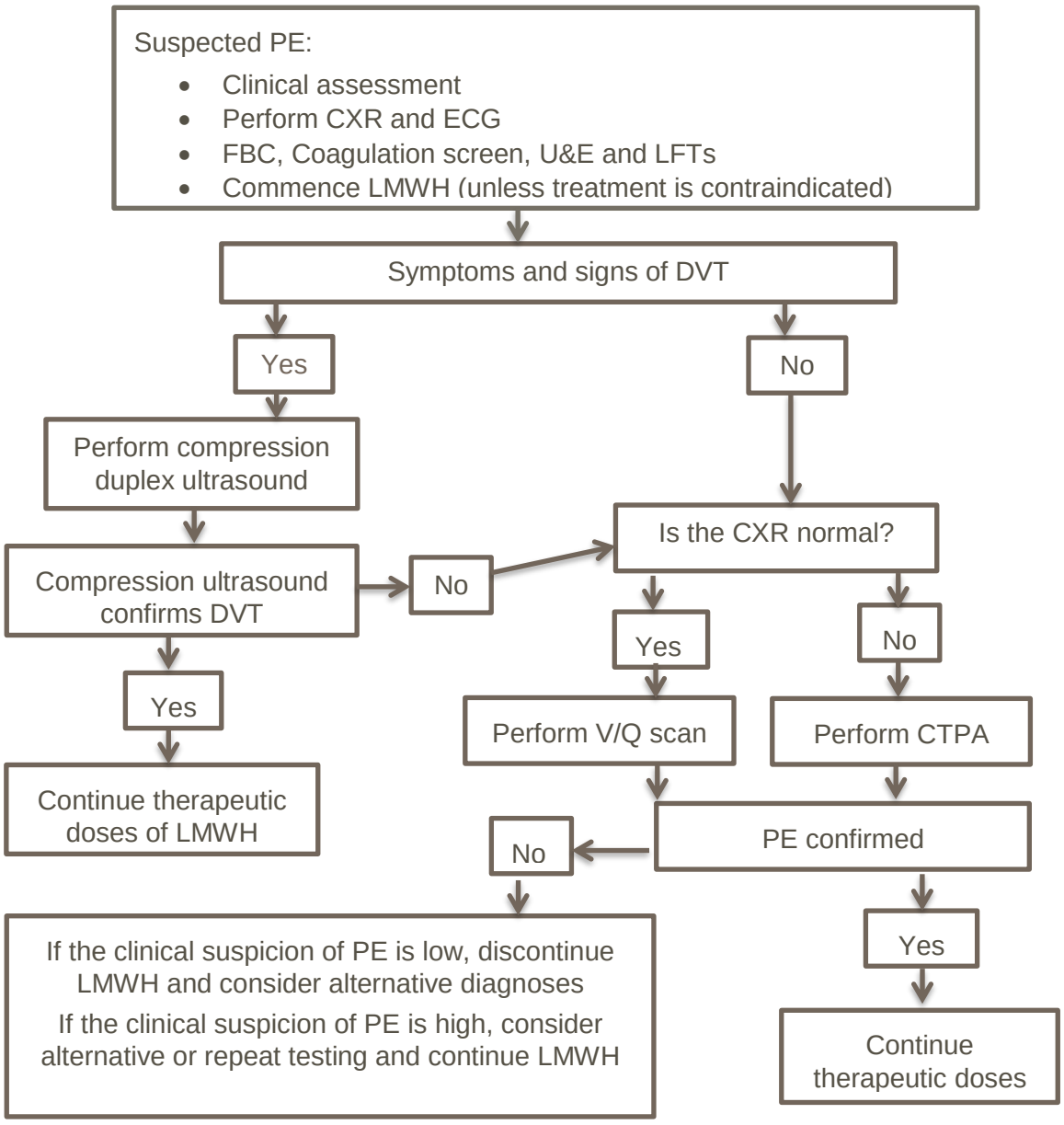
VENOUS THROMBOEMBOLISM IN PREGNANCY AND PUERPERIUM – DIAGNOSIS AND MANAGEMENT

CLINICAL GUIDELINE MCSA.MBC.2.1

Algorithm for the investigation and initial management of suspected Pulmonary Embolism (PE) in pregnancy and the puerperium **(RCOG Green-top Guideline 37b)**



The above algorithm should be followed for all cases of suspected venous thromboembolism (VTE) in pregnancy (also refer to Thromboprophylaxis in Pregnancy guideline).

Special investigations

Performing a thrombophilia screen prior to therapy is not recommended as the physiological changes of pregnancy as well as the pathophysiology of the acute thrombus can influence its results.

