

IRISH ASSOCIATION FOR EMERGENCY MEDICINE



IAEM Clinical Guideline

Management of Patients Presenting to the Emergency Department with Suspected Lower Limb Deep Vein Thrombosis

Version 1

August 2021

Authors: Dr Eduard Turcuman, Dr Canberk Meseli, Dr Farah Mustafa

Clinical Lead: Dr Tomas Breslin, Consultant in Emergency Medicine & Member of National VTE committee, in collaboration with IAEM Clinical Guideline Development committee.

DISCLAIMER

IAEM recognises that patients, their situations, Emergency Departments and staff all vary. These guidelines cannot cover all clinical scenarios. The ultimate responsibility for the interpretation and application of these guidelines, the use of current information and a patient's overall care and wellbeing resides with the treating clinician.

Contributors:

Dr Adrian Moughty, Consultant in Emergency Medicine, MMUH

Dr Niall O'Connor, Consultant in Emergency Medicine, OLOL

Dr Emily O'Connor, Consultant in Emergency Medicine, CHB

Dr Rachel Gilmore, Consultant in Emergency Medicine, CHB

Dr Jeremy Sargent, Consultant Haematologist, OLOL

Dr Ashraf Butt, Consultant in Emergency Medicine, CGH

GLOSSARY OF TERMS

Deep Vein Thrombosis: A condition in which a blood clot (thrombus) forms in a vein, most commonly in the deep veins of the legs or pelvis. The thrombus can dislodge and travel in the blood, particularly to the pulmonary arteries. This is known as Pulmonary Embolism.

D-dimer: A fibrin degradation product released into the circulation when a blood clot breaks down, either as a result of normal body processes or prescribed fibrinolytic medication. (1)

Renal impairment: Reduced renal function that may be acute or chronic. An estimated glomerular filtration rate of less than 90 ml/min/1.73 m² indicates a degree of renal impairment in chronic kidney disease. eGFR 80-45 (mild – moderate) / 44 – 15 (moderate - severe) / <15 (kidney failure). eGFR is a measure of Chronic Kidney Disease and it assumes that the disease process is stable. It is not a useful guide in patients with Acute Kidney Injury.

Wells Score: Clinical prediction rule for estimating the probability of DVT and PE. (2) (3) (4)

DOAC: Acronym endorsed by the International Society on Thrombosis and Haemostasis (ISTH) in 2015 which stands for Direct Oral Anti-Coagulants, a newer generation of anticoagulants that directly bind to specific factors (including factor Xa inhibitors such as Rivaroxaban and Apixaban, Edoxaban; and direct thrombin inhibitor such as dabigatran). (5)

GLOSSARY OF ABBREVIATIONS

ANP	Advanced Nurse Practitioner
CrCl	Creatinine Clearance
CRP	C-Reactive Protein
DOAC	Direct Oral Anti-Coagulants
DVT	Deep Vein Thrombosis
ED	Emergency Department
eGFR	Estimated Glomerular Filtration Rate
INR	International Normalised Ratio
IVDU	Intravenous Drug Users
LMWH	Low Molecular Weight Heparin
NICE	The National Institute for Health and Care Excellence
NIMS	National Incident Management System
NSAIDs	Non-Steroidal Anti-inflammatory Drugs
PE	Pulmonary Embolism
PoCUS	Point of Care Ultrasound
SMPC	Summary of Product Characteristic
SVT	Superficial Vein Thrombosis
UFH	Unfractionated Heparin
U&E	Urea and Electrolytes

