked proximal DVT if their risk of VTE recurrence is high and there is no additional risk of major bleeding. Discuss with the patient the benefits and risks of extending their VKA treatment. **[KPI 1.2.5]**
- Consider pharmacological systemic thrombolytic therapy for patients with PE and haemodynamic **instability** (see also recommendation 1.2.1 on pharmacological interventions for DVT and PE). **[1.2.7]**
- Do not offer pharmacological systemic thrombolytic therapy to patients with PE and haemodynamic **stability** (see also recommendation 1.2.1 on pharmacological interventions for DVT and PE). **[1.2.8]**
- Be aware that heparins are of animal origin and this may be of concern to some patients. (see Religion or belief: a practical guide for the NHS). For patients who have concerns about using animal products, consider offering synthetic alternatives based on clinical judgement after discussing their suitability, advantages and disadvantages with the patient. [This recommendation is from Venous thromboembolism: reducing the risk (NICE clinical guideline 92).] **[1.3.3]**

Additional information

When offering a choice of low molecular weight heparin (LMWH) or fondaparinux to patients with confirmed proximal DVT or PE (recommendation 1.2.1) the guidance developers noted that it is very important to consider the individual patient circumstances, such as comorbidities and contraindications in order to offer the most suitable agent for the patient. Important considerations include:

- **Renal status:** Dose adjustment and monitoring may be required as patients with renal impairment may accumulate excessive amounts of these drugs in the body. LMWH and fondaparinux should be used with caution for people with renal impairment, and UFH should be considered as an alternative. UFH has a short half-life and is predominantly metabolised in the liver compared to LMWHs that are predominantly excreted through the kidneys. UFH therefore may be more suitable for patients who are at risk of bleeding or have renal impairment.
- **Risk of bleeding or need for surgery or thrombolysis:** As in renal impairment patients, UFH is an alternative option for patients with uncertain risk of bleeding or if the patient may have to undergo surgical procedures or thrombolysis. Unfractionated heparin has a shorter half life and is more easily reversed if required.
- **Risk of HIT:** Based on clinical experience the guidance developers identified that there may be a lower risk of HIT in people receiving LMWH compared to UFH. If the patient has a history of HIT, fondaparinux is an alternative option because it is a synthetic pentasaccharide and not associated with HIT.
- **Appropriate dose:** Dosing errors in administering LMWH to patients have been the subject of a National Patient Safety Agency alert (NPSA Rapid response 14); doses were frequently not adjusted to the appropriate clinical indication, weight or renal function. Patients should be weighed prior to receiving LMWH to ensure that they are prescribed the correct dose, especially in obese patients. Renal function should also be considered in all patients, although renal function testing should not delay the first dose it should be taken into account for subsequent doses.
- **Patient preferences:** Both UFH and LMWH are of porcine origin. This may be a concern to some patients. If this is a concern, fondaparinux may be considered as a suitable alternative for some of these patients.
- **Route of administration for UFH:** Both the intravenous route and the subcutaneous route were included for UFH in the evidence review. However, the main group of patients where UFH is likely to be used are those with risk of bleeding or accumulation due to severe renal impairment. The intravenous route has advantages over the subcutaneous route in patients where

accumulation or bleeding may be problematic. If problems arise, the action of UFH can be limited by turning off the infusion. Protamine sulphate can be administered as indicated.

1.6 Question

Would you offer Helen systemic thrombolytic therapy or an inferior vena caval filter?

1.6 Answer

No, do not offer systemic thrombolytic therapy because Helen is not haemodynamically unstable.

Do not offer an inferior vena caval filter, because Helen can have anticoagulation treatment.

Relevant recommendations

- Do not offer pharmacological systemic thrombolytic therapy to patients with PE and haemodynamic **stability** (see also recommendation 1.2.1 in the NICE clinical guideline). **[1.2.8]**
- Offer temporary inferior vena caval filters to patients with proximal DVT or PE who cannot have anticoagulation treatment, and remove the inferior vena caval filter when the patient becomes eligible for anticoagulation treatment. **[1.2.10]**
- Consider inferior vena caval filters for patients with recurrent proximal DVT or PE despite adequate anticoagulation treatment only after considering alternative treatments such as:
  - increasing target INR to 3–4 for long-term high-intensity oral anticoagulant therapy **or**
  - switching treatment to LMWH. **[1.2.11]**

Related recommendation

- Ensure that a strategy for removing the inferior vena caval filter at the earliest possible opportunity is planned and documented when the filter is placed, and that the strategy is reviewed regularly. **[1.2.12]**

1.7 Question

Helen says her son, who has a mechanical heart valve, does his own INR blood tests, and asks whether she can do that?

1.7 Answer

Do not routinely offer Helen self-management or self-monitoring of her INR.

Relevant recommendation

- Do not routinely offer self-management or self-monitoring of INR to patients who have had DVT or PE and are having treatment with a VKA. **[1.4.1]**

1.8 Question

What information would you give Helen about her treatment?

1.8 Answer

Offer Helen verbal and written information about her anticoagulant treatment, including monitoring, side effects, interactions and lifestyle impacts. Provide her with an anticoagulant information booklet and an anticoagulant alert card. Advise her to carry the card at all times.

Relevant recommendations

- Give patients having anticoagulation treatment verbal and written information about:
  - how to use anticoagulants
  - duration of anticoagulation treatment
  - possible side effects of anticoagulant treatment and what to do if these occur
  - the effects of other medications, foods and alcohol on oral anticoagulation treatment
  - monitoring their anticoagulant treatment
  - how anticoagulants may affect their dental treatment
  - taking anticoagulants if they are planning pregnancy or become pregnant
  - how anticoagulants may affect activities such as sports and travel
  - when and how to seek medical help. **[1.3.1]**
- Provide patients who are having anticoagulation treatment with an 'anticoagulant information booklet' and an 'anticoagulant alert card' and advise them to carry the 'anticoagulant alert card' at all times. **[1.3.2]**
- Be aware that heparins are of animal origin and this may be of concern to some patients. (see Religion or belief: a practical guide for the NHS). For patients who have concerns about using animal products, consider offering synthetic alternatives based on clinical judgement after discussing their suitability, advantages and disadvantages with the patient. [This recommendation is from Venous thromboembolism: reducing the risk (NICE clinical guideline 92).] **[1.3.3]**

1.9 Question

Are there any further tests or investigations you would organise in relation to Helen’s diagnosis of PE?

1.9 Answer

No further investigations are needed. Helen's PE is provoked and likely to have been caused by her immobility due to the sprained ankle.

If Helen's PE had been unprovoked, and depending on anticoagulation plans, you would organise screening for cancer and thrombophilia.

