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122

Prevention and management of venous thromboembolism

Quick Reference Guide

December 2010

This Quick Reference Guide provides a summary of the main recommendations in **SIGN 122 Prevention and management of venous thromboembolism.**

Recommendations are graded **A B C D** to indicate the strength of the supporting evidence. Good practice points ✓are provided where the guideline development group wishes to highlight specific aspects of accepted clinical practice.

Details of the evidence supporting these recommendations can be found in the full guideline, available on the SIGN website: **www.sign.ac.uk**

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ASSESSMENT OF RISK FOR VENOUS THROMBOEMBOLISM

VTE is a multicausal disease, the result of the coincidence of several risk factors which can be grouped as:

- inherent to the individual and may be inherited, eg thrombophilia
- inherent to the individual and can be acquired, eg obesity, cancer and certain drug use (eg oral contraceptive pill)
- the result of an intercurrent illness or procedure, or other cause of temporary reduced mobility, eg following major trauma or surgery, serious medical disorder, pregnancy, or long-haul travel.

RISK FACTORS FOR VENOUS THROMBOEMBOLISM
Age: < 40 years annual incidence of 1/10,000, 60-69 years annual incidence of 1/1,000, > 80 years annual incidence of 1/100
Obesity: 2 to 3-fold risk if BMI > 30 kg/m^2
Varicose veins: 1.5 to 2.5-fold risk after major general/orthopaedic surgery
Family history of VTE
Thrombophilias
Other thrombotic states: cancer, heart failure, recent myocardial infarction/stroke, metabolic syndrome, severe acute infection, chronic HIV infection, inflammatory bowel disease, nephrotic syndrome, myeloproliferative disease, paraproteinaemia, Bechet's disease, paroxysmal nocturnal haemoglobinuria, sickle cell trait and sickle cell disease
Combined oral contraceptives: 3 to 6-fold increased risk **Oral oestrogen hormone replacement therapy**: 2.5-fold increased risk **Raloxifene and tamoxifen**: 2-3-fold increased risk
Pregnancy: 10-fold increased risk compared with non-pregnant **Puerperium:** 25-fold increased risk compared with non-pregnant/non-puerperal
Immobility: 10-fold increased risk with bed rest > 3 days, plaster cast, paralysis
Immobility during travel: 2 to 3-fold increased risk
Hospitalisation: 10-fold increased risk
Anaesthesia: 2 to 3-fold increased risk of postoperative VTE in general compared with spinal/epidural
Central venous catheters: femoral route 11.5-fold increased risk compared with subclavian access
RISK FACTORS FOR RECURRENT VENOUS THROMBOEMBOLISM (in patients not on long term anticoagulation)
Previous unprovoked VTE: recurrence rate 5% per year
Male sex
Obesity
Thrombophilias: risk of recurrence may be increased in patients with antithrombin deficiency

D	**All patients admitted to hospital or presenting acutely to hospital should be individually assessed for risk of VTE and bleeding. The risks and benefits of prophylaxis must be discussed with the patient.**
D	**The use of a risk assessment method checklist is recommended for this purpose.**
D	**The assessment should be repeated regularly and at least every 48 hours.**
D	**Routine laboratory screening for thrombophilias is not recommended.**

RATIONALE FOR PROPHYLAXIS

The rationale for prophylaxis is based on its efficacy, the clinically silent nature of VTE, its high prevalence in hospitalised patients, pregnant or puerperal women, and its potentially disabling or fatal consequences. There is evidence that routine prophylaxis reduces morbidity, mortality and costs in hospitalised patients at risk of deep vein thrombosis and pulmonary embolism.

Screening for asymptomatic DVT, and its treatment, is insensitive and not cost effective compared to routine prophylaxis in at-risk patients.

General measures

☑	Early mobilisation and leg exercises should be encouraged in patients recently immobilised.
☑	Adequate hydration should be ensured in immobilised patients.

THROMBOPROPHYLAXIS IN SURGICAL PATIENTS

General surgery

A	**Patients undergoing abdominal surgery who are at moderate to high risk should receive thromboprophylaxis with mechanical methods unless contraindicated and either subcutaneous low molecular weight heparin, unfractionated heparin or fondaparinux.**
A	**Anti-embolism stockings are recommended for prophylaxis in surgical patients, in the absence of contraindications.**
D	**Intermittent pneumatic compression devices are recommended for prophylaxis of DVT in surgical patients.**
A	**In patients undergoing abdominal surgery AES can be used alone when pharmacological agents are contraindicated, for example due to high bleeding risk.**
C	**Aspirin is not recommended as the sole pharmacological agent for VTE prophylaxis in surgical patients, as other available agents are more effective.**

