# Assessment & Treatment of patients with suspected / confirmed Deep Vein Thrombosis (DVT) in the Ambulatory DVT Clinic

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## 1. Introduction

**1.1** This guidelines covers assessment, investigation and treatment of deep vein thrombosis in the acute ambulatory service

**1.2** Further advice or guidance can be found by contacting the Acute Ambulatory DVT Service at UHL. Their hotline number is **0116 258 5972**

**1.3** It is also advisable to get specialist advice from the appropriate consultant or service for patients with complex conditions or presentations.

## 2. Scope

**2.1** These guidelines cover patients with suspected and confirmed DVT in the acute ambulatory setting.

**2.2** Other relevant UHL guidelines that might apply to patients with suspected or confirmed venous thromboembolism:

- Venous thromboembolism UHL musculoskeletal guideline C10/2013
- Venous thromboembolism in pregnancy UHL Obstetric guideline C5/2001
- Anticoagulation bridging therapy for elective surgery and procedures B30/2016
- Prothrombin Complex Concentrate (PCC - Octaplex or Beriplex P/N) - Clinician Pack C265/2016
- Massive haemorrhage UHL policy C263/2016
- Pulmonary embolism policies

**2.3** These guidelines are all available on the intranet in the policies and guidelines library

**2.5** These guidelines are designed for nurses and doctors and sonographers working in the acute ambulatory DVT service UHL.

## 3. Recommendations, Standards and Procedural Statements

### Referrals to the DVT Service

The Leicester Acute Ambulatory DVT Service accepts adult patients (aged 18 or over) suspected of having a lower limb DVT who are suitable for out-patient assessment and treatment. It operates five days a week, 8-8 Mon-Fri and 8-4 Bank Holidays. On Christmas Day, Boxing Day and New Year's Day the service is closed. New patients need to arrive at least one hour before the clinic closes. Referrals are by telephone to bed bureau ext 4858. They will take details and also ask for a brief letter to accompany the patient.

Exclusion criteria

- Pregnancy (patients >15 weeks gestation go to pregnancy assessment unit and to GPAU if under 16 weeks gestation)
- Suspected upper limb DVT
- In-patients (unless investigation complete and being discharged)
- Unable to transfer from chair to chair by self.
- Suspected pulmonary embolism
- >180 kg
- Active bleeding
- Known to be at increased risk of bleeding, e.g.
    - o Active peptic ulceration
    - o Liver disease (INR ≥ 1.5)
    - o Renal insufficiency: creatinine >200 µmol/L with unknown eGFR or
        - eGFR< 20 mL/min/1.73m$^2$, or
        - Cockcroft-Gault creatinine clearance (CG CrCl) <30ml/min
    - o Uncontrolled hypertension (>200/110 mmHg)
    - o Recent (<1/12) eye or CNS surgery
    - o Recent (<1/12) haemorrhagic stroke

    Patients with inherited bleeding disorders or thrombocytopenia (platelets <100) or with an Hb <100g/L should be discussed with a doctor in the Haemophilia and Thrombosis Centre or with the on-call haematology registrar.
- On bank holidays we cannot accept patients who require hospital transport.

**Referrals from the following:**

1. **Mental health patients** from Bradgate unit(GGH), Brandon unit(LGH)
2. **Community Hospital patients** from Coalville, Lutterworth, Melton, Loughborough or Market Harborough.
3. Patients from **HM Welford Road and Glen Parva prisons**

Patients can attend the DVT clinic on an outpatient basis if escorted by an appropriate member of staff.

When discharged from the DVT Service, the patient's anticoagulant care will be the responsibility of these hospitals or prisons.

**Out of Hours Referrals**

A GP seeing a patient with suspected DVT out of hours should decide whether they are suitable for out-patient assessment and treatment (see exclusion list above). If they are not suitable, the patient should be referred to the on-call medical team.

If they are suitable a dose of either, Low Molecular Weight Heparin (LMWH), Apixaban or Rivaroxaban should be given (dosing below) pending a DVT clinic appointment the following day.

If GP can't give LMWH, Apixaban or Rivaroxaban they should phone Bed Bureau who can arrange a visit to the GP & Ambulatory Unit (GPAU) to arrange a dose of LMWH to be given.

**A blood sample for D-dimer testing MUST be taken before anticoagulation is given - if Wells<2. Note: D-dimers cannot be used as part of the diagnostic algorithm once patients have received a dose of anticoagulant, and this sample is therefore critical for effective diagnosis and use of resources.**

**Dose of Dalteparin**

| Weight (Kg) | dalteparin (Units) |
|---|---|
| <46 | 7,500 |
| 46-56 | 10,000 |
| 57-68 | 12,500 |
| 69-82 | 15,000 |
| >82 | 18,000 |

**Dose of Rivaroxaban:** 15 mg bd (supply two to three 15 mg tablets in order to ensure a dose is not missed before review at DVT clinic).

**Dose of Apixaban:** 10 mg bd (supply four to six 5 mg tablets in order to ensure a dose is not missed before review at DVT clinic).

Apixaban and Rivaroxaban should not be used in pregnancy.

The patient should be given a referral letter and asked to attend the DVT Service at the appointment time given by Bed Bureau.

The GP should either write or fax (0116 2587299) a referral.

If transport is needed for the first visit, this will need to be arranged via Bed Bureau.