Relevant recommendation

- Do not offer thrombophilia testing to patients who have had provoked DVT or PE. **[1.6.4]**

Related recommendations

- Offer all patients diagnosed with unprovoked DVT or PE who are not already known to have cancer the following investigations for cancer:
  - a physical examination (guided by the patient's full history) **and**
  - a chest X-ray **and**
  - blood tests (full blood count, serum calcium and liver function tests) **and**
  - urinalysis. **[1.5.1]**
- Consider further investigations for cancer with an abdomino-pelvic CT scan (and a mammogram for women) in all patients aged over 40 years with a first unprovoked DVT or PE who do not have signs or symptoms of cancer based on initial investigation (see recommendation □ above). **[KPI 1.5.2]**
- Do not offer thrombophilia testing to patients who are continuing anticoagulation treatment. **[1.6.1]**
- Consider testing for antiphospholipid antibodies in patients who have had unprovoked DVT or PE if it is planned to stop anticoagulation treatment. **[1.6.2]**
- Consider testing for hereditary thrombophilia in patients who have had unprovoked DVT or PE and who have a first-degree relative who has had DVT or PE if it is planned to stop anticoagulation treatment. **[1.6.3]**
- Do not routinely offer thrombophilia testing to first-degree relatives of people with a history of DVT or PE and thrombophilia. **[1.6.5]**

Case scenario 2: Harry

Presentation

Harry is an 81-year-old man who presents to your A&E department with a 3-day history of breathlessness. He reports coughing up fresh blood and a sharp pain on the left side of his chest on taking a deep breath.

2.1 Question

You believe Harry has symptoms of a suspected PE. What would you do next?

2.1 Answer

Carry out an assessment of his general medical history, a physical examination and a chest X-ray to exclude other causes.

Relevant recommendation

- If a patient presents with signs or symptoms of PE, carry out an assessment of their general medical history, a physical examination and a chest X-ray to exclude other causes **[1.1.7]**

On examination his respiratory rate is 20 breaths per minute, blood pressure 145/90 mmHg, heart rate 72 beat per minute. His temperature is 37.5°C and SpO_2 92% on air. Upon auscultation of his lungs you hear crackles at the left base. Chest X-ray shows a small left-sided pleural effusion. Upon further questioning you find out that Harry has been in bed for the past 4 days because he felt unwell, but 'did not like to bother anyone because it was a bank holiday'.

2.2 Question

You still suspect pulmonary embolism. What would you do next?

2.2 Answer

Use the two-level PE Wells score to estimate the clinical probability of PE.

Relevant recommendation

- If PE is suspected, use the two-level PE Wells score (see appendix 2 or table 2 in the NICE clinical guideline) to estimate the clinical probability of PE. **[1.1.8]**

- Immobilisation for more than 3 days or surgery in the previous 4 weeks = 1.5
- Haemoptysis = 1

You calculate the two-level PE Wells score to be 2.5 (PE unlikely)[2]. You consider than an alternative diagnosis (pneumonia) is as likely or more likely that PE.

2.3 Question

Although the two-level PE Wells score is unlikely, you still suspect a PE. What would you do next?

[2] Recommendations 1.1.7 and 1.1.8 are likely to happen simultaneously. For example, it is not likely that in reality the clinician would wait for the chest X-ray result before commencing a Wells score. The cases have been presented in this manner in order to illustrate the application of each of the recommendations.

2.3 Answer

Offer Harry a D-dimer test and, if positive an immediate CTPA or immediate interim parenteral anticoagulant therapy followed by CTPA.

Relevant recommendation

- Offer patients in whom PE is suspected and with an **unlikely** two-level PE Wells score a D-dimer test and if the result is positive offer **either**:
  - an immediate CTPA **or**
  - immediate interim parenteral anticoagulant therapy followed by a CTPA, if a CTPA cannot be carried out immediately **[KPI 1.1.10]**

Related recommendation

- For patients who have an allergy to contrast media, or who have renal impairment, or whose risk from irradiation is high:
  - Assess the suitability of a ventilation/perfusion single photon emission computed tomography (V/Q SPECT) scan or, if a V/Q SPECT scan is not available, a V/Q planar scan, as an alternative to CTPA.
  - If offering a V/Q SPECT or planar scan that will not be available immediately, offer interim parenteral anticoagulant therapy. **[1.1.11]**

2.4 Question

The D-dimer test is positive and the CTPA does not show any PE but shows evidence of consolidation of the left lower lobe of the lung.

What would you do next?

2.4 Answer

Start Harry on antibiotics for his left lower lobe pneumonia[3]. Advise him that it is not likely that he has a PE and discuss with him the signs and symptoms of PE, and when and where to seek further medical help.

Relevant recommendation

- Take into consideration alternative diagnoses in the following two groups of patients:
  - Patients with an **unlikely** two-level PE Wells score and **either**:
    - ◊ a negative D-dimer test **or**
    - ◊ a positive D-dimer test and a negative CTPA.
  - Patients with a **likely** two-level PE Wells score and **both**:
    - ◊ a negative CTPA **and**
    - ◊ no suspected DVT.

  Advise these patients that it is not likely they have PE and discuss with them the signs and symptoms of PE, and when and where to seek further medical help. **[1.1.13]**

[3] This potential diagnosis has been added to make the case more realistic but diagnosis of pneumonia is beyond the scope of this clinical guideline and therefore local protocols and relevant NICE guidance relating to pneumonia, and not this case, should be adhered to when diagnosing and managing pneumonia.

Case scenario 3: Kwasi

Presentation

Kwasi is a 25-year-old man who presents to your A&E department having recently been immobile for 6 weeks. He has been in a plaster cast for a left sided Achilles tendon injury, and the cast was removed last week. He has noticed that he is short of breath and is complaining of chest pain. On admission SpO_2 is 92% in air.

3.1 Question

You believe Kwasi has symptoms of PE. What would you do next?

3.1 Answer

Carry out an assessment of his general medical history, a physical examination and a chest X-ray to exclude other causes.

Relevant recommendation

- If a patient presents with signs or symptoms of PE, carry out an assessment of their general medical history, a physical examination and a chest X-ray to exclude other causes **[1.1.7]**

3.2 Question

On admission Kwasi's blood pressure is 89/62 mmHg, pulse rate 110 beats per minute, temperature 36.7^0c respiratory rate 15 breaths per minute. There are no clinical signs of a DVT. He has no other significant past medical history. You still suspect PE. What would you do next?

3.2 Answer

Use the two-level PE Wells score to estimate the clinical probability of PE.

Relevant recommendation

If PE is suspected, use the two-level PE Wells score (see appendix 2) to estimate the clinical probability of PE. **[1.1.8]**

- Alternative diagnosis less likely than PE = 3
- Heart rate >100 beats per minute = 1.5
- Immobilisation for more than 3 days or surgery in the previous 4 weeks = 1.5

You calculate the two-level PE wells score to be 6 (PE likely)[4].