Orthopaedic surgery

A	**Patients undergoing total hip or total knee replacement surgery should receive pharmacological prophylaxis** *(with LMWH, fondaparinux, rivaroxaban or dabigatran)* **combined with mechanical prophylaxis unless contraindicated.**
A	**Extended prophylaxis should be considered.**
C	**As other agents are more effective for prevention of DVT, aspirin is not recommended as the sole pharmacological agent for VTE prophylaxis in orthopaedic patients.**
C	**Patients with increased risk of bleeding should be given mechanical prophylaxis alone.**
C	**If the bleeding risk has become acceptable then pharmacological prophylaxis should be added.**
A	**Pneumatic foot pumps can be considered for prophylaxis as an alternative to IPC in orthopaedic surgery patients.**

Cardiothoracic surgery

D	**Patients undergoing thoracic surgery should be offered mechanical prophylaxis with IPC or AES.**
D	**Patients undergoing thoracic surgery who are not at high risk of bleeding should be offered pharmacological thromboprophylaxis with UFH or LMWH in addition to mechanical thromboprophylaxis.**
D	**Patients undergoing coronary artery bypass graft surgery should be offered mechanical thromboprophylaxis where feasible.**
D	**Patients undergoing coronary artery bypass graft surgery who are not at high risk of bleeding can be offered pharmacological thromboprophylaxis with UFH or LMWH in addition to mechanical thromboprophylaxis.**

THROMBOPROPHYLAXIS IN MEDICAL PATIENTS

A	**When the assessment of risk favours use of thromboprophylaxis, UFH, LMWH or fondaparinux should be administered.**
C	**Aspirin is not recommended as the sole pharmacological agent for VTE prophylaxis in medical patients.**

Acute stroke

A	**AES should not be used routinely in stroke patients.**
A	**In patients with non-haemorrhagic stroke at high risk of VTE, LMWH can be considered.**
A	**Use of IPC should be considered during hospitalisation in patients with acute stroke, if tolerated.**

Cancer

A	**Patients with cancer are generally at high risk of VTE and should be considered for prophylaxis with LMWH, UFH or fondaparinux whilst hospitalised.**

PREGNANCY AND THE PUERPERIUM

D	**All women should be assessed for risk factors for VTE when booking for antenatal care and at each subsequent maternity contact.**

Antenatal thromboprophylaxis

D	**Women with a previous unprovoked VTE; or VTE linked to oestrogen** *(including pregnancy)***; or minimally provoked VTE** *(related to travel)***; or previous recurrent VTE; or other additional risk factors for VTE; should be offered antenatal thromboprophylaxis with LMWH.**
D	**Women considered to be at high risk of VTE because of multiple risk factors** *(three or more)* **should be offered thromboprophylaxis with LMWH antenatally** *(first trimester)***.**
C	**Vitamin K antagonists have adverse fetal effects and should generally be avoided in pregnancy. In women with mechanical heart valves, however, the risks and benefits of VKA and heparin should be assessed on an individual basis.**
C	**Women of childbearing age using VKA should be clearly informed of the risk of teratogenesis associated with these agents and should be advised to seek appropriate medical advice if they are planning to become pregnant or as soon as possible** *(and within two weeks following a first missed period)* **if they suspect that they may be pregnant.**
D	**Pregnant women considered to be at increased risk of VTE should be advised to wear AES when immobilised/hospitalised.**

Postnatal thromboprophylaxis

D	**All women should be assessed after delivery for risk factors for VTE.**
D	**Women with multiple risk factors for VTE should be considered for postnatal thromboprophylaxis.**
D	**All women who have had an emergency Caesarean section and those who have an elective Caesarean section who have one or more additional risk factors for VTE, should receive thromboprophylaxis with LMWH for seven days.**
D	**Women with a previous VTE should receive LMWH for six weeks following delivery.**
D	**Women receiving prophylaxis antenatally should continue thromboprophylactic doses for six weeks following delivery.**

TRAVEL-RELATED THROMBOSIS

☑	The risks and possible benefits of any intervention should always be discussed with the patient before travelling.
D	**Travellers should be advised to remain as ambulant as safely possible before, during and after journeys.**
D	**The use of AES for prevention of VTE during and after long-haul travel is not routinely recommended.**

DIAGNOSIS OF VENOUS THROMBOEMBOLISM

Acute venous thromboembolism should be suspected in patients with a combination of suggestive symptoms and/or signs:

- **DVT:** unilateral leg pain, swelling, tenderness, increased temperature, pitting oedema, prominent superficial veins
- **PE:** breathlessness, chest pain, haemoptysis, collapse, tachycardia, hypotension, tachypnoea, raised jugular venous pressure, focal signs in chest, hypoxia/cyanosis and/or predisposing factors (see risk factors).

Most patients with confirmed PE do not have clinically evident DVT and around 30% of patients with symptomatic DVT have asymptomatic PE.

