Guidelines For The Prevention Of Thromboembolism In Adults

Appendix

Introduction

Dear Colleagues,

It's our pleasure to introduce these state-of-the-art guidelines for venous thrombo-embolism (VTE) prophylaxis, which is based on the most recently issued ACCP, IUA, ASRA & RCOG guidelines.

Recent evidence indicates that VTE is a major health problem. The Agency for Healthcare Research and Quality ranked 79 patient safety interventions based on the strength of the evidence supporting more widespread implementation of these procedures. The highest ranked safety practice was the appropriate use of prophylaxis to prevent VTE in patients at risk. Despite all this evidence, the risk remains underestimated and its management is suboptimal.

With the help of VTE committee in our institute, we will try to cover the wide variety of topics including VTE prophylaxis for different types of patients (critically ill patients, general medical, surgical, Obstetric, etc…) in this booklet. Trying to cover important issues related to our daily practice and answer outstanding questions in VTE.

This protocol with other tool provided for all health care professionals in our institute, will help us to raise VTE awareness as well as increase prophylaxis rate, for the sake of our patients.

Finally we are very confident that by your help, cooperation & compliance to the guidelines, we will find this project "DVT Safety Zone" a very helpful, informative tool. We are sure that, this program will be reflected on a better care for our patients.

Best regards

VTE Committee members

Table 2 – Rational for Thrombophylaxis in Hospitalized Patients

Rational	Description
High prevalence of VTE	Most hospitalized patients have risk factors for VTE DVT is common in many hospitalized patient groups Hospital-acquired DVT and PE are usually clinically silent Difficult to predict which at-risk patients will develop symptomatic thromboembolic Complications Screening at-risk patients using physical examination or noninvasive testing is neither effective nor cost-effective
Adverse consequence of unprevented VTE	Symptomatic DVT and PE Fatal PE Costs of investigating symptomatic patients Risks and costs of treating unprevented VTA, especially bleeding Increased future risk of recurrent VTE Chronic post thrombotic syndrome
Efficacy and effectiveness of thromboprophylaxis	Thromboprophylaxis is highly efficacious at preventing DVT and proximal DVT Thromboprophylaxis is highly effective at preventing symptomatic VTE and fatal PE The prevention of DVT also prevents PE Cost-effectiveness of prophylaxis has repeatedly been demonstrated

General recommendations

- All hospitalized patients should be assessed for their risk of venous thromboembolic disease and considered for prophylaxis.
- Early ambulation should be considered for all patients as soon as the clinical condition permits.
- We recommend that mechanical methods of prophylaxis be used primarily in patients who are at high risk of bleeding **(Grade 1C+)** or as an adjunct to anticoagulant-based prophylaxis **(Grade 2A)**. We recommend that careful attention be directed toward ensuring the proper use of, and optimal compliance with, the mechanical device **(Grade 1C+)**.
- We recommend against the use of aspirin alone as prophylaxis against VTE for any patient group **(Grade 1A)**.
- For each of the antithrombotic agents, we recommend that clinicians consider the manufacturer's suggested dosing guidelines **(Grade 1C)**.

- We recommend consideration of renal impairment when deciding on doses of LMWH, fondaparinux, the direct thrombin inhibitors, and other antithrombotic drugs that are cleared by the kidneys, particularly in elderly patients and those who are at high risk for bleeding. **(Grade 1C+)**.

(Refer to page 51 for dose adjustment)

- In all patients undergoing neuraxial anesthesia or analgesia, we recommend special caution when using anticoagulant prophylaxis **(Grade 1C)**.
- For patients at both extreme body weight, dose should be adjusted according to the manufacturer's guidelines.
- With the exception of VTE prophylaxis during pregnancy, there is no need for laboratory monitoring for patients receiving VTE prophylaxis.

Grading recommendation

Grade 1
If the guideline developers are very certain that benefits do, or do not, outweigh risks, burdens, and costs, they will make a strong recommendation.

Grade 2
If they are less certain of the magnitude of the benefits and the risks, burdens, and costs, and thus of their relative impact. they make a weaker recommendation.