TABLE OF CONTENTS

INTRODUCTION

INTRODUCTION	5
--------------------	---

PARAMETERS.....	6
-----------------	---

AIMS	6
------------	---

RISK FACTORS FOR THROMBOSIS	7
-----------------------------------	---

ASSESSMENT

ASSESSMENT PATHWAY.....	7
-------------------------	---

Assessment Flowchart.....	9
---------------------------	---

D-dimer Testing.....	11
----------------------	----

Imaging.....	11
--------------	----

Bleeding Risk Assessment.....	12
-------------------------------	----

MANAGEMENT

TREATMENT WITH ANTICOAGULANTS	13
-------------------------------------	----

Treatment for Suspected DVT	13
-----------------------------------	----

Treatment for Confirmed DVT	14
-----------------------------------	----

Symptomatic Treatment.....	16
----------------------------	----

MANAGEMENT OF BLEEDING IN PATIENTS ON ANTICOAGULANTS	16
--	----

DISPOSITION AND FOLLOW UP.....	17
--------------------------------	----

SPECIAL CONSIDERATIONS

SPECIAL CONSIDERATIONS	18
------------------------------	----

Oncology & Pregnant patients	18
------------------------------------	----

Superficial Vein Thrombosis	19
-----------------------------------	----

APPENDICES	19
------------------	----

1. DVT Management Booklet.....	19
--------------------------------	----

2. Take home Packs.....	19
-------------------------	----

3. Anticoagulation Discharge Advice Sheet	19
---	----

4. Safe prescribing.....	19
--------------------------	----

5. Implementation recommendations.....	19
--	----

6. References.....	19
--------------------	----

Management of Patients Presenting to the Emergency Department with Suspected Lower Limb Deep Vein Thrombosis

INTRODUCTION

Undifferentiated lower limb swelling and pain is a common ED presentation, with DVT being one of the possible diagnoses. DVT and PE are collectively referred to as Venous Thromboembolism (VTE).

VTE is responsible for almost 500,000 deaths a year in Europe, but the absence of specific data for Ireland means the mortality rate here is not known. However, Irish Doctors estimate that there are approximately 4,000 deaths per year from hospital acquired VTE of which 1,900 are preventable. Blood clots affect around 11,000 people in Ireland every year and are the biggest cause of preventable death in hospitals. (6)

A systematic approach to these patients is needed in order to safely manage them, select the appropriate investigations and give the correct treatment. Failing to do so may lead to undesirable complications and medico-legal issues. Current NICE guidelines recommend ultrasound imaging to be performed within 4 hours for those patients where DVT is likely. ([NG158], 2020)

We understand that most Irish Hospitals would not have 24-hour Ultrasound Imaging service available, which makes rigorous assessments and robust safety-netting even more important for safe and efficient practice.

PARAMETERS

Target audience	This guideline is intended for all ED staff managing patients with suspected acute lower limb DVT
Patient population	This document provides assessment and treatment guidance for patients presenting to the ED with suspected acute lower limb DVT.
Exclusion criteria	<p>Any signs or symptoms of PE.</p> <p>Suspected (Proximal) Iliac vein DVT - Phlegmasia Alba Dolens and Phlegmasia Cerulea Dolens are vascular emergencies.</p> <p>Upper Limb DVT.</p> <p>Severe acute venous obstruction with significant swelling & pain.</p> <p>Limb ischemia.</p>

AIMS

The aim of this guideline is to provide a safe and effective pathway for assessing and treating patients presenting to the ED with a suspected acute lower limb DVT.

PROVOKED AND UNPROVOKED DVT

It can be further classified into

- **Provoked:** caused by a known event (see below) – a cause can now be identified in over 80%
- **Unprovoked:** no identifiable cause is evident

This has implications on the investigations, specialist input required and follow-up plan.

RISK FACTORS FOR THROMBOSIS (7)

- Inherited thrombophilia, prior thrombotic event, Antiphospholipid syndrome
- Recent major surgery
- Presence of a central venous catheter
- Trauma
- Immobilization, recent or current hospitalisation
- Malignancy
- Myeloproliferative disorders
- Pregnancy
- Use of oral contraceptives
- Intravenous drug users
- Use of heparin (Heparin-Induced Thrombocytopenia)
- Immobility for more than 48 hours in the preceding month
- Major medical illnesses

ASSESSMENT PATHWAY

A thorough assessment, risk stratification and prompt access to ultrasound scanning is paramount to avoid complications and initiate appropriate treatment.