3.3 Question

With this Wells score result what would you do next?

[4] It is acknowledged that the implementation of recommendations 1.1.7 and 1.1.8 are likely to happen simultaneously. For example, it is not likely that in reality the clinician would wait for the chest X-ray result before commencing a Wells score. The cases have been presented in this manner in order to illustrate implementation of each of the recommendations

3.3 Answer

Offer an immediate CPTA.

On this occasion CTPA is available for Kwasi immediately. The consultant in charge assesses Kwasi and deems him stable for transfer for CTPA. The CT department agree to accept him for CTPA and he is transferred with medical escort.

Relevant recommendation

- Offer patients in whom PE is suspected and with a **likely** two-level PE Wells score **either**:
  - an immediate computed tomography pulmonary angiogram (CTPA) **or**
  - immediate interim parenteral anticoagulant therapy followed by a CTPA, if a CTPA cannot be carried out immediately.

  Consider a proximal leg vein ultrasound scan if the CTPA is negative and DVT is suspected. **[KPI 1.1.9]**

Related recommendation

- For patients who have an allergy to contrast media, or who have renal impairment, or whose risk from irradiation is high:
  - Assess the suitability of a ventilation/perfusion single photon emission computed tomography (V/Q SPECT) scan or, if a V/Q SPECT scan is not available, a V/Q planar scan, as an alternative to CTPA.
  - If offering a V/Q SPECT or planar scan that will not be available immediately, offer interim parenteral anticoagulant therapy. **[1.1.11]**

3.4 Question

Kwasi's CTPA is positive for PE and he remains haemodynamically unstable. What would you do next?

3.4 Answer

Diagnose PE and treat as soon as possible. Because of Kwasi's hemodynamic instability start unfractionated heparin and consider offering systematic thrombolytic therapy.

In considering systematic thrombolytic therapy, expert clinical opinion advises provision of adequate monitoring facilities. Kwasi agrees to being treated with systemic thrombolytic therapy and appropriate facilities are made immediately available to safely administer and monitor systematic thrombolytic therapy.

Following the acute management phase Kwasi is stabilised and continues on UFH until the international normalised ratio (INR) (adjusted by a VKA) is 2 or above for at least 24 hours.

Relevant recommendations

- Diagnose PE and treat (see section 1.2 of the guideline) patients with a positive CTPA or in whom PE is identified with a V/Q SPECT or planar scan. **[1.1.12]**
- Offer a choice of low molecular weight heparin (LMWH) or fondaparinux to patients with confirmed proximal DVT or PE, taking into account comorbidities, contraindications and drug costs, with the following exceptions:
  - For patients with severe renal impairment (estimated glomerular filtration rate [eGFR] < 30 ml/minute/1.73 m^2) offer unfractionated heparin (UFH) with dose adjustments based on the APTT (activated partial thromboplastin time) or LMWH with dose adjustments based on an anti-Xa assay.
  - For patients with an increased risk of bleeding consider UFH.
  - For patients with PE and haemodynamic instability, offer UFH and consider thrombolytic therapy (see recommendations 1.2.7 and 1.2.8).

  Start the LMWH, fondaparinux or UFH as soon as possible and continue it for at least 5 days or until the international normalised ratio (INR) (adjusted by a vitamin K antagonist [VKA]; see recommendation 1.2.3) is 2 or above for at least 24 hours, whichever is longer. **[KPI 1.2.1]**

- Consider pharmacological systemic thrombolytic therapy for patients with PE and haemodynamic **instability** (see also recommendation 1.2.1 above). **[1.2.7]**

Related recommendation

- Do not offer pharmacological systemic thrombolytic therapy to patients with PE and haemodynamic **stability** (see also recommendation 1.2.1 on pharmacological interventions for DVT and PE). **[1.2.8]**

Additional information

When offering a choice of low molecular weight heparin (LMWH) or fondaparinux to patients with confirmed proximal DVT or PE (recommendation 1.2.1) the guidance developers noted that it is very important to consider the individual patient circumstances, such as comorbidities and contraindications in order to offer the most suitable agent for the patient. Important considerations include:

- **Renal status:** Dose adjustment and monitoring may be required as patients with renal impairment may accumulate excessive amounts of these drugs in the body. LMWH and fondaparinux should be used with caution for people with renal impairment, and UFH should be considered as an alternative. UFH has a short half-life and is predominantly metabolised in the liver compared to LMWHs that are predominantly excreted through the kidneys. UFH therefore may be more suitable for patients who are at risk of bleeding or have renal impairment.
- **Risk of bleeding or need for surgery or thrombolysis:** As in renal impairment patients, UFH is an alternative option for patients with uncertain risk of bleeding or if the patient may have to undergo surgical procedures or thrombolysis. Unfractionated heparin has a shorter half life and is more easily reversed if required.
- **Risk of HIT:** Based on clinical experience the guidance developers identified that there may be a lower risk of HIT in people receiving LMWH compared to UFH. If the patient has a history of HIT, fondaparinux is an alternative option because it is a synthetic pentasaccharide and not associated with HIT.

- **Appropriate dose:** Dosing errors in administering LMWH to patients have been the subject of a National Patient Safety Agency alert (NPSA Rapid response 14); doses were frequently not adjusted to the appropriate clinical indication, weight or renal function. Patients should be weighed prior to receiving LMWH to ensure that they are prescribed the correct dose, especially in obese patients. Renal function should also be considered in all patients, although renal function testing should not delay the first dose it should be taken into account for subsequent doses.
- **Patient preferences:** Both UFH and LMWH are of porcine origin. This may be a concern to some patients. If this is a concern, fondaparinux may be considered as a suitable alternative for some of these patients.
- **Route of administration for UFH:** Both the intravenous route and the subcutaneous route were included for UFH in the evidence review. However, the main group of patients where UFH is likely to be used are those with risk of bleeding or accumulation due to severe renal impairment. The intravenous route has advantages over the subcutaneous route in patients where accumulation or bleeding may be problematic. If problems arise, the action of UFH can be limited by turning off the infusion. Protamine sulphate can be administered as indicated.

3.5 Question

Once stabilised, what other treatment would you offer after diagnosis of PE?

3.5 Answer

Offer a VKA. Ensure that an outpatient clinic appointment is booked for Kwasi in 3 months time to allow you to assess his progress, benefits and risks of continuing VKA treatment.

The NICE recommendations say that the VKA should be offered within 2 hours of diagnosis. However expert opinion suggests that for cases such as Kwasi's, in which the patient is haemodynamically unstable, it is not likely to be started until the patient has stabilised.