Diagnostic algorithms

A variety of clinical decision rules (CDR) can be used to assess clinical probability of having DVT and PE. Most commonly used are the Wells score for DVT and PE, and the Geneva score and the revised Geneva score for PE.

☑	The diagnosis of suspected DVT or PE in hospitalised patients and pregnant women should be by the appropriate imaging.
B	**A validated clinical decision rule should be used in the initial assessment of outpatients presenting with suspected deep vein thrombosis or pulmonary embolism.**
B	**Wells score, Geneva score and revised Geneva score should be used either in their 3 level** *(low, intermediate or high risk)* **or in their 2 level** *(likely or unlikely)* **formats to assess clinical probability of diagnosis of venous thromboembolism in appropriate patients for whom the clinical decision rule is validated.**
☑	Patients with high clinical probability or 'DVT or PE likely' should proceed to imaging to confirm or exclude VTE.

B	**Patients with low or moderate probability CDR or 'DVT or PE unlikely' but a positive D-dimer test should proceed to imaging to confirm or exclude a diagnosis of VTE.**
D	**Patients assessed as low or 'unlikely'clinical probability and with a negative D-dimer should be informed that a diagnosis of VTE may become apparent during three months of follow up.**

Confirmation of clinically suspected deep vein thrombosis

C	**Venous ultrasound is the imaging investigation of choice for patients with suspected DVT.**
C	**Patients who have a negative or inadequate initial scan but who have a persisting clinical suspicion of DVT or whose symptoms do not settle should have a repeat ultrasound scan.**
☑	Patients who have an initial negative ultrasound scan should be considered for repeat ultrasound scanning at 5-7 days if: ▪ they have a high probability clinical decision rule ▪ they have moderate or 'likely' CDR with a positive D-dimer result ▪ on clinical review the suspicion of DVT remains high or increases.

Confirmation of clinically suspected pulmonary embolism

A	**Computed tomography pulmonary angiography using multidetector computed tomography should be the first line investigation of pulmonary embolism.**
C D	**Isotope lung scintigraphy may be considered if computed tomography pulmonary angiography is unavailable and the patient is clinically stable** *(ie, no right heart strain and no hypotension)***, and is of most use in:** ▪ **patients with a normal chest X-ray and no underlying chronic lung disease** ▪ **patients with a contraindication for computed tomography pulmonary angiography** ▪ **pregnant women who have a normal chest X-ray.**

PRELIMINARY ASSESSMENT

D	**All patients presenting with VTE should have a full clinical history and examination undertaken with the aim of detecting underlying conditions contributing to the development of thrombosis and assessing suitability for antithrombotic therapy.**
D	**Patients commencing treatment with UFH, LMWH and warfarin should have a baseline assessment of renal function, prothrombin time and activated partial thromboplastin time.**
☑	Patients commencing treatment with UFH, LMWH and warfarin should have a full blood count to: ▪ monitor for the development of heparin induced thrombocytopenia ▪ exclude overt myeloproliferative disease as a contributing factor in the development of VTE ▪ assess bleeding risk.
☑	Patients for whom anticoagulation is planned should be assessed for their risk of anticoagulant induced bleeding.

INITIAL MANAGEMENT OF VENOUS THROMBOEMBOLISM

Pulmonary embolism

A	**Patients with suspected PE should be treated with therapeutic doses of heparin or fondaparinux until the diagnosis has been deemed very unlikely.**
D	**Patients with intermediate-risk PE should not routinely receive thrombolytic therapy.**
☑	Patients with intermediate-risk PE should be monitored in hospital and be considered for thrombolysis should they deteriorate.

Lower limb DVT

A	**Patients with suspected DVT should be treated with therapeutic doses of LMWH until the diagnosis has been deemed very unlikely or oral anticoagulant therapy has been established.**
B	**Intravenous UFH may be an appropriate alternative in certain circumstances, eg if thrombolysis is being considered, in the immediate postoperative period or where there is particular risk of bleeding.**

Superficial Thrombophlebitis

D	**Patients with clinical signs of superficial thrombophlebitis affecting the proximal long saphenous vein should have an ultrasound scan to exclude concurrent deep vein thrombosis.**
B	**Patients with superficial thrombophlebitis should have anti-embolism stockings and be considered for treatment with prophylactic doses of LMWH for up to 30 days or fondaparinux for 45 days.**
B	**If low molecular weight heparin is contraindicated, 8-12 days of oral non-steroidal anti-inflammatory drugs should be offered.**

Upper extremity DVT

☑	Management of upper extremity DVT needs to be on an individual patient basis and should include management of any underlying condition.