A patient with symptoms consistent with lower limb venous thrombosis is initially assessed with a clinical prediction rule (Wells score, Revised and Simplified Geneva score, and the Charlotte rule) (8) (9), and categorised as being likely or unlikely of having a DVT. Clinical prediction rules such as the Wells score are recommended in clinical guidelines and are an important part of the patient pathway in routine clinical practice. (10)

Patients then undergo further testing, usually D-dimer or imaging (compression ultrasound, ascending venography or computer tomography venography). Uncertainty exists about the most accurate method to diagnose DVT, and this creates a great deal of variation in clinical practice. (11)

Your hospital may have an established DVT policy. Please make sure you are familiar with the local guidelines as they may differ from this document.

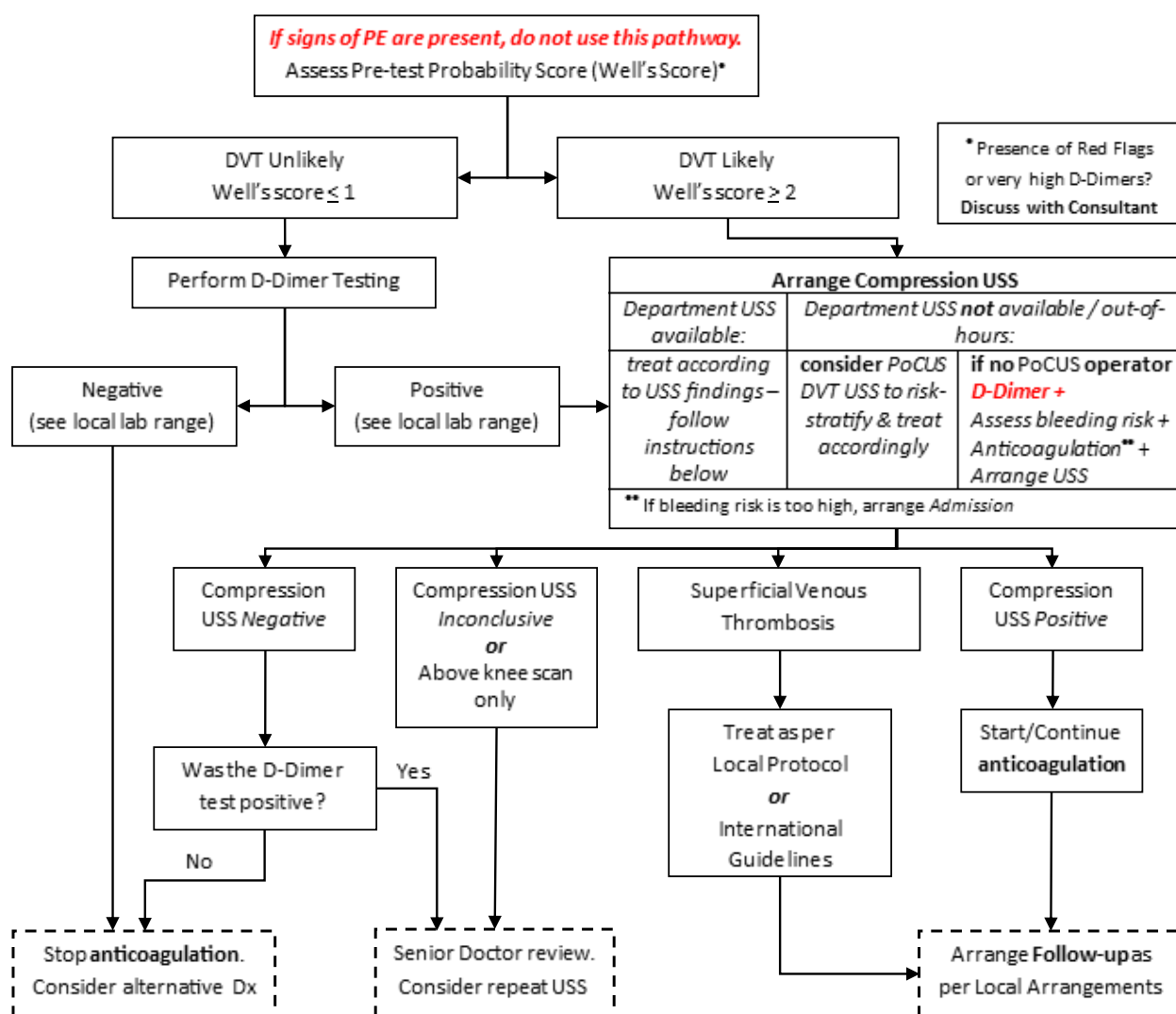
Differential Diagnoses

- Superficial Vein Thrombosis (SVT)
- Post-phlebitic (-thrombotic) syndrome
- Cellulitis
- Gout
- Skin changes associated with chronic lower extremity venous disease i.e., Varicose eczema, Lipodermatosclerosis
- Proximal abscess (especially in the IVDU population – remember to inspect the entire affected limb and compare both where possible)
- Baker's cyst
- Lymphoedema
- Oedema secondary to cardiac / renal / liver failure
- External venous compression (i.e. tumour causing mass effect)
- Musculoskeletal injury (i.e. calf / thigh muscle strain, muscle rupture, tendon rupture, haematoma, Tibial stress syndrome, fracture)

This is by no means an exhaustive list of all alternative diagnoses for undifferentiated lower limb swelling and pain, but it should highlight the range of possible causes and reinforce the need for a thorough assessment. Tools are included to help provide systematic management of patients with DVT. Please refer to the **Management Booklet** in [Appendix 1](#) for more details.

Assessment Flowchart