Relevant recommendation

- Offer a VKA to patients with confirmed proximal DVT or PE within 24 hours of diagnosis and continue the VKA for 3 months. At 3 months, assess the risks and benefits of continuing VKA treatment (see recommendations □ and □). **[1.2.3]**

Related recommendations

- Offer a VKA beyond 3 months to patients with an unprovoked PE, taking into account the patient's risk of VTE recurrence and whether they are at increased risk of bleeding. Discuss with the patient the benefits and risks of extending their VKA treatment. **[KPI 1.2.4]**
- Consider extending the VKA beyond 3 months for patients with unprovoked proximal DVT if their risk of VTE recurrence is high and there is no additional risk of major bleeding. Discuss with the patient the benefits and risks of extending their VKA treatment. **[KPI 1.2.5]**

3.6 Question

What information would you give to Kwasi about his treatment? Would you offer him self-management of his INR?

3.6 Answer

Offer Kwasi verbal and written information about his anticoagulant treatment, including monitoring, side effects, interactions and lifestyle impacts. Provide him with an anticoagulant information booklet and an anticoagulant alert card. Advise him to carry the alert card at all times.

Do not offer Kwasi self-management or self-monitoring of his INR.

Relevant recommendations

- Give patients having anticoagulation treatment verbal and written information about:
  - how to use anticoagulants
  - duration of anticoagulation treatment
  - possible side effects of anticoagulant treatment and what to do if these occur
  - the effects of other medications, foods and alcohol on oral anticoagulation treatment
  - monitoring their anticoagulant treatment
  - how anticoagulants may affect their dental treatment
  - taking anticoagulants if they are planning pregnancy or become pregnant
  - how anticoagulants may affect activities such as sports and travel
  - when and how to seek medical help. **[1.3.1]**
- Provide patients who are having anticoagulation treatment with an 'anticoagulant information booklet' and an 'anticoagulant alert card' and advise them to carry the 'anticoagulant alert card' at all times. **[1.3.2]**
- Be aware that heparins are of animal origin and this may be of concern to some patients. (see Religion or belief: a practical guide for the NHS). For patients who have concerns about using animal products, consider offering synthetic alternatives based on clinical judgement after discussing their suitability, advantages and disadvantages with the patient. [This recommendation is from Venous thromboembolism: reducing the risk (NICE clinical guideline 92).] **[1.3.3]**
- Do not routinely offer self-management or self-monitoring of INR to patients

who have had DVT or PE and are having treatment with a VKA. **[1.4.1]**

Case scenario 4: Joyce

Presentation

Joyce is a 60-year-old woman with inoperable colonic cancer undergoing palliative chemotherapy. She is admitted to your A&E department with sudden-onset of shortness of breath. She is hypoxic.

4.1 Question

You believe Joyce has symptoms of a suspected pulmonary embolism. What would you do next?

4.1 Answer

Carry out an assessment of her general medical history, a physical examination and a chest X-ray to exclude other causes.

Relevant recommendation

- If a patient presents with signs or symptoms of PE, carry out an assessment of their general medical history, a physical examination and a chest X-ray to exclude other causes **[1.1.7]**

On admission Joyce is hypoxic, $Sp0_2$ is 92% in air, respiratory rate is 26 breaths per minute, heart rate 110 beats per minute, blood pressure 125/90 mmHg, temperature 37.1^0c and her jugular venous pressure is elevated. On her chest X-ray there are no metastases and her lungs are clear. There are no clinical signs of DVT.

4.2 Question

You still suspect PE what would you do next?

4.2 Answer

Use the two-level PE Wells score to estimate the clinical probability of PE.

Relevant recommendation

- If PE is suspected, use the two-level PE Wells score (see appendix 2 or table 2 in the NICE clinical guideline) to estimate the clinical probability of PE. **[1.1.8]**

- An alternative diagnosis is less likely than a PE = 3
- Heart rate >100 beats per minute = 1.5
- Malignancy = 1

The two-level PE Wells score is 5.5 (PE likely)[5]. You suspect PE.

4.3 Question

With a Wells score of 'PE likely', what would you do next?

[5] It is acknowledged that the implementation of recommendations 1.1.7 and 1.1.8 are likely to happen simultaneously. For example, it is not likely that in reality the clinician would wait for the chest X-ray result before commencing a Wells score. The cases have been presented in this manner in order to illustrate implementation of each of the recommendations

4.3 Answer

Offer CTPA.

On this occasion CTPA is available immediately, therefore you organise it.

Relevant recommendation

- Offer patients in whom PE is suspected and with a **likely** two-level PE Wells score **either**:
  - an immediate computed tomography pulmonary angiogram (CTPA) **or**
  - immediate interim parenteral anticoagulant therapy followed by a CTPA, if a CTPA cannot be carried out immediately.

  Consider a proximal leg vein ultrasound scan if the CTPA is negative and DVT is suspected. **[KPI 1.1.9]**

Related recommendation

- For patients who have an allergy to contrast media, or who have renal impairment, or whose risk from irradiation is high:
  - Assess the suitability of a ventilation/perfusion single photon emission computed tomography (V/Q SPECT) scan or, if a V/Q SPECT scan is not available, a V/Q planar scan, as an alternative to CTPA.
  - If offering a V/Q SPECT or planar scan that will not be available immediately, offer interim parenteral anticoagulant therapy. **[1.1.11]**

4.4 Question

The CTPA is positive for PE. What would you do next?

4.4 Answer

Diagnose PE and start treatment.

Joyce is amenable to daily subcutaneous injections so you start treatment with low molecular weight heparin. This should continue for 6 months.

Ensure that an outpatient appointment is booked for Joyce for 6 months time to assess the risks and benefits of continuing anticoagulation.

When developing their recommendations, the GDG noted that current international guidelines and UK clinical practice recommend continuing anticoagulation lifelong in patients with active cancer, based on expert clinical experience, case series and opinion, in the absence of randomised controlled trials.

Relevant recommendations

- Diagnose PE and treat (see section 1.2 of the NICE clinical guideline) patients with a positive CTPA or in whom PE is identified with a V/Q SPECT or planar scan. **[1.1.12]**
- Offer LMWH to patients with active cancer and confirmed proximal DVT or PE, and continue the LMWH for 6 months[6]. At 6 months, assess the risks and benefits of continuing anticoagulation[7]. **[KPI 1.2.2]**

Additional information

The evidence suggested that using LMWH instead of VKAs offered an overall benefit, for patients with proximal DVT or PE and active cancer (recommendation 1.2.2). However, this means that patients will be having daily subcutaneous injections instead of taking oral tablets. Therefore, patient preference and practicalities, such as whether patients can reliably self-inject or

[6] At the time of publication (June 2012) some types of LMWH do not have a UK marketing authorisation for 6 months of treatment of DVT or PE in patients with cancer. Prescribers should consult the summary of product characteristics for the individual LMWH and make appropriate adjustments for renal impairment. Informed consent for off-label use should be obtained and documented.