FURTHER MANAGEMENT OF VENOUS THROMBOEMBOLISM

Choice of anticoagulant

A	**After a first episode of limb deep vein thrombosis or pulmonary embolism, treatment with a vitamin K antagonist should be initiated.**
A	**Use of LMWH is an alternative and can be considered if VKA therapy is problematic, for example due to poor compliance/erratic intensity of anticoagulation.**
A	**LMWH rather than warfarin should be considered in VTE associated with cancer.**
C	**Neither aspirin nor statin is recommended for the prevention of recurrent VTE after discontinuation of VKA therapy.**

Intensity of anticoagulation

B	**After a first episode of limb deep vein thrombosis or pulmonary embolism the target INR should be 2.5.**
D	**A higher target INR** *(3.5)* **may be considered if there is recurrent VTE whilst in the target range.**
B	**In patients with antiphospholipid syndrome and VTE, anticoagulation with a VKA, target INR 2.5, should be implemented.**

Duration of anticoagulation

A	**After a first episode of proximal limb deep vein thrombosis or pulmonary embolism, treatment with a VKA should be continued for at least three months.**

☑	Uninterrupted, long term continuation of VKA therapy after a first episode of VTE may be appropriate in some patients and can be based on individual assessment of risk factors including: ▪ an unprovoked first event ▪ the site and severity of the first event ▪ the presence of persistent comorbidities, eg cancer ▪ the presence of persistent antiphospholipid antibodies ▪ male sex ▪ bleeding risk on anticoagulant treatment ▪ patient compliance and preference.

Graduated elastic compression stockings

A	**After deep vein thrombosis affecting a lower limb, the use of well fitted below-knee graduated elastic compression stockings for two years should be encouraged to reduce the risk of post-phlebitic syndrome.**

MONITORING THE ANTICOAGULANT EFFECT

D	**Therapeutic dosing of UFH should be monitored by use of a locally calibrated APTT assay.**
C	**Routine laboratory monitoring of LMWH is not recommended.**

Warfarin has a narrow therapeutic window and there is considerable inter-individual as well as temporal intra-individual variability which necessitates regular monitoring. The PT, with the result expressed as INR, is the best measure of intensity of VKA therapy. A moderately sensitive INR reagent (with an International Sensitivity Index (ISI) <1.7) is recommended, as is assay validation within the individual laboratory.

A	**Computer-assisted dosing algorithms are recommended.**
D	**Patient self testing and self management supported by a dedicated and well trained anticoagulant team may be considered for selected patients.**

ADVERSE EFFECTS OF VTE PROPHYLAXIS AND TREATMENT

Bleeding

D	**In choosing pharmacological thromboprophylaxis the risks of bleeding and other complications need to be considered alongside the likely benefits.**
D	**Major bleeding in patients who are receiving warfarin or other VKAs should be treated by immediate reversal of anticoagulation. This is best achieved by administration of intravenous vitamin K and prothrombin complex concentrate.**
D	**Minor bleeding in patients who are anticoagulated with warfarin should be reversed using low doses of vitamin K** *(1-2.5 mg)* **given either intravenously or orally depending on the clinical circumstances and assessment of the bleeding.**

Heparin induced thrombocytopenia

Heparin induced thrombocytopenia (HIT) is a complication of the use of heparins. It is a prothrombotic state which presents with either asymptomatic thrombocytopenia or with venous or arterial thrombosis, skin lesions or rarely with a generalised systemic reaction which can be severe or even fatal. HIT may occur in any patient who is receiving heparin (UFH and LMWH).

A	**To minimise the incidence of HIT, LMWH should be used in preference to UFH.**
☑	Patients at high risk of developing HIT, and who should be monitored by serial platelet counts between days 4–14 are: ▪ all post-operative patients receiving UFH ▪ patients post-cardiopulmonary bypass receiving LMWH.
D	**All patients who are to receive UFH or LMWH for prophylaxis or treatment of VTE should have a platelet count performed in the 24 hours before receiving treatment.**
D	**Monitoring patients for the development of HIT should be by performing serial platelet counts.**
D	**Patients who have previously received UFH or LMWH within 100 days or in whom the history of recent exposure to heparins is not clear should have a platelet count performed within 24 hours of receiving the first dose of treatment.**
D	**All other patients for whom monitoring is indicated should have platelet counts performed every two to three days from day four to day14 of exposure.**
☑	HIT should be suspected if the platelet count falls by 30% or more or if there is thrombocytopenia ($<150 \times 10^9$/l).

SOURCES OF FURTHER INFORMATION

LIFEBLOOD – THE THROMBOSIS CHARITY

c/o the Thrombosis and Haemostasis Centre

Level 1, North Wing, St Thomas' Hospital

London SE1 7EH

Tel: 0207 633 9937

www.thrombosis-charity.org.uk

Lifeblood's website includes a range of information on various conditions linked with thrombosis.

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