Anticoagulant therapy may need to be adjusted for renal and hepatic dysfunction and can influence the platelet count. Blood should therefore be taken to confirm that these are normal before commencing treatment.

Treatment – general principles

In clinically suspected deep venous thrombosis (DVT) or pulmonary embolism (PE), treatment with low-molecular-weight heparin (LMWH) should be commenced immediately until the diagnosis is excluded by objective testing, unless treatment is strongly contraindicated.

LMWH is preferred over unfractionated heparin due to its reduced risk of bleeding and this is of particular relevance in obstetric practice where obstetric haemorrhage remains the most common cause of severe obstetric morbidity. In women at risk of bleeding, LMWH should be postponed until objective testing has confirmed the diagnosis of VTE and careful consideration has been given to the balance of risks of haemorrhage and clotting.

LMWH should be given in doses titrated against the woman's booking or early pregnancy weight.

Initial doses of different LMWHs

Table 1a. Initial dose of enoxaparin (Clexane®)

Booking or early pregnancy weight	Initial dose of Enoxaparin
< 50 kg	40 mg twice daily or 60 mg once daily
50–69 kg	60 mg twice daily or 90 mg once daily
70–89 kg	80 mg twice daily or 120 mg once daily
90–109 kg	100 mg twice daily or 150 mg once daily
110–125 kg	120 mg twice daily or 180 mg once daily
> 125 kg	Discuss with haematologist

Table 1b. Initial dose of dalteparin (Fragmin®):

Booking or early pregnancy weight	Initial dose of Dalteparin
< 50 kg	5000iu twice daily or 10 000iu once daily
50–69 kg	6000iu twice daily or 12 000iu once daily
70–89 kg	8000iu twice daily or 16 000iu once daily
90–109 kg	10000iu twice daily or 20 000iu once daily
110–125 kg	12000iu twice daily or 24 000iu daily
> 125 kg	Discuss with haematologist

Table 1c. Initial dose of tinzaparin (Nadroparine®):

175 units/kg once daily (based on booking or early pregnancy weight)

- Lower doses of LMWH should be employed if the creatinine clearance is less than 30 ml/minute (enoxaparin and dalteparin) or less than 20 ml/minute with tinzaparin.
- Routine measurement of peak anti-Xa activity for patients on LMWH for treatment of acute VTE in pregnancy or postpartum is not recommended except in women at extremes of body weight (less than 50 kg and 90 kg or more) or with other complicating factors (for example, with renal impairment or recurrent VTE).
- Routine platelet count monitoring is not indicated during LMWH treatment, but postoperative obstetric patients treated with unfractionated heparin should have platelet count monitoring every 2–3 days from days 4 to 14 or until heparin is stopped.

Management of massive life-threatening PE

- Collapsed, shocked women who are pregnant or in the puerperium should be assessed by a team of experienced clinicians. Management should involve a multidisciplinary team including senior physicians, obstetricians and radiologists.
- Management should be individualised regarding intravenous unfractionated heparin, thrombolytic therapy or thoracotomy and surgical embolectomy
- Intravenous unfractionated heparin (UFH) is the preferred, initial treatment in massive PE with cardiovascular compromise because of its rapid effect and since it can be adjusted more readily if thrombolytic therapy is administered. Initial bolus dosage of 80units/kg followed by continuous infusion of 18 units/kg/hr. The infusion is titrated every 6 hours to achieve a therapeutic aPTT of 60 – 90s. Once achieved it should be rechecked once or twice daily
- If massive PE confirmed, or in extreme circumstances prior to confirmation, immediate thrombolysis should be considered

Additional therapies

- In the initial management of DVT, the leg should be elevated and a graduated compression stocking applied to reduce oedema. Mobilisation with graduated elastic compression stockings should be encouraged
- Consideration should be given to the use of a temporary inferior vena cava filter in the peripartum period for patients with iliac vein VTE to reduce the risk of PE or in patients with proven DVT and who have recurrent PE despite adequate anticoagulation.

Maintenance treatment of VTE

- Treatment with therapeutic doses of subcutaneous LMWH should be employed during the remainder of the pregnancy and the first 6 weeks postnatally AND until at least 3 months of treatment has been given in total.
- Women should be taught to self-inject LMWH and arrangements made to allow safe disposal of needles and syringes.
- Outpatient follow-up should include clinical assessment and advice with monitoring of platelets and peak anti-Xa levels if appropriate (see page 3 above).
- Pregnant women who develop heparin-induced thrombocytopenia or have heparin allergy and require continuing anticoagulant therapy should be managed with an alternative anticoagulant under specialist advice.
- Because of their adverse effects on the fetus, vitamin K antagonists, such as warfarin, should not be used for antenatal VTE treatment.
- Consideration should be given to the use of newer anticoagulants e.g., fondaparinux (Arixtra®), argatroban (or r-hirudin) in pregnant women who are unable to tolerate heparin (LMWH or unfractionated heparin) or danaparoid and who require continuing anticoagulant therapy.