[7] Although this use is common in UK clinical practice, at the time of publication (June 2012) none of the anticoagulants has a UK marketing authorisation for the treatment of DVT or PE beyond 6 months in patients with cancer. Informed consent for off-label use should be obtained and documented.

have a carer (such as a relative or district nurse) to help to administer the injection needs to be taken into account. The ability of patients to adhere to the treatment plan is important for its success.

Additional benefits to LMWH for people with cancer:

- It is difficult to maintain good INR control (which puts patients at risk of bleeding or more VTE events) while patients are on chemotherapy. This makes it a strong case for the use of LMWH for those patients with new VTE, and active cancer, particularly if undergoing chemotherapy.
- Patients with cancer have a higher risk of major bleeding on anticoagulation compared to patients without cancer, which may relate to the underlying cancer and propensity for bleeding (e.g. ulcerated gastric cancer).
- Patients with impaired renal function can receive LMWH at a reduced dose, and would therefore not be excluded. There may be an additional cost to Factor X monitoring for such patients, however probably few actual tests need to be conducted when patients are stabilised.

At 6 months, the need to continue anticoagulation should be reassessed and discussed with the patient. The current recommendation of international guidelines and UK clinical practice is to continue anticoagulation lifelong in patients with active cancer, based on expert clinical experience, case series and opinion, in the absence of randomised controlled trials (Khorana AA, Streiff MB, Farge D, Mandala M, Debourdeau P, Cajfinger F et al. Venous thromboembolism prophylaxis and treatment in cancer: a consensus statement of major guidelines panels and call to action. Journal of Clinical Oncology: Official Journal of the American Society of Clinical Oncology. 2009; 27(29):4919-4926.)

4.5 Question

Would you offer Joyce systemic thrombolytic therapy or insertion of an inferior venal caval filter?

4.5 Answer

No, do not offer systemic thrombolytic therapy because she is not haemodynamically unstable.

Do not offer insertion of an inferior venal caval filter, because she is able to have anticoagulation treatment.

Relevant recommendation

- Do not offer pharmacological systemic thrombolytic therapy to patients with PE and haemodynamic **stability** (see also recommendation 1.2.1 in the NICE clinical guideline). **[1.2.8]**

Related recommendations

- Offer temporary inferior vena caval filters to patients with proximal DVT or PE who cannot have anticoagulation treatment, and remove the inferior vena caval filter when the patient becomes eligible for anticoagulation treatment. **[1.2.10]**
- Consider inferior vena caval filters for patients with recurrent proximal DVT or PE despite adequate anticoagulation treatment only after considering alternative treatments such as:
  - increasing target INR to 3–4 for long-term high-intensity oral anticoagulant therapy **or**
  - switching treatment to LMWH. **1.2.11]**
- Ensure that a strategy for removing the inferior vena caval filter at the earliest possible opportunity is planned and documented when the filter is placed, and that the strategy is reviewed regularly. **[1.2.12]**

4.6 Question

What information would you give Joyce about her treatment?

4.6 Answer

Offer Joyce verbal and written information about her anticoagulant treatment, including monitoring, side effects, interactions and lifestyle impacts. Provide her with an anticoagulant information booklet and an anticoagulant alert card. Advise her to carry the alert card at all times.

Relevant recommendations

- Give patients having anticoagulation treatment verbal and written information about:
  - how to use anticoagulants
  - duration of anticoagulation treatment
  - possible side effects of anticoagulant treatment and what to do if these occur
  - the effects of other medications, foods and alcohol on oral anticoagulation treatment
  - monitoring their anticoagulant treatment
  - how anticoagulants may affect their dental treatment
  - taking anticoagulants if they are planning pregnancy or become pregnant
  - how anticoagulants may affect activities such as sports and travel
  - when and how to seek medical help. **[1.3.1]**
- Provide patients who are having anticoagulation treatment with an 'anticoagulant information booklet' and an 'anticoagulant alert card' and advise them to carry the 'anticoagulant alert card' at all times. **[1.3.2]**
- Be aware that heparins are of animal origin and this may be of concern to some patients. (see Religion or belief: a practical guide for the NHS). For patients who have concerns about using animal products, consider offering synthetic alternatives based on clinical judgement after discussing their suitability, advantages and disadvantages with the patient. [This recommendation is from Venous thromboembolism: reducing the risk (NICE clinical guideline 92).] **[1.3.3]**

4.7 Question

Joyce's PE is considered to be unprovoked (other than by her colonic cancer), Given this, are there any further investigations and tests you would organise?

4.7 Answer

No further tests are needed. Although Joyce's PE is considered 'unprovoked' by the definitions in the NICE clinical guideline, further testing for cancer or thrombophilia is not needed because Joyce is known to have active cancer.

Relevant recommendations

- Offer all patients diagnosed with unprovoked DVT or PE who are not already known to have cancer the following investigations for cancer:
  - a physical examination (guided by the patient's full history) **and**
  - a chest X-ray **and**
  - blood tests (full blood count, serum calcium and liver function tests) **and**
  - urinalysis. **[1.5.1]**
- Consider further investigations for cancer with an abdomino-pelvic CT scan (and a mammogram for women) in all patients aged over 40 years with a first unprovoked DVT or PE who do not have signs or symptoms of cancer based on initial investigation (see recommendation above). **[KPI 1.5.2]**
- Do not offer thrombophilia testing to patients who are continuing anticoagulation treatment. **[1.6.1]**
- Consider testing for antiphospholipid antibodies in patients who have had unprovoked DVT or PE if it is planned to stop anticoagulation treatment. **[1.6.2]**
- Consider testing for hereditary thrombophilia in patients who have had unprovoked DVT or PE and who have a first-degree relative who has had DVT or PE if it is planned to stop anticoagulation treatment. **[1.6.3]**

Related recommendation

- Do not routinely offer thrombophilia testing to first-degree relatives of people with a history of DVT or PE and thrombophilia. **[1.6.5]**

Case scenario 5: Gary

Please note this case scenario also appears in the DVT clinical case scenarios.

Presentation

Gary is a 52-year-old man who is an endurance cyclist. He presents to your A&E department following referral from his GP. He reports shortness of breath at rest and chest pain. On direct questioning he admits to pain in the right calf for a month, which he put down to muscle sprain.

5.1 Question

You believe Gary has symptoms of a suspected PE and DVT. Which diagnostic route should you take?

5.1 Answer

Take into consideration the 'additional information' below in making your decision.