Grade A
Consistent results from RCTs

Grade C+
Observational studies with very strong effects or secure generalizations from randomized clinical trials (RCTs) .

Grade B
Inconsistent results from RCTs

Grade C
Observational studies

We now use the language **"we recommend"** for strong recommendations (ie, Grades 1A, 1C+, 1B, and 1C) and **"we suggest"** for weaker recommendations (ie, Grades 2A, 2C+, 2B, and 2C).

VTE risk factors

Table 3 – Risk Factors for VTE
Surgery
Trauma (major or lower extremity)
Immobility, paresis
Malignancy
Cancer therapy (hormonal, chemotherapy, or radiotherapy)
Previous VTE
Increasing age
Pregnancy and the postpartum period
Estrogen-containing oral contraception or (HRT)
Selective estrogen receptor modulators
Acute medical illness
Heart or respiratory failure
Inflammatory bowel disease
Nephritic syndrome
Myeloproliferative disorders
Paroxysmal nocturnal hemoglobinuria
Obesity
Smoking
Varicose veins
Central venous catheterization
Inherited or acquired thrombophilia

N.B:

Please refer to Page 55 for "VTE Risk Assessment Model" RAM for medical & surgical patients, in order to have a guide in stratifying your patients at risk of developing DVT or PE (ie, very high, high, moderate, or low risk).

General surgery

- **In low-risk general surgery patients**
  Who are undergoing a minor procedure, are <40 years of age, and have no additional risk factors.

  we recommend against the use of specific prophylaxis other than early and persistent mobilization **(Grade 1C+)**.

- **Moderate-risk general surgery patients**
  Are those patients undergoing a non major procedure and are between the ages of 40 and 60 years, Or have additional risk factors.
  Patients who are undergoing major operations and are <40 years of age with no additional risk factors.

  We recommend prophylaxis with LMWH, e.g. Enoxaparin 20 mg once daily LDUH, 5,000 U bid (both **Grade 1A**).

- **Higher-risk general surgery patients**
  Are those undergoing non major surgery and are > 60 years of age or have additional risk factors.
  Patients undergoing major surgery who are >40 years of age or have additional risk factors.

  We recommend thromboprophylaxis with LMWH, e.g. Enoxaparin 40 mg once daily or LDUH, 5,000 U tid(both **Grade 1A**).

- **High-risk general surgery patients with multiple Risk factors**

  We recommend that pharmacologic methods (LMWH ie, Enoxaparin 40 mg once daily or LDUH, tid) be Combined with the use of GCS and/or IPC **(Grade 1C+)**.

- **In general surgery patients with a high risk of Bleeding**

  We recommend the use of mechanical prophylaxis with properly fitted GCS or IPC, at least initially until the bleeding risk decreases **(Grade 1A)**.

- **In selected high-risk general surgery patients** Including those who have undergone major cancer surgery.

  We suggest post-hospital discharge prophylaxis with LMWH (Enoxaparin 40 mg once daily) **(Grade 2A)**.

Enoxaparin to be started 1-2 hrs pre-operative

N.B:

Please refer to the VTE **RAM** "risk Assessment Model", in order to have a better tool to assess the level of risk for your patient, which is a function of exposing (associated with clinical settings) & predisposing (associated with patient) risk factors.

Vascular surgery

- In patients undergoing vascular surgery **who do not have** additional thromboembolic risk factors

  We suggest that clinicians not routinely use thromboprophylaxis **(Grade 2B)**.

- For patients undergoing major vascular surgical procedures **who have** additional thromboembolic risk factors,

  We recommend prophylaxis with LDUH or LMWH (e.g. Enoxaparin 40 mg) **(Grade 1C+)**.

Enoxaparin to be started 1-2 hrs pre-operative

N.B:

Please refer to the VTE **RAM** "risk Assessment Model", in order to have a better tool to assess the level of risk for your patient, which is a function of exposing (associated with clinical settings) & predisposing (associated with patient) risk factors.