If symptoms or signs of PE are present, investigate for PE, as it represents a more severe form of VTE. Do not use this pathway if PE is suspected. Please consider admission for patients that are deemed high-risk or not suitable for out-patient investigations and treatment.



Pre-test Probability Score:

DVT Risk Assessment using modified Well's Score	Circle
Paralysis, paresis or recent cast immobilisation of lower extremity	+1
Recently bedridden (more than 3 days) or major surgery within past 4 weeks	+1
Localized tenderness in the deep vein system	+1
Swelling of the entire leg	+1
Calf swelling 3 cm greater than the other leg (measured 10 cm below the tibial tuberosity) <u>Calf circumference:</u> Left: _____ cm Right: _____ cm	+1
Pitting oedema greater in the symptomatic leg	+1
Collateral non-varicose superficial veins	+1
Past history of confirmed DVT	+1
Active cancer or cancer treated within 6 months	+1
Alternative diagnosis more likely than DVT	- 2
Total score:	

Select Pre-test Clinical Probability of a DVT:

<input type="checkbox"/> Unlikely:	≤ 1
<input type="checkbox"/> Likely:	≥ 2

D-dimer Testing

The result of the D-dimer test can be used as part of probability assessment when DVT or PE is suspected. (12) Although D-dimer testing is limited due to low specificity, convenience to perform the test and the high sensitivity and negative predictive value makes it a highly valuable screening test for DVT.

A recent study showed that the sensitivity of D-dimer for DVT was 92.0%, specificity was 44.8%, negative predictive value was 98.8% and positive predictive value was 10.3%. (13)

Please ensure that a blood sample for D-dimer testing is sent before anticoagulation is given – as the DOAC treatment will interfere with next day D-dimer testing.

Imaging

When a DVT is suspected, compression ultrasound scans of the affected leg should be performed within 4 hours of being requested as recommended by current NICE guidelines. If this is not possible, an ultrasound scan should be performed within 24 hours of being requested with interim anticoagulation after assessment of bleeding risk to the patient.