Because of Gary's chest pain and shortness of breath, you decide to carry out initial diagnostic investigations for PE.

Relevant recommendation

- If a patient presents with signs or symptoms of both DVT (for example a swollen and/or painful leg) and PE (for example chest pain, shortness of breath or haemoptysis), carry out initial diagnostic investigations for either DVT or PE, basing the choice of diagnostic investigations on clinical judgement. **[1.1.14]**

Additional information

When developing the guideline the developers discussed the advantages and disadvantages to the patient in following each pathway (either DVT or PE):

- The ultrasound scan used in the DVT algorithm avoids radiation exposure and the administration of contrast compared with CTPA which is used in the PE diagnostic algorithm. A CTPA is approximately equivalent to 3.6 years of natural background radiation (UK average 2.2 mSv per year taken from referral guideline from the Royal College of Radiologists)
- One advantage of CTPA is that it also looks at all of the other structures within the chest including whether there is evidence of right ventricular dilatation which has prognostic implications and can identify other causes for the patient's symptoms.
- The DVT diagnosis algorithm may be chosen for a patient with a possible provoked DVT and PE because there will be no change to the pharmacological treatment as a result of diagnosis and they would be exposed to no radiation or intravenous contrast.

5.2 Question

What would you do next to diagnose PE?

5.2 Answer

Carry out an assessment of his general medical history, a physical examination and a chest X-ray to exclude other causes.

Relevant recommendation

- If a patient presents with signs or symptoms of PE, carry out an assessment of their general medical history, a physical examination and a chest X-ray to exclude other causes. **[1.1.7]**

5.3 Question

On admission Gary's SpO_2 is 93% in air, heart rate is 102 beats per minute, respiratory rate 17 breaths per minute, blood pressure 110/70 mmHg, temperature 37^0c. You still suspect PE: what would you do next?

5.3 Answer

Use the two-level PE Wells score to estimate the clinical probability of PE.

Relevant recommendation

- If PE is suspected, use the two-level PE Wells score (see appendix 2 or table 2) to estimate the clinical probability of PE. **[1.1.8]**

5.4 Question

You calculate the two-level PE Wells score to be 7.5 (PE likely)[8]:

- Clinical signs and symptoms of DVT = 3.
- Alternative diagnosis less likely than PE = 3.
- Heart rate >100 beats per minute = 1.5.

You suspect PE. With this Wells score result, what would you do next?

[8] It is acknowledged that the implementation of recommendations 1.1.7 and 1.1.8 are likely to happen simultaneously. For example, it is not likely that in reality the clinician would wait for the chest X-ray result before commencing a Wells score. The cases have been presented in this manner in order to illustrate implementation of each of the recommendations

5.4 Answer

Offer CTPA.

On this occasion immediate CTPA is available so you offer this.

Relevant recommendation

- Offer patients in whom PE is suspected and with a **likely** two-level PE Wells score **either**:
  - an immediate computed tomography pulmonary angiogram (CTPA) **or**
  - immediate interim parenteral anticoagulant therapy followed by a CTPA, if a CTPA cannot be carried out immediately.

  Consider a proximal leg vein ultrasound scan if the CTPA is negative and DVT is suspected. **[KPI 1.1.9]**

Related recommendation

- For patients who have an allergy to contrast media, or who have renal impairment, or whose risk from irradiation is high:
  - Assess the suitability of a ventilation/perfusion single photon emission computed tomography (V/Q SPECT) scan or, if a V/Q SPECT scan is not available, a V/Q planar scan, as an alternative to CTPA.

  If offering a V/Q SPECT or planar scan that will not be available immediately, offer interim parenteral anticoagulant therapy. **[1.1.11]**

5.5 Question

The CTPA is positive showing several pulmonary emboli. What would you do next?

5.5 Answer

Diagnose PE and start treatment.

Based on your clinical decision you offer LMWH immediately and continue this for at least 5 days or until the INR is 2 or above for at least 24 hours (whichever is longer). You also start VKA within 24 hours of diagnosis of the PE and continue this for 3 months. You also ensure an outpatient appointment is booked for Gary in 3 months' time to assess benefits and risks of continuing the VKA.

Relevant recommendations

- Diagnose PE and treat (see section 1.2 of the NICE guideline) patients with a positive CTPA or in whom PE is identified with a V/Q SPECT or planar scan. **[1.1.12]**
- Offer a choice of low molecular weight heparin (LMWH) or fondaparinux to patients with confirmed proximal DVT or PE, taking into account comorbidities, contraindications and drug costs, with the following exceptions:
  - For patients with severe renal impairment (estimated glomerular filtration rate [eGFR] < 30 ml/minute/1.73 m^2) offer unfractionated heparin (UFH) with dose adjustments based on the APTT (activated partial thromboplastin time) or LMWH with dose adjustments based on an anti-Xa assay.
  - For patients with an increased risk of bleeding consider UFH.
  - For patients with PE and haemodynamic instability, offer UFH and consider thrombolytic therapy (see recommendations 1.2.7 and 1.2.8 below).

  Start the LMWH, fondaparinux or UFH as soon as possible and continue it for at least 5 days or until the international normalised ratio (INR) (adjusted by a vitamin K antagonist [VKA]; see recommendation 1.2.3) is 2 or above for at least 24 hours, whichever is longer. **[KPI 1.2.1]**
- Offer a VKA to patients with confirmed proximal DVT or PE within 24 hours of diagnosis and continue the VKA for 3 months. At 3 months, assess the risks and benefits of continuing VKA treatment (see recommendations 1.2.4

and 1.2.5). **[1.2.3]**

Related recommendations

- Offer a VKA beyond 3 months to patients with an unprovoked PE, taking into account the patient's risk of VTE recurrence and whether they are at increased risk of bleeding. Discuss with the patient the benefits and risks of extending their VKA treatment. **[KPI 1.2.4]**
- Consider extending the VKA beyond 3 months for patients with unprovoked proximal DVT if their risk of VTE recurrence is high and there is no additional risk of major bleeding. Discuss with the patient the benefits and risks of extending their VKA treatment. **[KPI 1.2.5]**
- Consider pharmacological systemic thrombolytic therapy for patients with PE and haemodynamic **instability** (see also recommendation 1.2.1 on pharmacological interventions for DVT and PE). **[1.2.7]**
- Do not offer pharmacological systemic thrombolytic therapy to patients with PE and haemodynamic **stability** (see also recommendation 1.2.1 on pharmacological interventions for DVT and PE). **[1.2.8]**

Additional information

When offering a choice of low molecular weight heparin (LMWH) or fondaparinux to patients with confirmed proximal DVT or PE (recommendation 1.2.1) the guidance developers noted that it is very important to consider the individual patient circumstances, such as comorbidities and contraindications in order to offer the most suitable agent for the patient. Important considerations include:

- **Renal status:** Dose adjustment and monitoring may be required as patients with renal impairment may accumulate excessive amounts of these drugs in the body. LMWH and fondaparinux should be used with caution for people with renal impairment, and UFH should be considered as an alternative. UFH has a short half-life and is predominantly metabolised in the liver compared to LMWHs that are predominantly excreted through the kidneys. UFH therefore may be more suitable for patients who are at risk of bleeding or have renal impairment.