Gynecologic surgery

- For gynecologic surgery patients undergoing brief procedures of ≤30 min for benign disease

  We recommend against the use of specific prophylaxis other than early and persistent mobilization **(Grade 1C+)**.

- For patients undergoing laparoscopic gynecologic procedures, in whom additional VTE risk factors are present

  We recommend the use of thromboprophylaxis with one or more of the following: LDUH, LMWH, IPC, or GCS (all **Grade 1C**).

- For patients undergoing major gynecologic surgery for benign disease, without additional risk factors,

  We recommend LDUH, 5,000 U bid **(Grade 1A)**. Alternatives include once-daily prophylaxis with LMWH e.g. Enoxaparin 40 mg **(Grade 1C+)**, or IPC started just before surgery and used continuously while the patient is not ambulating. **(Grade 1B)**.

- For patients undergoing extensive surgery for malignancy, and for patients with additional VTE risk factors

We recommend routine prophylaxis with LDUH, 5,000 U tid **(Grade 1A)**, or higher doses of LMWH (e.g. Enoxaparin 40 mg) **[Grade 1A]**. Alternative considerations include IPC alone continued until hospital discharge **(Grade 1A)**, or a combination of LDUH or LMWH plus mechanical prophylaxis with GCS or IPC (all **Grade 1C**).

- For patients undergoing major gynecologic procedures

  We suggest that prophylaxis continue until discharge from the hospital **(Grade 1C)**.

- For patients who are at particularly high risk, including those who have undergone cancer surgery and are > 60 years of age or have previously experienced VTE

  We suggest continuing prophylaxis for 2 to 4 weeks after hospital discharge **(Grade 2C)**.

N.B:

Please refer to the VTE **RAM** "risk Assessment Model", in order to have a better tool to assess the level of risk for your patient, which is a function of exposing (associated with clinical settings) & predisposing (associated with patient) risk factors.

Please refer to medical patients section for medical setting.

Urologic surgery

- In patients undergoing transurethral or other Low-risk urologic procedures

  We recommend against the use of specific prophylaxis other than early and persistent mobilization **(Grade 1C+)**.

- For patients undergoing major, open urologic Procedures

  We recommend routine prophylaxis with LDUH twice daily or three times daily **(Grade 1A).**
  Acceptable alternatives include prophylaxis with IPC and/or GCS **(Grade 1B)** or LMWH **(Grade 1C+)**.

- For urologic surgery patients who are actively bleeding, or are at very high risk for bleeding

  we recommend the use of mechanical prophylaxis with GCS and/or IPC at least until the bleeding risk decreases **(Grade 1C+).**

- For patients with multiple risk factors

  We recommend combining GCS and/or IPC with LDUH or LMWH **(Grade 1C+).**

Laparoscopic surgery

- We recommend against routine thromboprophylaxis in these patients, other than aggressive mobilization **(Grade 1A)**.

- For patients undergoing laparoscopic procedures, and who have additional thromboembolic risk factors

  We recommend the use of thromboprophylaxis with one or more of the following: LDUH, LMWH, IPC, or GCS **(Grade 1C+)**.

N.B:

Please refer to the VTE **RAM** "risk Assessment Model", in order to have a better tool to assess the level of risk for your patient, which is a function of exposing (associated with clinical settings) & predisposing (associated with patient) risk factors.

Orthopaedic surgery

Elective hip arthroplasty

- For patients undergoing elective THR

  We recommend the routine use of one of the following three anticoagulants:
  (1) LMWH (at a usual high-risk dose Enoxaparin 40 mg once daily, started 12 h before surgery or 12 to 24 h after surgery, or 4 to 6 h after surgery at half the usual high-risk dose and then increasing to the usual high-risk dose the following day).

  (2) fondaparinux (2.5 mg started 6 to 8 h after surgery).

  or (3) adjusted-dose VKA started preoperatively or the evening after surgery (INR target, 2.5; INR range, 2.0 to 3.0)
  [All Grade 1A]

Underlying values and preferences. We have not recommended the use of fondaparinux over LMWH and VKA, or the use of LMWH over VKA, because we place a relatively low value on the prevention of venographic thrombosis, and a relatively high value on minimizing bleeding complications.