**DIAGNOSTIC ALGORITHM FOR SUSPECTED DVT**

**Pre-test probability** assessment: Patients will initially have a pre-test probability assessment (Keeling, et al 2004, Wells, et al 1997, Wells, et al 2003, Wells, et al 1995) and be classified as unlikely or likely to have a DVT (see below).

They will then follow the algorithm in the figure overleaf.

| | Points |
|---|---|
| Active cancer (patient receiving treatment for cancer within the previous six months or currently receiving palliative treatment) | 1 |
| Paralysis, paresis, or recent plaster immobilisation of the lower extremities | 1 |
| Recently bedridden for 3 days or more, or major surgery within previous twelve weeks | 1 |
| Localised tenderness along the distribution of the deep venous system | 1 |
| Entire leg swollen | 1 |
| Calf swelling at least 3 cm larger than the asymptomatic leg (measured ten cm below tibial tuberosity) | 1 |
| Pitting oedema confined to the symptomatic leg | 1 |
| Collateral superficial veins (non-varicose) | 1 |
| Previously documented venous thromboembolism | 1 |
| Alternative diagnosis at least as likely as deep vein thrombosis | -2 |

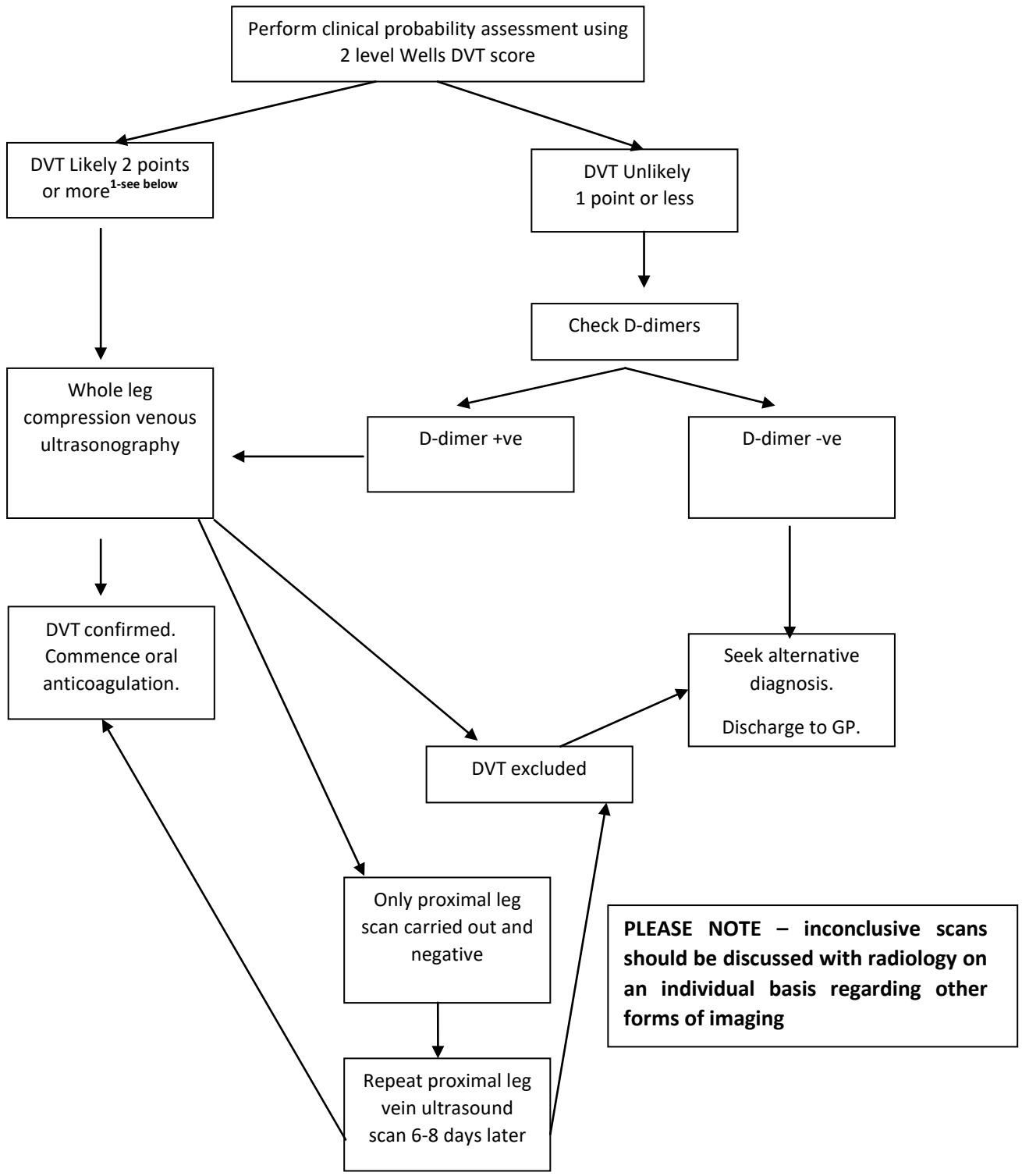
In cases in which it is unclear as to whether there is an alternative diagnosis, the assumption of no alternative diagnosis will ensure the highest level of safety.

**Score Probability**

≤1 Unlikely

≥2 Likely

**Flow chart for clinical assessment of suspected DVT**




Patients with a suspected deep vein thrombosis are given an interim therapeutic dose of anticoagulant therapy (weight-based treatment dose of low molecular weight heparin or treatment dose of direct oral

anticoagulant) *if diagnostic investigations are expected to take longer than 4 hours from the time of first clinical suspicion*.