- **Risk of bleeding or need for surgery or thrombolysis:** As in renal impairment patients, UFH is an alternative option for patients with uncertain risk of bleeding or if the patient may have to undergo surgical procedures or thrombolysis. Unfractionated heparin has a shorter half-life and is more easily reversed if required.
- **Risk of HIT:** Based on clinical experience the guidance developers identified that there may be a lower risk of HIT in people receiving LMWH compared to UFH. If the patient has a history of HIT, fondaparinux is an alternative option because it is a synthetic pentasaccharide and not associated with HIT.
- **Appropriate dose:** Dosing errors in administering LMWH to patients have been the subject of a National Patient Safety Agency alert (NPSA Rapid response 14); doses were frequently not adjusted to the appropriate clinical indication, weight or renal function. Patients should be weighed prior to receiving LMWH to ensure that they are prescribed the correct dose, especially in obese patients. Renal function should also be considered in all patients, although renal function testing should not delay the first dose it should be taken into account for subsequent doses.
- **Patient preferences:** Both UFH and LMWH are of porcine origin. This may be a concern to some patients. If this is a concern, fondaparinux may be considered as a suitable alternative for some of these patients.
- **Route of administration for UFH:** Both the intravenous route and the subcutaneous route were included for UFH in the evidence review. However, the main group of patients where UFH is likely to be used are those with risk of bleeding or accumulation due to severe renal impairment. The intravenous route has advantages over the subcutaneous route in patients where accumulation or bleeding may be problematic. If problems arise, the action of UFH can be limited by turning off the infusion. Protamine sulphate can be administered as indicated.

5.6 Question

Would you offer Gary systemic thrombolytic therapy, catheter-directed thrombolytic therapy or an inferior vena caval filter to treat his PE and DVT?

5.6 Answer

No, do not offer systemic thrombolytic therapy to treat Gary's PE because he is not haemodynamically unstable.

Do not offer an inferior vena caval filter because Gary is able to have anticoagulation treatment.

Relevant recommendations

- Consider catheter-directed thrombolytic therapy for patients with symptomatic iliofemoral DVT who have:
  - symptoms of less than 14 days' duration **and**
  - good functional status **and**
  - a life expectancy of 1 year or more **and**
  - a low risk of bleeding. **[KPI 1.2.6]**
- Do not offer pharmacological systemic thrombolytic therapy to patients with PE and haemodynamic **stability** (see also recommendation 1.2.1 in the NICE guideline). **[1.2.8]**
- Offer temporary inferior vena caval filters to patients with proximal DVT or PE who cannot have anticoagulation treatment, and remove the inferior vena caval filter when the patient becomes eligible for anticoagulation treatment. **[1.2.10]**
- Consider inferior vena caval filters for patients with recurrent proximal DVT or PE despite adequate anticoagulation treatment only after considering alternative treatments such as:
  - increasing target INR to 3–4 for long-term high-intensity oral anticoagulant therapy **or**
  - switching treatment to LMWH. **[1.2.11]**

Related recommendation

- Ensure that a strategy for removing the inferior vena caval filter at the earliest possible opportunity is planned and documented when the filter is placed, and that the strategy is reviewed regularly. **[1.2.12]**
- Consider pharmacological systemic thrombolytic therapy for patients with PE and haemodynamic **instability** (see also recommendation 1.2.1 on

pharmacological interventions for DVT and PE). **[1.2.7]**

- Do not offer pharmacological systemic thrombolytic therapy to patients with PE and haemodynamic **stability** (see also recommendation 1.2.1 on pharmacological interventions for DVT and PE). **[1.2.8]**

5.7 Question

A few days after Gary's admission the acute PE phase has been managed and Gary is stable. You noted on admission that Gary complained of a sore leg. You now note that his entire leg is swollen, he has calf swelling of more than 3 cm on his sore leg. You are still concerned about DVT: what would you do next?

5.7 Answer

The anticoagulation treatment for pulmonary embolism is very similar to that for deep vein thrombosis. Therefore if Gary does have a DVT, the treatment he has been receiving would also be treating any possible DVT. However, the treatment for DVT also includes graduated compression stocking to prevent the development of post thrombotic limb. It is therefore helpful to confirm if Gary has a DVT. You would therefore offer a proximal leg vein ultrasound.

Relevant recommendation

- Offer patients in whom DVT is suspected and with a **likely** two-level DVT Wells score **either**:
  - a proximal leg vein ultrasound scan carried out within 4 hours of being requested and, if the result is negative, a D-dimer test **or**
  - a D-dimer test and an interim 24-hour dose of a parenteral anticoagulant (if a proximal leg vein ultrasound scan cannot be carried out within 4 hours) and a proximal leg vein ultrasound scan carried out within 24 hours of being requested.

  Repeat the proximal leg vein ultrasound scan 6–8 days later for all patients with a positive D-dimer test and a negative proximal leg vein ultrasound scan. **[1.1.3]**

5.8 Question

The proximal leg vein ultrasound scan shows a proximal DVT. What would you do next? Would you consider catheter-directed thrombolytic therapy?

5.8 Answer

Do not offer Gary catheter-directed thrombolytic therapy because he has had symptoms for longer than 14 days. Additionally the ultrasound did not identify iliofemoral DVT.

In addition to the LMWH and VKA (see answer 4.5), a week after diagnosis or when swelling is reduced sufficiently Gary should be offered below-knee graduated compression stockings with an ankle pressure greater than 23 mmHg, if there are no contraindications.

By this point it is likely that Gary will have left the acute setting, so to ensure he receives this treatment refer him at the time of diagnosis to the relevant healthcare professional/department responsible for providing stockings (this may be his GP or the orthotic department).

Also ask his GP to ensure that the stockings are worn for at least 2 years, are replaced two or three times a year and are worn in line with the manufacturer's instructions.