- We recommend against the use of aspirin, dextran, LDUH, GCS, IPC, or VFP as the only method of thromboprophylaxis in these patients **(Grade 1A)**.

Elective knee arthroplasty

- For patients undergoing elective TKA

  we recommend routine thromboprophylaxis using LMWH (at the usual high-risk dose e.g. Enoxaparin 40 mg once daily), fondaparinux, or adjusted-dose VKA (target INR, 2.5; INR range, 2.0 to 3.0) [all **Grade 1A**].

Underlying values and preferences. We have not recommended the use of fondaparinux over LMWH and VKA, or the use of LMWH over VKA, because we place a relatively low value on the prevention of venographic thrombosis, and a relatively high value on minimizing bleeding complications

- The optimal use of IPC is an alternative option to anticoagulant prophylaxis **(Grade 1B)**.

- We recommend against the use of any of the following as sole methods of thromboprophylaxis: aspirin **(Grade 1A)**; LDUH **(Grade 1A)**; or VFP **(Grade 1B)**.

Knee arthroscopy

- We suggest clinicians do not use routine thromboprophylaxis in these patients, other than early mobilization **(Grade 2B)**.

- For patients undergoing arthroscopic knee surgery Who are at higher than usual risk, based on preexisting VTE risk factors or following a prolonged or complicated procedure,

  We suggest thromboprophylaxis with LMWH **(Grade 2B)**.

N.B:

Please refer to the VTE **RAM** "risk Assessment Model", in order to have a better tool to assess the level of risk for your patient, which is a function of exposing (associated with clinical settings) & predisposing (associated with patient) risk factors.

Hip fracture surgery

- For patients undergoing HFS

  We recommend the routine use of fondaparinux **(Grade 1A)**, LMWH at the usual high-risk dose e.g. Enoxaparin 40 mg once daily **(Grade 1C+)**, adjusted-dose VKA [target INR, 2.5; INR range, 2.0 to 3.0] **(Grade 2B)**, or LDUH **(Grade 1B)**.

- We recommend against the use of aspirin alone **(Grade 1A)**.

- If surgery will likely be delayed

  We recommend that prophylaxis with either LDUH or LMWH be initiated during the time between hospital admission and surgery **(Grade 1C+)**.

- If anticoagulant prophylaxis is contraindicated because of a high risk of bleeding

  We recommend mechanical prophylaxis **(Grade 1C+)**.

Other prophylaxis issues in major orthopedic surgery

Timing of prophylaxis initiation

For major orthopedic surgical procedures, we recommend that a decision about the timing of the initiation of pharmacologic prophylaxis be based on the efficacy-to-bleeding tradeoffs for that particular agent **(Grade 1A)**.

For LMWH, there are only small differences between starting preoperatively or postoperatively, and both options are acceptable **(Grade 1A)**.

Pre-hospital discharge screening for DVT

We recommend against the routine use of DUS screening at the time of hospital discharge in asymptomatic patients following major orthopedic surgery **(Grade 1A)**.

Duration of prophylaxis

- We recommend that patients undergoing **THR, TKA,** or **HFS**

  Receive thromboprophylaxis with LMWH (e.g. using a high-risk dose Enoxaparin 40 mg once daily), fondaparinux (2.5 mg daily), or a VKA (target INR, 2.5; INR range, 2.0 to 3.0) for at least 10 days **(Grade 1A)**.

- We recommend that patients undergoing **THR** or **HFS**

  Be given extended prophylaxis for up to 28 to 35 days after surgery **(Grade 1A)**.

  The recommended options for THR include:
  - LMWH **(Grade 1A)**
  - VKA **(Grade 1A)**
  - Fondaparinux **(Grade 1C+)**.

  The recommended options following HFS are
  - Fondaparinux **(Grade 1A)**
  - LMWH **(Grade 1C+)**
  - VKA **(Grade 1C+)**

Elective spine surgery

- For spinal surgery patients with no additional risk Factors

  We recommend against the routine use of any thromboprophylaxis modality, apart from early and persistent mobilization **(Grade 1C)**.