If proximal leg scan has been carried out and is negative, anticoagulants are withheld until the repeat scan result is known. Patients are warned to contact the DVT clinic or A&E out of hours if they experience any worsening symptoms.

**D-dimers**

D-dimer values rise with age, hampering its specificity in older patients. Adjusting values to improve its diagnostic utility in this population where DVT is prevalent may improve specificity. One meta-analysis of 13 cohorts (12,497 patients) compared the sensitivity and specificity of conventional cut off values for D-dimer (<500 ng/mL) to age-adjusted values (defined as age [years] x 10 ng/mL for patients aged over 50 years). Compared to a conventional cut off value, higher specificities were reported for age-adjusted cut off values (age 51 to 60 years: 63 versus 58 percent; 61 to 70 years: 50 versus 39 percent; 71 to 80 years: 44 versus 24 percent; >80 years: 35 versus 15 percent) Shouten et al. Despite improved specificity, age-adjusted values for D-dimer require validation in clinical practice before they can be applied routinely in clinical practice, for the diagnosis of DVT. We have validated our own CobasH D-dimer test retrospectively (Strong et al 2016) and are now using age related D-dimers and prospectively auditing.

**Patients on anticoagulation**

A patient with suspected recurrence will all get an initial ultrasound scan and a D-dimer. For these referrals, the referring doctor should ring Bed Bureau and arrange a scan slot in the DVT Clinic. A doctor will use both the ultrasound and D-dimer plus clinical assessment to decide if a new clot has occurred.

**Ultrasound**

Patients in whom a DVT cannot be ruled out by clinical examination and D-dimers will be given LMWH, Rivaroxaban or Apixaban if scanning is delayed by 4 hours or more. The scan should take place within 24 hours.

If the initial ultrasound was out of hours in the emergency department these patients should be referred onto the acute ambulatory DVT service for education and anticoagulation, rather than the anticoagulation clinic.

**Patients with bilateral symptoms**

Most patients with bilateral leg swelling will not have a DVT but will have a systemic condition such as heart failure, hypoalbuminaemia, renal failure or severe anaemia. However bilateral DVT was found in 4.4% (1 in 23) of DVT patients in the RIETE registry. If a patient has bilateral symptoms, ask the GP to speak with Bed Bureau to arrange assessment in the GP Ambulatory Unit (GPAU).

**Patients with high clinical suspicion, a grossly swollen leg, but a negative scan**

If a patient has a grossly swollen leg but a negative scan consider a CT venogram to look for isolated iliac or pelvic vein thrombosis or pelvic pathology causing external compression of pelvic veins. This should be arranged and coordinated via the acute medical unit.

**Diagnosis of a recurrence in the ipsilateral leg**.

If the scan is abnormal, but only in sites known to be abnormal on a previous scan (or no previous scan is available) it is often difficult to know whether there is new clot or residual vein thrombosis. Ultrasound findings suggestive of a prior DVT are non-occlusive DVT, disconnected DVT, echoes and signs of flow within the DVT, and DVT at a location that does not fit with the clinical signs. The scan, the clinical situation and the D-dimers should all be considered by the doctor in forming a management plan.

**Second ultrasound** – in some patients (likely pre-test probability with a positive D-dimer) proximal DVT will have been excluded by the first ultrasound but the patient could still have a distal DVT. They will be asked to re-attend for second ultrasound in one week. If the ultrasound becomes positive they will be treated for

proximal DVT. If it remains negative they will be discharged without treatment. Those whose ultrasound remains negative will not be further investigated and will not see a doctor on the unit.

**Patients who have a DVT excluded** - the patient will be referred back to their GP with this information. They will not be further investigated and will not see a doctor on the unit.

**Patients who have a DVT diagnosed** – these patients will be treated as out-patients and have their case medically reviewed at the weekly MDT positives meeting. Patients will be ambulant but we suggest it prudent to avoid vigorous exercise and air travel within six weeks of a new venous thromboembolism.

**Investigations**

All should have:

FBC

U&E/LFT/glucose/Calcium

PT/INR and APTT

Pregnancy test for women of child bearing potential uncertain about their contraception.

**Investigation for cancer in patients with unprovoked DVT**

All patients should have a full history and examination. Patients with any concerning symptoms or signs should have targeted further investigations to investigate for an underlying cancer.

In patients over 40 years with a first unprovoked VTE, but who do not have any concerning clinical symptoms or signs, NICE (clinical guideline 144), based on a randomised trial (Piccioli, et al 2004), said consider the possibility of further investigation with an abdomino-pelvic CT scan (and a mammogram for women), though a non-randomised concurrent-controlled cohort study (Van Doormaal, et al 2011) did not support this. A recent large randomised controlled trial (Carrier, et al 2015) has however shown that routine screening with CT of the abdomen and pelvis did not provide a clinically significant benefit. This trial did offer targeted additional tests as part of a limited screen so following this trial we would suggest a

- CXR (If significant smoking history)

and if not performed in the past year

- Breast examination in women over 50 years of age
- PSA in men over 60 years of age.