Anticoagulant therapy during labour and delivery

- When VTE occurs at term, consideration should be given to the use of intravenous unfractionated heparin which is more easily manipulated.
- The woman on LMWH for maintenance therapy should be advised that once she is in established labour or thinks that she is in labour, she should not inject any further heparin.
- Where delivery is planned, either by elective caesarean section or induction of labour, LMWH maintenance therapy should be discontinued 24 hours prior to planned delivery.
- Regional anaesthetic or analgesic techniques should not be undertaken until at least 24 hours after the last dose of therapeutic LMWH.

- LMWH should not be given for 4 hours after the use of spinal anaesthesia or after the epidural catheter has been removed, and the epidural catheter should be removed based on the following risk categories for epidural bleeding.
    - “Normal risk” - for removal of the catheter more than 24 hours after a therapeutic dose of LMWH.
    - “Increased risk” - for removal between 12 and 24 hours.
    - “High risk” - for removal between 6 and 12 hours.
- In patients receiving therapeutic doses of LMWH, wound drains (abdominal and rectus sheath) should be considered at caesarean section and the skin incision should be closed with interrupted sutures to allow drainage of any haematoma.
- Any woman who is considered to be at high risk of haemorrhage, and in whom continued heparin treatment is considered essential, should be managed with intravenous unfractionated heparin until the risk factors for haemorrhage have resolved.

Postnatal anticoagulation

- Therapeutic anticoagulant therapy should be continued for at least 6 weeks postnatally and until at least 3 months of treatment has been given in total. Before discontinuing treatment the continuing risk of thrombosis should be assessed.
- Women should be offered a choice of LMWH or oral anticoagulant for postnatal therapy after discussion about the need for regular blood tests for monitoring of warfarin, particularly during the first 10 days of treatment.
- Postnatal warfarin may be started 2 days after caesarean delivery and 24 hours after vaginal delivery.
- Women should be advised that neither heparin (unfractionated or LMWH) nor warfarin is contraindicated in breastfeeding.

Prevention of post-thrombotic syndrome

- Women should be advised that prolonged use of LMWH (more than 12 weeks) is associated with a significantly lower chance of developing post-thrombotic syndrome.
- Following a DVT, graduated elastic compression stockings should be worn on the affected leg to reduce pain and swelling. Clinicians should be aware that the role of compression stockings in the prevention of post-thrombotic syndrome is unclear.

Definitions

Term, Acronym or abbreviation	Definition
CTPA	Computer tomography pulmonary angiogram
CXR	Chest X-Ray
DVT	Deep vein thrombosis
FBC	Full Blood Count
LFTs	Liver Function Tests
U&E	Urea and Creatinine
LMWH	Low-molecular weight heparin
PE	Pulmonary embolism
VQ scan	Ventilation Perfusion Scan

References

1. Adam, S. & Soma-Pillay, P. 2018. Obstetric Essentials. 3rd Edition. University of Pretoria
2. RCOG Green Top Guideline No 37b (2015). Thrombosis and Embolism during Pregnancy and the Puerperium: Acute Management.
3. RCOG Addendum – Green-top Guideline August 2018. Addendum to Section 9: Anticoagulant therapy during labour

Authorship

These guidelines were drafted by a clinical team from Mediclinic and were reviewed by a panel of experts from SASOG and the BetterObs™ clinical team in 2019 and revised by the Scientific Committee of BetterObs™ in 2022. All attempts were made to ensure that the guidance provided is clinically safe, locally relevant and in line with current global and South African best practise. Succinctness was considered more important than comprehensiveness.

All guidelines must be used in conjunction with clinical evaluation and judgement; care must be individualised when appropriate. The writing team, reviewers and SASOG do not accept accountability for any untoward clinical, financial or other outcome related to the use of these documents. Comments are welcome and will be used at the time of next review.

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History and version control

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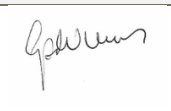
Approval and sign-off

Approved by

Department/ Area/ Group/ Forum	Representative name	Signature	Designation	Date
Clinical Department	Dr Gerrit de Villiers		Chief Clinical Officer	2023 04 27