We acknowledge that access to imaging services can vary significantly i.e., out-of-hours, weekends, and we strongly encourage striving for whole week ultrasound service or prompt access within 24 hours wherever possible.

PoCUS for DVT has been shown to be sensitive for diagnosis of DVT (14) (15), however the accuracy depends on the training and experience of the person performing it. It is not currently used to rule out DVT in Ireland, however in certain centres it can guide decisions about anticoagulation while waiting for a departmental scan.

Bleeding Risk Assessment

All patients requiring anticoagulation should be assessed for risk of bleeding. Senior or specialist decision making is recommended if the risk of bleeding is considered moderate to high. Assess the patient for:

- Congenital or acquired bleeding disorders
- Uncontrolled severe arterial hypertension (>200/110 mmHg)
- Active ulcerative gastrointestinal disease
- Recent gastrointestinal ulcerations
- Liver disease (INR \geq 1.5), including cirrhotic patients with Child Pugh scores B & C
- Moderate to severe renal impairment (CrCl <50 ml/min)
- Vascular retinopathy
- Recent intracranial / intracerebral haemorrhage
- Intraspinal or intracerebral vascular abnormalities
- Recent brain, spinal or ophthalmological surgery
- Bronchiectasis or history of pulmonary bleeding
- Patients on other drugs which may affect haemostasis, including:
 - NSAIDs i.e. Ibuprofen & Diclofenac
 - Antiplatelet agents i.e. Aspirin & Clopidogrel
- [HAS-BLED](#) Score of 2 signifies moderate risk and \geq 3 signifies high risk of bleeding.

Anti-coagulate with caution after a discussion with the EM Consultant or Haematologist and consider admission if anticoagulation is required. (16)

TREATMENT WITH ANTICOAGULANTS

Warfarin, LMWH and DOACs are viable treatment options for DVT. The agent choice can be tailored to your patient's specific needs and clinical circumstance.

The HSE has created an Anticoagulation Guide that includes DVT treatment and specific considerations for each anticoagulant class. This document can be found at: <https://www.hse.ie/eng/about/who/cspd/ncps/medicines-management/oral-anticoagulants/anticoagulation-prescribing-tips.pdf>. Local policies may differ, so please be familiar with your Local Guidelines or seek senior help if unsure how to proceed.

More details can be found in Summary of Product Characteristics (SMPC) on www.medicines.ie or <https://www.hpra.ie/> (17)

Treatment for Suspected DVT

The current NICE DVT Guideline supports DOAC as first line agent for suspected and confirmed DVT treatment. (18) In Ireland, DOAC are currently used to treat suspected DVT in most EDs, even though it was not licensed yet for treatment of suspected DVT. At present, their license only extends to confirmed DVT. The data available on safety and efficacy is constantly evolving and we foresee they will be approved for the treatment of both confirmed and suspected DVT.

Clinicians must weigh up the risks and benefits when deciding whether to prescribe therapeutic anticoagulation while waiting for scanning. Factors involved in this decision should include bleeding risk, differential diagnosis (i.e. calf muscle tear), Wells score, duration to scanning, ability to perform point of care ultrasound, pregnancy, etc and if in doubt senior review and/or advice should be sought.

Guidance on DOAC use should be obtained from your Drug and Therapeutics Committee before including them in the treatment plan of suspected DVT. The majority of ED patients

with suspected DVT will require only 1-3 days of treatment while waiting for their ultrasound scan. Please refer to **Take Home Packs** in [appendix 2](#).

Treatment for Confirmed DVT

Choosing between the three main classes of anticoagulant agents (Warfarin, LMWH, DOAC) should be made with care and consideration for each patient based on their characteristics (i.e. age, frailty, renal function, drug interactions, pregnancy/breast feeding, alcohol/drug addiction etc).