**OUT-PATIENT TREATMENT OF DVT**

This can be either with A) Apixaban, B) Rivaroxaban or C) LMWH and warfarin

**A) Treatment with Apixaban**
Apixaban, a direct inhibitor of factor Xa, is given orally for the treatment of DVT and PE and for the secondary prevention of recurrent DVT and PE (Agnelli, et al 2013a, Agnelli, et al 2013b). Apixaban does not require therapeutic monitoring (nor concurrent initial treatment with heparin).

It should not be used in those less than 18 years of age.

**Dose**
10 mg twice daily for 7 days, then 5 mg twice daily.
On the first day the second dose can be taken later that evening even if the first dose is given in the afternoon.
The licenced dose for prevention of recurrent DVT and/or PE following completion of 6 months of treatment for DVT or PE is 2.5 mg twice a day (but see page 18) which considers this possibility after 3 months).

**Renal impairment**
No dose adjustment is necessary in patients with mild or moderate renal impairment. In patients with severe renal impairment (CG CrCl 15-29 mL/min) apixaban is to be used with caution. We will not routinely use apixaban if CG CrCl < 30 mL/minute but in selected patients it can be considered for use if the CG CrCl is 15-30 ml/min.

**Hepatic impairment**
Avoid in liver disease with coagulopathy.

**Pregnancy or breast feeding** – avoid.

**Missed doses** - If a dose is missed the patient should take the missed dose immediately and take the next dose on time (if the next dose is due a double dose can be taken).

**Interaction with other medicinal products**

The use of factor Xa inhibitors is not recommended in patients receiving concomitant systemic treatment with azole-antimycotics (such as ketoconazole, itraconazole, voriconazole and posaconazole) or HIV protease inhibitors (such as ritonavir). These active substances are strong inhibitors of both CYP3A4 and P-gp and therefore may increase rivaroxaban and apixaban plasma concentrations to a clinically relevant degree. Co-administration of factor Xa inhibitors with strong CYP3A4 inducers e.g. rifampicin, phenytoin, carbamazepine, phenobarbital or St. John's Wort, may lead to reduced rivaroxaban and apixaban plasma concentrations. We therefore recommend that strong CYP3A4 inducers should not be co-administered with factor Xa inhibitors when treating acute venous thromboembolism. Macrolide antibiotics, such as clarithromycin and erythromycin, may inhibit metabolism of factor Xa inhibitors and therefore caution should be applied if co-prescribed.

**Prescription**
Initially one week's treatment should be prescribed, followed by a reduced dose which should complete a 3 month course in total. The GP should prescribe if an ongoing treatment is required after this point.

**B) Treatment with rivaroxaban**
Rivaroxaban, a direct inhibitor of factor Xa, is given orally for the treatment of DVT and PE and for the secondary prevention of recurrent DVT and PE (Bauersachs, et al 2010). Rivaroxaban does not require therapeutic monitoring (nor concurrent initial treatment with heparin).

It should not be used in those less than 18 years of age.

**Dose**
15 mg twice daily with food for 21 days, then 20 mg once daily with food.

**Renal impairment**
If CG CrCl is 15–49 mL/minute initially 15 mg twice daily for 21 days, thereafter, the recommended dose is the standard 20 mg once daily but a reduction of the dose from 20 mg once daily to 15 mg once daily should be considered if the patient's assessed risk for bleeding outweighs the risk for recurrent DVT and PE. The SPC says use with caution if CG CrCl 15-29 mL/minute and avoid if CG CrCl less than 15 mL/minute.

We will not routinely use Rivaroxaban if CG CrCl < 30 L/minute. Hepatic impairment – avoid in liver disease with coagulopathy.

**Pregnancy or breast feeding** – avoid.

**Missed doses** - If a dose is missed during the 15 mg twice daily treatment phase (day 1 - 21), the patient should take the missed dose immediately and take the next dose on time (if the next dose is due two 15 mg tablets can be taken together). The patient should then continue with 15 mg twice daily.

If a dose is missed during the once daily treatment phase (day 22 and onwards), the patient should take the missed dose immediately, and continue on the following day with the once daily intake as recommended. The dose should not be doubled within the same day to make up for a missed dose.

**Interaction with other medicinal products**
The use of factor Xa inhibitors is not recommended in patients receiving concomitant systemic treatment with azole-antimycotics (such as ketoconazole, Itraconazole, Voriconazole and Posaconazole) or HIV protease inhibitors (such as ritonavir). These active substances are strong inhibitors of both CYP3A4 and P-gp and therefore may increase Rivaroxaban and Apixaban plasma concentrations to a clinically relevant degree. Co-administration of factor Xa inhibitors with strong CYP3A4 inducers e.g. rifampicin, phenytoin, carbamazepine, phenobarbital or St. John's Wort, may lead to reduced Rivaroxaban and Apixaban plasma concentrations. We therefore recommend that strong CYP3A4 inducers should not be co-administered with factor Xa inhibitors when treating acute venous thromboembolism. Macrolide antibiotics, such as clarithromycin and erythromycin, may inhibit metabolism of factor Xa inhibitors and therefore caution should be applied if co-prescribed. Co-administration of Rivaroxaban and Dronedarone should be avoided given the limited clinical data.

**Prescription**
Initially three weeks should be prescribed, followed by a reduced dose which should complete a 3 month course in total. The GP should prescribe if an ongoing treatment is required after this point.