Relevant recommendations

- Consider catheter-directed thrombolytic therapy for patients with symptomatic iliofemoral DVT who have:
  - symptoms of less than 14 days' duration **and**
  - good functional status **and**
  - a life expectancy of 1 year or more **and**
  - a low risk of bleeding. **[KPI 1.2.6]**
- Offer below-knee graduated compression stockings with an ankle pressure greater than 23 mmHg to patients with proximal DVT a week after diagnosis or when swelling is reduced sufficiently and if there are no contraindications[9], and:
  - advise patients to continue wearing the stockings for at least 2 years
  - ensure that the stockings are replaced two or three times per year or according to the manufacturer's instructions

[9] Prescribers should refer to specific product information and contraindications before offering graduated compression stockings.

– advise patients that the stockings need to be worn only on the affected leg or legs. **[1.2.9]**

5.9 Question

What information would you give to Gary about his treatment? Would you offer him self-management of his INR?

5.9 Answer

Offer Gary verbal and written information about his anticoagulant treatment including monitoring, side effects, interactions and lifestyle impacts. Provide him with an anticoagulant information booklet and an anticoagulant alert card. Advise him to carry the anticoagulant alert card at all times.

You would not routinely offer Gary self-management of his INR.

Relevant recommendations

- Give patients having anticoagulation treatment verbal and written information about:
  - how to use anticoagulants
  - duration of anticoagulation treatment
  - possible side effects of anticoagulant treatment and what to do if these occur
  - the effects of other medications, foods and alcohol on oral anticoagulation treatment
  - monitoring their anticoagulant treatment
  - how anticoagulants may affect their dental treatment
  - taking anticoagulants if they are planning pregnancy or become pregnant
  - how anticoagulants may affect activities such as sports and travel
  - when and how to seek medical help. **[1.3.1]**
- Provide patients who are having anticoagulation treatment with an 'anticoagulant information booklet' and an 'anticoagulant alert card' and advise them to carry the 'anticoagulant alert card' at all times. **[1.3.2]**
- Be aware that heparins are of animal origin and this may be of concern to some patients (see Religion or belief: a practical guide for the NHS). For patients who have concerns about using animal products, consider offering synthetic alternatives based on clinical judgement after discussing their suitability, advantages and disadvantages with the patient. [This recommendation is from Venous thromboembolism: reducing the risk (NICE clinical guideline 92).] **[1.3.3]**
- Advise patients about the correct application and use of below-knee graduated compression stockings, how long they should be worn and when

they should be replaced. **[1.3.4]**

- Do not routinely offer self-management or self-monitoring of INR to patients who have had DVT or PE and are having treatment with a VKA. **[1.4.1]**

5.10 Question

Following this recent episode of unprovoked PE and DVT, are there any further tests you would offer Gary?

5.10 Answer

Yes, offer the following investigations for cancer: a physical examination (guided by his full history) and a chest X-ray and blood tests (full blood count, serum calcium and liver function tests) and urinalysis.

If these tests do not identify signs and symptoms of cancer in Gary, consider further investigation with an abdomino-pelvic CT scan for cancer.

If active cancer is identified it may be necessary to re-assess Gary's PE and DVT treatment plan.

If the plan is to stop anticoagulant treatment you should also consider thrombophilia testing.

Relevant recommendations

- Offer all patients diagnosed with unprovoked DVT or PE who are not already known to have cancer the following investigations for cancer:
  - a physical examination (guided by the patient's full history) **and**
  - a chest X-ray **and**
  - blood tests (full blood count, serum calcium and liver function tests) **and**
  - urinalysis. **[1.5.1]**
- Consider further investigations for cancer with an abdomino-pelvic CT scan (and a mammogram for women) in all patients aged over 40 years with a first unprovoked DVT or PE who do not have signs or symptoms of cancer based on initial investigation (see recommendation 1.5.1 above). **[KPI 1.5.2]**
- Do not offer thrombophilia testing to patients who are continuing anticoagulation treatment. **[1.6.1]**
- Consider testing for antiphospholipid antibodies in patients who have had unprovoked DVT or PE if it is planned to stop anticoagulation treatment. **[1.6.2]**
- Consider testing for hereditary thrombophilia in patients who have had unprovoked DVT or PE and who have a first-degree relative who has had DVT or PE if it is planned to stop anticoagulation treatment. **[1.6.3]**

Related recommendations

- Do not routinely offer thrombophilia testing to first-degree relatives of people with a history of DVT or PE and thrombophilia. **[1.6.5]**
- Offer LMWH to patients with active cancer and confirmed proximal DVT or PE, and continue the LMWH for 6 months[10]. At 6 months, assess the risks and benefits of continuing anticoagulation[11]. **[KPI 1.2.2]**

[10] At the time of publication (June 2012) some types of LMWH do not have a UK marketing authorisation for 6 months of treatment of DVT or PE in patients with cancer. Prescribers should consult the summary of product characteristics for the individual LMWH and make appropriate adjustments for renal impairment. Informed consent for off-label use should be obtained and documented.

[11] Although this use is common in UK clinical practice, at the time of publication (June 2012) none of the anticoagulants has a UK marketing authorisation for the treatment of DVT or PE beyond 6 months in patients with cancer. Informed consent for off-label use should be obtained and documented.

Other implementation tools

NICE has developed tools to help organisations implement the clinical guideline on Venous thromboembolic diseases. These are available on the NICE website (www.nice.org.uk/guidance/CG144).

- DVT training plan, clinical case scenarios and slide set.
- Costing statement – details of the likely costs and savings when the cost impact of the guideline is not considered to be significant.
- Audit support including electronic data tools – for monitoring local practice.

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Appendix 1 Two-level DVT Wells score[a]

Clinical feature	Points
Active cancer (treatment ongoing, within 6 months, or palliative)	1
Paralysis, paresis or recent plaster immobilisation of the lower extremities	1
Recently bedridden for 3 days or more or major surgery within 12 weeks requiring general or regional anaesthesia	1
Localised tenderness along the distribution of the deep venous system	1
Entire leg swollen	1
Calf swelling at least 3 cm larger than asymptomatic side	1
Pitting oedema confined to the symptomatic leg	1
Collateral superficial veins (non-varicose)	1
Previously documented DVT	1
An alternative diagnosis is at least as likely as DVT	−2
Clinical probability simplified score	
DVT *likely*	2 points or more
DVT *unlikely*	1 point or less
[a] Adapted with permission from Wells PS et al. (2003) Evaluation of D-dimer in the diagnosis of suspected deep-vein thrombosis.	

A template patient record Two-level DVT Wells score which you can print, complete and then add to patient records can be downloaded from the NICE website

Appendix 2 Two-level PE Wells score[a]

Clinical feature	Points
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
Immobilisation 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
[a] Adapted with permission from Wells PS et al. (2000) Derivation of a simple clinical model to categorize patients' probability of pulmonary embolism: increasing the model's utility with the SimpliRED D-dimer.	

A template patient record Two-level PE Wells score which you can print, complete and then add to patient records can be downloaded from the NICE website