We have provided below a list of parameters (Table 1) to be taken into account when choosing the appropriate anticoagulant agent for your patient. DOAC significantly simplifies the treatment of lower limb thrombosis because they are given in a fixed dose and no routine monitoring is needed. (19) The Irish Health Products Regulatory Authority (HPRA) and the European Medicines Agency (EMA) have licensed 4 DOACs for the treatment of DVT.

Apixaban and Rivaroxaban are factor Xa inhibitors preventing cleavage of prothrombin to thrombin. They have been extensively studied for the treatment and prophylaxis of VTE, long term anticoagulation for Atrial Fibrillation, and Acute Coronary Syndrome. (20) (21) (22) The literature proves that Apixaban and Rivaroxaban have an equal efficacy and a lower risk of major bleeding compared with LMWH followed by Vitamin K antagonist/Warfarin. (23) (24)

Unlike Apixaban and Rivaroxaban, Dabigatran and Edoxaban requires parenteral LMWH bridging which limits its use in suspected DVT while awaiting ultrasound scanning. Please refer to [appendix 4](#) for safe prescribing document before starting patients on anticoagulants.

Once a DVT is confirmed, the average duration of anticoagulant treatment is 3 months. This may be extended based on patient factors, thrombus characteristics and Haematology advice.

Table 1: Considerations when choosing therapeutic agent

Contraindications	<ul style="list-style-type: none"> - Known allergy or sensitivity to the active substance or excipients - Caution in Pregnancy & Breast feeding - Active, clinically significant bleeding - Lesion or condition if considered a significant risk of major bleeding - Concomitant treatment with any other anticoagulants - Hepatic disease & Cirrhotic patient with Child Pugh scores B & C - Drug interaction that may have synergistic effect
Drug Interactions	<p>Caution with concomitant use:</p> <ul style="list-style-type: none"> - CYP3A4 inducers (i.e. Rifampicin, Phenytoin, Carbamazepine, Phenobarbitone, St John's Wort) - reduced effect of Rivaroxaban / Apixaban - Antiplatelet agents (i.e. Aspirin, Clopidogrel, Prasugrel, Ticagrelor), Clarithromycin, Erythromycin, SSRIs, SNRIs - increased risk of bleeding. (25) (26)
Renal Dose Adjustment	Agent & eGFR dependant – Please check SMPC or HSE guidance
Bridging Bridging	<p>Required for Warfarin, Edoxaban and Dabigatran</p> <p>Not required for Apixaban and Rivaroxaban</p>
Monitoring	<p>Required for Warfarin – Regular INR testing due to variable effect</p> <p>Not required for DOACs – Coagulation parameters may be abnormal</p>
Outpatient suitability – consider admission if any of the following apply:	<ul style="list-style-type: none"> - Patient already on Warfarin or LMWH with high pre-test probability - Alcohol dependence - Age under 18 years - Patients with active bleeding or patients at significant risk of bleeding (severe liver disease, brain tumour, bleeding disorder) - Significant renal impairment (creatinine >200 µmol/L or CrCl<30 ml/min or eGFR<30 ml/min) - Any patient with increased risk of fall should be considered for admission (i.e. frail, elderly, limited mobility, alcohol dependence) - Compliance issues (i.e. Intravenous drug users, intellectual disability, alcohol dependence)
Spinal puncture delay	<p>Agent dependent – extremely varied Half-Life</p> <p>Please find below a useful link to BMJ Guide when Lumbar Puncture is required in the context of Antiplatelet & Anticoagulant treatment:</p> <p>https://pn.bmj.com/content/practneurol/early/2018/08/28/practneurol-2017-001820.full.pdf</p>

Symptomatic Treatment

1. **Provide adequate analgesia** – pain is often the main presenting symptom and may be high on your patient's list of priorities. Satisfactory resolution of pain can lead to better adherence with the anticoagulant treatment and minimize return visits. Avoid **NSAIDs** with anticoagulants.
2. Consider Elastic Compression Stockings when oedema is a significant component. They can be worn for the entire duration of DVT treatment (3-6 months) and reduce the risk of developing chronic DVT and oedema. Advise your patient to only wear them during the day (when up and about) and to remove them when going to bed.
3. Consider elevating the leg above the level of the heart when resting.
4. Encourage the patient to mobilize and be as active as tolerated to take advantage of the calf muscle pump action in promoting venous return.