**CHECK LIST FOR ALL PATIENTS ON DIRECT ORAL ANTICOAGULANTS:**

- **DAWN DOAC module and prescriber checklist completed**
- **Patient consented with decision aid and information**
- **Patients given DOAC card and patient information booklet**
- **Patient given prescription and appointment for DOAC dose reduction**
- **Patient given phone number to contact if any issues/side effects**
- **AVOID at extremes of body weight:<50kg or BMI<20kg/m2.**

**C) Treatment with low molecular weight heparin and warfarin**

USE FIXED DOSE SYRINGES and give Dalteparin subcutaneously once a day*

| WEIGHT (kg) | DOSE (U) |
|---|---|
| <40 | 5,000 |
| 40-45 | 7,500 |
| 46-56 | 10,000 |
| 57-68 | 12,500 |
| 69-82 | 15,000 |
| 83-99 | 18,000 |
| 100-124* | 10,500 twice daily |
| 124-140* | 12,500 twice daily |
| 141-169* | 15,000 twice daily |
| 170-180* | 18,000 twice daily |

*for patients >100 kg give bd (but give 18,000 units first dose if giving a single injection whilst awaiting a scan the next day).

There is no need to routinely monitor anti-Xa levels in patients who weigh less than 130 kg. This weight and above should have an anti Xa after the 3rd dose, and the LMWH dose should be adjusted accordingly.

Dalteparin should be continued until the INR has been ≥ 2 for at least two consecutive days or for five days – whichever is the longer.

Monitoring the platelet count for heparin-induced thrombocytopenia and potassium level for hyperaldosteronism is still done, as DVT patients are a heterogeneous group and can include orthopaedic and cardiac surgery patients.

INCREASED BLEEDING RISK DALTEPARIN DOSING CHART eGFR>29ml/min, no active bleeding

| **WEIGHT (kg)** | **FIRST STAT DOSE (U)** | **ON-GOING TREATMENT (starting 12-24 Hrs later)** |
|---|---|---|
| <40 | 5,000 stat | 2,500 twice daily |
| 40-45 | 7,500 stat | 5,000am,<br>2,500 pm |
| 46-56 | 10,000 stat | 5,000 twice daily |
| 57-68 | 12,500 stat | 7,500am,<br>5,000 pm |
| 69-82 | 15,000 stat | 7,500 twice daily |
| 83-99 | 18,000 stat | 10,000am,<br>7,500pm |
| 100-124 | 18,000 stat | 10,000 twice daily |
| 125-130 | 18,000 stat | 12,500 twice daily |
| >130 | 18,000 stat | seek specialist advice from Haematology |

If the weight is 130kg or above further dose escalation should be considered i.e. 100U/kg twice daily after an initial stat dose of 18,000u sc on an individualised basis. Timed anti Xa levels should be taken after the 3rd dose.

RENAL IMPAIRMENT DALTEPARIN DOSING CHART eGFR between 20-29ml/min inclusive.

| **WEIGHT (kg)** | **FIRST STAT DOSE (U)** | **ON-GOING TREATMENT (starting 24 Hrs later)** |
|---|---|---|
| <46 | 5,000 stat | 2,500 twice daily |
| 46-62 | 7,500 stat | 5,000am<br>2500pm |
| 63-80 | 7,500 stat | 5,000am twice daily |
| 81-98 | 10,000 stat | 7,500am<br>5,000pm |
| 99-116 | 10,000 stat | 7,500 twice daily |
| 117-134 | 12,500 stat | 10,000am<br>7,500pm |
| >134 | 15,000 stat | 10,000 twice daily |
| >150 | Seek specialist advice from Haematology | Seek specialist advice from Haematology |

In renal impairment the risk of bleeding may be increased – the above represents guidance on dose reduction.

Timed anti-Xa levels should be taken 3-4 hours after the 3rd dose.

PRESCRIBING LMWH IF eGFR less than 20ml/min

1. Calculate CG CrCl (UHL Insite Creatinine clearance calculator)
2. IF CG CrCl between 20 - 29ml/min inclusive follow prescribing table above
3. IF CG CrCl is less than 20ml/min the patient is not suitable for ambulatory care and should be discussed with either the on-call Renal team or Medical team in GPAU for consideration of unfractionated heparin or closely renal supervised LMWH.

**Warfarin**

We follow the Tait and Sefcick slow warfarin initiation protocol (Tait RO, Sefcick A 1998).

If the initial INR ≤1.3 the patient will receive 5mg of warfarin once daily on days 1 - 4. The INR is checked on days 5, 8 and 12 and the warfarin dose is adjusted according to the schedule.

| INR day5 | Warfarin dose Day5 | INR day 8 | Warfarin dose from day8 |
|---|---|---|---|
| <1.7 | 5mg | ≤1.7 | 6mg |
| | | 1.8-2.4 | 5mg |
| | | 2.5-3.0 | 4mg |
| | | >3.0 | 3mg for 4days |
| 1.8-2.2 | 4mg | ≤1.7 | 5mg |
| | | 1.8-2.4 | 4mg |
| | | 2.5-3.0 | 3.5mg |
| | | 3.1-3.5 | 3mg for 4 days |
| | | >3.5 | 2.5mg for 4 days |
| 2.3-2.7 | 3mg | ≤1.7 | 4mg |
| | | 1.8-2.4 | 3.5mg |
| | | 2.5-3.0 | 3mg |
| | | 3.1-3.5 | 2.5mg for 4 days |
| | | >3.5 | 2mg for 4 days |
| 2.8-3.2 | 2mg | ≤1.7 | 3mg |
| | | 1.8-2.4 | 2.5mg |
| | | 2.5-3.0 | 2mg |
| | | 3.1-3.5 | 1.5mg for 4 days |
| | | >3.5 | 1mg for 4 days |
| 3.3-3.7 | 1mg | ≤1.7 | 2mg |
| | | 1.8-2.4 | 1.5mg |
| | | 2.5-3.0 | 1mg |
| | | 3.1-3.5 | 0.5mg for 4 days |
| | | >3.5 | Omit for 4 days |
| >3.7 | 0mg | <2.0 | 1.5mg for 4 days |
| | | 2.0-2.9 | 1mg for 4 days |
| | | 3.0-3.5 | 0.5mg for 4 days |