Missed Dose

- If your patient has missed a dose of anticoagulant, they must take it immediately after they become aware and resume the anticoagulant treatment as prescribed.
- Warn them against taking a double dose or to contact their GP/ pharmacist if unsure.
- Please follow the SMPC when counselling your patient about missed doses.

MANAGEMENT OF BLEEDING IN PATIENTS ON ANTICOAGULANTS

Bleeding complications are common complication associated with anticoagulant use, and it can present a challenge to manage quickly and safely in the ED. It is important to contact the on-call Haematologist for guidance, especially in the context of trauma. Most hospitals have well established Major Haemorrhage Protocols and Anticoagulation Reversal Policies in place. Follow your local protocol for Anticoagulant bleeding management.

Management should include stabilising the patient and reversing anticoagulation by:

1. ABC management
2. Cross match and transfuse appropriate blood products as required, consider activating the Major Haemorrhage protocol
3. Administer Tranexamic acid
4. Haemorrhage control measures such as applying pressure for external and surgical treatment for internal haemorrhage
5. Vitamin K and Prothombin Complex Concentrate administration if indicated.
6. Specific reversal agent – where available

DISPOSITION AND FOLLOW UP

In most centres in Ireland, confirmed DVT is managed by medical teams. Some have dedicated VTE clinics or ANPs trained to review these patients. Please become familiar with your local services and DVT policy.

In general

- Provoked DVT – discharge to GP care is appropriate once the DVT is confirmed and treatment is started.
- Unprovoked DVT (when an obvious cause is not identified), please send a referral to the Haematology team or arrange VTE follow-up clinic review according to your local arrangement.

SPECIAL CONSIDERATIONS

Oncology & Pregnant patients

Oncology & Pregnant patients	<p>Higher risk of VTE due to the inherently hypercoagulable state.</p> <p>Care should be taken when treating DVT in this patient group as not all anticoagulant agents are licensed for this use. Please check the SMPC before commencing treatment.</p>
Pregnancy	<p>Please be aware that D-dimer testing is not validated for use in pregnant patients as a slightly raised D-dimer value can be normal. Your hospital may have specific guidance on how to manage VTE in pregnancy. Consult with your senior if in doubt.</p> <p>LMWH has long been used safely in pregnancy for prevention and treatment of VTE and it is the agent of choice.</p> <p>Warfarin is contraindicated in pregnancy as it causes congenital malformations and foetal death. (27)</p> <p>DOAC safety and efficacy have not been established in pregnancy and are not currently licensed for this use</p>
Injectable Drug Users	<p>Wells score and D-dimer test are not validated risk-stratifying tools to rule out DVT, thus imaging should be arranged irrespective of their Well's score and D-dimer results if VTE is clinically suspected</p>

Superficial Vein Thrombosis

SVT, also known as Thrombophlebitis is an inflammatory process that causes a blood clot to form and block one or more superficial veins, usually in the legs. SVT is generally a benign, self-limited disorder. However, when the larger axial veins are involved, propagation into the deep vein system (DVT) and even PE can occur.¹⁶

Patient with SVT can be further risk-stratified based on the thrombus characteristic:

- Length of thrombosed segment (≥ 5 cm) and
- Proximity to the deep venous junction (within 3-5 cm). (28) (29)

Patient with high-risk SVT features is considered a DVT equivalent by International Guidelines (NICE, EBM, UpToDate) and treated with anticoagulation.

APPENDICES

1. DVT Management Booklet
2. Take home Packs
3. Anticoagulation Discharge Advice Sheet
4. Safe prescribing
5. Implementation recommendations
6. References