After day 12, until the INR is > 2.0 for two consecutive days, a senior thrombosis nurse or doctor will continue to amend the warfarin dose based on the INR result.

**Selecting an anticoagulant**

Warfarin will be used if CG CrCl is < 30 ml/min, or if there is liver dysfunction.

Choice of anticoagulant should be discussed with the patient, some may prefer to opt for a drug with a longer history of use, or have warfarin again if they've been on it before.

The efficacy of Rivaroxaban and Apixaban are similar to that of warfarin. If there is no medical reason to favour warfarin, and if there is no patient preference for warfarin we will use a Xa inhibitor. Compared to warfarin, both are significantly less likely to cause major bleeding.

The ACCP (CHEST 2016;149(2):315-352) now recommend direct oral anticoagulants over vitamin K antagonist therapy in patients with DVT of the leg or PE and no cancer as long-term (first 3 months) anticoagulant therapy (grade 2B).

**Differentiating anticoagulant therapy**

| **Objective** | **Anticoagulant** |
|---|---|
| Minimize bleeding | Apixaban |
| Once daily dosing | Rivaroxaban |
| All oral therapy | Rivaroxaban/Apixaban |
| CG CrCl less than 30ml/min | Warfarin |
| Cancer | LMWH – see below |

**Continuing LMWH in patients with cancer**

Patients with an underlying malignancy will be considered for continuing LMWH rather than oral anticoagulation. However, in those who do not want to inject, an oral Xa inhibitor (that is Apixaban or Rivaroxaban) is a reasonable alternative. If continuing LMWH the patient will need to be able to administer their own LMWH or have a carer do it. Compared to warfarin, LMWH carries a similar risk of bleeding but halves recurrences in patients with cancer (Lee*, et al* 2003). **Full dose LMWH is given for the first month** (see page 12). We give a prescription for the first 4 weeks supply of Dalteparin, and after that time the GP should prescribe it.

After the first month the dose is reduced to the pre-filled syringe in the band below (unless patient <46 kg or >98 kg when dose is unaltered) (see table below). Please give clear instructions to the GP.

Dose after the first month

| Weight | Dose |
|---|---|
| <57kg | 7,500units |
| 57-68kg | 10,000units |
| 69-82kg | 12,500units |
| 83-98kg | 15,000units |
| >98kg | 18,000units |

At three months, review the patient to decide on subsequent management. Treatment of cancer-associated VTE is for a minimum of six months, and if cancer is not cured some form of continuing anticoagulation is usually recommended. If this is with LMWH, there is no data as to whether the dose can be reduced to a prophylactic dose.

**Anticoagulation in high BMI and body weight patients with acute VTE**

The use of DOAC to treat patients with a BMI >40 kg/$m^2$ or >120 kg was previously not recommended due to the concern of decreased drug exposure in this group of patients given the lack of evidence. However, there is increasing data now to support the utilization of DOAC in patients with high BMI or >120 kg. In 2021, the ISTH SCC (International Society on Thrombosis and Haemostasis Subcommittee on Control of Anticoagulation) provided updated guidance recommendations. They suggest that standard doses of Rivaroxaban or Apixaban are appropriate anticoagulant options for patients with acute VTE *regardless of high BMI and weight*. Dabigatran or Edoxaban should not be used due to lack of evidence. Treatment or prevention of VTE with DOAC in the acute setting after bariatric surgery is not supported. This ISTH guidance has been adopted in our UHL DVT Ambulatory Service.

**Antiplatelet medication**

For patients with stable coronary artery disease patients (> 12 months from ACS, NSTEMI, STEMI, CABG or stent), antiplatelet therapy can be stopped when anticoagulated, unless there is a high risk of future coronary events (prior stenting of the left main, proximal LAD, proximal bifurcation, recurrent MIs), in which case cardiology advice should be sought. Patients with more recent coronary artery disease should have their antiplatelet and anticoagulant regimen discussed with the relevant interventional cardiologist.

**Thrombolytic therapy**

Consider referral to vascular surgeons for consideration of catheter-directed thrombolytic therapy for patients with symptomatic ilio-femoral DVT who have all of:

- Symptoms of less than 14-day duration.
- Good functional status.
- A life expectancy of 1 year or more.
- A low risk of bleeding.

**Duration of treatment and follow up**

Patients with proximal DVT should be treated for at least 3 months. An analysis of data from seven trials (Boutitie*, et al* 2011) concluded that three months of treatment achieves a similar risk of recurrent venous thromboembolism after stopping anticoagulation as a longer course of treatment. This was also found in a British study (Campbell*, et al* 2007).

**Isolated calf DVT:** As the diagnostic strategy used will identify isolated calf DVTs, we will usually be treating them as the patient has been referred with symptoms. If a first isolated calf vein DVT is identified the option is serial scanning (ACCP suggest scanning at one *and* two weeks) or treatment for three months (Kearon*, et al* 2012).

For a **first proximal DVT associated with transient risk factors** treatment will stop at three months.

Transient risk factors (TRF):

- surgery (the various studies used within 6 weeks/8 weeks/3 months)
- significant trauma e.g. fracture, plaster cast

- COC/HRT
- pregnancy/puerperium

A weaker TRF is temporary immobility in previous 4 weeks e.g. confined to bed ≥ 3 days or a flight > 6 hours. In this case, a three month review is appropriate. In this group, treatment should be continued until thrombosis clinic follow up review.

Long–term treatment will be *considered* for

- recurrent thrombosis
- patients with an on-going risk factor such as cancer
- a first unprovoked proximal DVT (or PE).

**Follow-up**

All patients with a thrombosis or superficial thrombophlebitis encroaching on the deep venous system are reviewed at the weekly multidisciplinary team meeting, where follow up pathway and urgency, and further investigations are decided.

All patients are reviewed either by a DVT clinical nurse specialist or doctor. Those who may require long-term anticoagulation will be reviewed by a doctor at three months, to decide whether to stop or whether to continue indefinitely.

If it is decided to continue anticoagulation therapy beyond 3-6 months of treatment, Apixaban 2.5 mg bd or Rivaroxaban 10 mg od can be considered as treatment options for secondary prophylaxis.

Patients who have had a DVT will be offered a routine follow-up either in a Nurse-Led Clinic, or for those with unprovoked DVTs in a Consultant-Led Clinic.

| **3 months** | **3 months then consider long-term** |
|---|---|
| 1st proximal DVT with TRF* | Recurrent thrombosis |
| 1st isolated calf vein DVT | 1st unprovoked proximal DVT |

* If temporary immobility e.g. confined to bed ≥ 3 days or a flight > 6 hours is the only transient risk factor, the patient should have a review at three months.

Patients with unprovoked proximal DVT or PE are at a higher risk of recurrence than those with a transient precipitating factor (Lorio*, et al* 2010), and it is therefore recommended that they should be considered for long-term anticoagulation (Kearon*, et al* 2012). We should take into account information that may help predict risk of recurrence in the individual patient.

Recurrences after unprovoked VTE are more likely in:

- males
- those with raised D-dimers (>500 µg/l FEU) after completing anticoagulation

Prediction scores such as HER DOO2 (Rodger, et al 2008) and DASH (Tosetto, et al 2012) have been proposed.

It is important to take into account that patients with an initial symptomatic PE are 3 to 4 times more likely to suffer recurrence as PE rather than DVT as compared with patients who present with an initial DVT (Baglin, et al 2010, Murin, et al 2002).

Each patient should be counselled as to the risk of recurrence if anticoagulation is stopped and the risk of bleeding if it is continued. Bleeding risk increases in those > 75 years old and in those patients on warfarin who have a low time in therapeutic range (TTR).

The most important initial considerations are male vs female and PE vs DVT. Patients may express a clear preference for stopping or continuing, but, for those in whom the best course of action is not clear a D-dimer one month after stopping treatment may be the best way to decide.

The table below summaries the approximate risk of recurrence **after a first unprovoked VTE**

| D-dimer Result | **+ve** | **+ve** | **not done** | **not done** | **-ve** | **-ve** |
|---|---|---|---|---|---|---|
| | **1 year** | **5 year** | **1 year** | **5 year** | **1 year** | **5 year** |
| **Male** | 15% | 50-60% | 10% | 35-40% | 5% | 20-25% |
| **Female** | 7.5% | 30-35% | 5% | 20-25% | 2.5% | 10-15% |

**TESTING FOR THROMBOPHILIA**

Do not offer routine thrombophilia testing to patients who are continuing anticoagulation treatment.

Test for antiphospholipid antibodies in patients who have had unprovoked or recurrent DVT or PE if it is planned to stop anticoagulation treatment.

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.

Do not routinely offer thrombophilia testing to patients who have had provoked DVT or PE. .

Do not routinely offer thrombophilia testing to first-degree relatives of patients with thromboembolic disease and thrombophilia.

Consider testing asymptomatic female relatives planning a pregnancy who have a first degree relative with unprovoked (or hormone-related) VTE

Testing may be helpful to assist counselling regarding COC and HRT in asymptomatic female relatives in selected thrombosis-prone families with high risk thrombophilia

Testing is usually performed one month after discontinuing anticoagulation and the doctor should clearly indicate which of the following are require:

- Testing for heritable thrombophilia
- Testing for antiphospholipid antibodies
- D-dimers

**Compression stockings**

Initial studies suggested that stockings with 40 mm Hg (Brandjes*, et al* 1997) or 30-40 mm Hg (Prandoni*, et al* 2004) compression at the ankle can halve the incidence of post-thrombotic syndrome. However, the randomised SOX Trial (Kahn*, et al* 2013) which was much larger and which blinded doctors and patients by comparing stockings with 30-40 mmHg pressure with placebo stockings gave negative results. Compliance rates were however poor in this study.

**Stockings should no longer be prescribed routinely** but only used selectively in patients to treat symptoms.

Absolute contra-indications are advanced peripheral arterial occlusive disease, decompensated heart failure, septic phlebitis, and phlegmasia caerulea dolens (DVT leading to severe swelling of the whole leg). Relative contra-indications are suppurative dermatoses, intolerance of compression stocking fabric, advanced neuropathy, and chronic arthritis.

**Superficial Thrombophlebitis / Superficial Vein Thrombosis (SVT)**

SVT has been considered to be a benign and self-limiting condition. However, it is now appreciated that a significant proportion of those presenting with SVT are at significant risk of development DVT or PE (Scott et al 2015). Endovascular laser treatment of varicose veins will cause a phlebitic reaction – if the patient is within 4-6 weeks of this treatment, the policy is to refer them back to the vascular team.

The most commonly affected superficial veins are the long (great) and short saphenous veins of the leg. SVT is adjacent to (within 3 cm of) the sapheno-femoral junction (SFJ) has such a high risk of progression of DVT(14-70%) that such patients are no longer included in interventional trials in SVT, but rather advised therapeutic anticoagulation as for DVT (Tait et al 2012)

- Patients with superficial thrombophlebitis within 3cm of the SFJ should be treated with therapeutic anticoagulation (as for DVT) for three months
- For patients with SVT more than 5cm in length but more than 3cm from the SFJ, we recommend Rivaroxaban 15mg od (Webster, Strong et al 2016 poster157 BSH 2016 abstract/poster 157) or intermediate dose of LMWH for six weeks (Cosmi et al 2012, Scott et al 2015). This has been shown to provide better symptomatic relief. We use Dalteparin at approximately 125units/kg od (rounding to the nearest syringe). Prophylactic dose of Fondaparinux (2.5mg od) is an alternative (Decousus et al 2010).
- Patients with SVT less than 5cm in length and more than 3cm from the SFJ can be treated with non-steroidal anti-inflammatory drugs (NSAIDs).

**Incidentally discovered asymptomatic DVTs and PEs**

In patients who are unexpectedly found to have asymptomatic DVT or PE, the ACCP recommend the same initial and long-term anticoagulation as for comparable patients with symptomatic VTE (Kearon*, et al* 2012).

**Women on the combined oral contraceptive pill (COCP)**

The COCP should be stopped at least one month before anticoagulation is discontinued and an alternative form of contraception should be organised. The patient should be warned of the risks of pregnancy on warfarin, Apixaban or Rivaroxaban.

**DVT patients who when reviewed are suspected to have concomitant symptomatic PE**

These patients do not necessarily need to be investigated for PE as the treatment is the same. However, consider whether they should be referred to the medics for consideration of admission. They should if they have any of:

- Age > 80 years
- Pulse ≥ 110 bpm
- Systolic BP < 100 mm Hg
- Sat < 90%
- Cancer
- Chronic cardiopulmonary disease

(i.e. a positive sPESI), as this indicates a higher early mortality.

**Floating clot**

Patients with free floating thrombus (FFT) are at no higher risk for pulmonary embolus and there is data to support the safety of ambulatory therapy in clinically stable patients. Most FFT followed non-invasively by duplex scanning do not embolise but instead become attached to the vein wall or resolve. These patients are informed of the signs and symptoms of pulmonary embolus and the need for urgent review should these occur.(Parcouret et al 1997, Ramasamy et al,2005, Baldridge et al 1990)

**Calf muscle vein thrombosis (soleal and gastrocnemius)**

The natural history of isolated symptomatic thrombus involving the deep veins draining the gastrocnemius and soleus muscles in the calf is unclear, but thrombosis confined to the muscular veins appear to have a lower risk of extension than true isolated distal DVT(Sales et al 2010). Our local policy is to treat these DVTs for 6 weeks with intermediate dose LMWH (ie125u/kg sc od) or Rivaroxaban (15mg od).

**Education and training**

All DVT staff is trained in the acute ambulatory clinic and attends educational meetings e.g. CLOT conference, DAWN user group, British Society of Haematology, International Society of thrombosis and Haemostasis

**Monitoring and audit**

The Trent Regional VTE group have proposed the following**:**

| Key performance indicator/monitor | Method of assessment | Frequency | Lead |
|---|---|---|---|
| **% patients seen on day of referral** | | | |
| **Treatment given or diagnosis excluded within 4 hrs of suspicion of VTE** | | | |
| **+ve rates:**<br>**DVT**<br>**SVT**<br>**Overall** | | | |
| **% rescan** | | | |
| **% extension at rescan** | | | |
| **% patients anticoagulated with a DOAC** | | | |
| **% patients with ileo-femoral DVT receiving catheter directed thrombolysis** | | | |
| **% patients receiving GCS 2 within 3 weeks diagnosis** | | | |
| **% patients discussed at MDT** | | | |
| **% of spontaneous events** | | | |
| **% spontaneous events undergoing review and testing for malignancy** | | | |
| **Average duration and range of time to clinic review:**<br>**Spontaneous**<br>**Provoked** | | | |
| **% patients with spontaneous DVT reviewed within 3 months** | | | |
| **% patients with spontaneous SVT reviewed within 6 weeks** | | | |

**Legal liability guideline statement**

Guidelines and procedures issued and approved by the Trust are considered to represent best practice. Staff may only exceptionally depart from any relevant Trust guidelines or procedures and always only providing that such departure is confined to the specific needs of the individual circumstances. In healthcare delivery such departure shall only be undertaken where in the judgement of the responsible healthcare professional, it is fully appropriate and justifiable – such decision to be fully documented in the patient's notes.

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