- In patients undergoing spinal surgery, who exhibit additional risk factors, such as advanced age, known malignancy, presence of a neurologic deficit, previous VTE, or an anterior surgical approach

  We recommend that some form of prophylaxis be used**(Grade 1B)**

- For patients with additional risk factors

  We recommend any of the following prophylaxis options:
  - postoperative LDUH alone **(Grade 1C+)**
  - postoperative LMWH alone **(Grade 1B)**
  - perioperative IPC alone **(Grade 1B)**
  - Other considerations include perioperative GCS alone **(Grade 2B)**
  - perioperative IPC combined with GCS **(Grade 2C)**.

  In patients with multiple risk factors for VTE, we recommend combining LDUH or LMWH with GCS and/or IPC **(Grade 1C+)**.

Neurosurgery

- We recommend that thromboprophylaxis be routinely used in patients undergoing major neurosurgery **(Grade 1A)**.
- We recommend the use of IPC with or without GCS in patients undergoing intracranial neurosurgery **(Grade 1A)**.
- Acceptable alternatives to the above options are prophylaxis with LDUH **(Grade 2B)** or postoperative LMWH (Enoxaparin 40 mg) **(Grade 2A)**.
- We suggest the combination of mechanical prophylaxis (ie, GCS and/or IPC) and pharmacologic prophylaxis (ie, LDUH or LMWH) in high-risk neurosurgery patients **(Grade 2B)**.

Trauma

- We recommend that all trauma patients with at least one risk factor for VTE
  receive thromboprophylaxis, if possible **(Grade 1A)**.

- In the absence of a major contraindication

  We recommend that clinicians use LMWH (Enoxaparin 30 mg, bid) prophylaxis starting as soon as it is considered safe to do so **(Grade 1A)**.

- If LMWH prophylaxis is delayed or if it is currently contraindicated due to active bleeding or a high risk for hemorrhage

  We recommend that mechanical prophylaxis with IPC, or possibly with GCS alone, be **(Grade 1B)**.

- In patients who are at high risk for VTE (eg, in the presence of a SCI, lower extremity or pelvic fracture, major head injury, or an indwelling femoral venous line) and who have received suboptimal prophylaxis or no prophylaxis

  We recommend DUS screening **(Grade 1C)**.

- We recommend against the use of IVCFs as primary prophylaxis in trauma patients **(Grade 1C).**

- We recommend the continuation of thromboprophylaxis until hospital discharge, including the period of inpatient rehabilitation **(Grade 1C+)**

- We suggest continuing prophylaxis after hospital discharge

  With LMWH (Enoxaparin 40 mg, od) or a VKA (target INR, 2.5; INR range, 2.0 to 3.0) in patients with major impaired mobility **(Grade 2C).**

Acute SCI

- We recommend that thromboprophylaxis be provided for all patients with acute SCIs **(Grade 1A).**
- We recommend against the use of LDUH, GCS, or IPC as single prophylaxis modalities **(Grade 1A).**
- In patients with acute SCI

  We recommend prophylaxis with LMWH (e.g. Enoxaparin 30 mg, bid), to be commenced once primary hemostasis is evident **(Grade 1B)**. We suggest the combined use of IPC and either LDUH **(Grade 2B)** or LWMH **(Grade 2C)** as alternatives to LMWH.
- When anticoagulant prophylaxis is contraindicated early after injury

  We recommend the use of IPC and/or GCS **(Grade 1C+).**
- We recommend against the use of an IVCF as primary prophylaxis against PE **(Grade 1C).**
- During the rehabilitation phase following acute SCI, we recommend the continuation of LMWH (e.g. Enoxaparin 40 mg, od) prophylaxis or conversion to an oral VKA (INR target, 2.5; INR range, 2.0 to 3.0) **[Grade 1C].**

Burns

- Burn patients with additional risk factors for VTE, including one or more of the following: advanced age, morbid obesity, extensive or lower extremity burns, concomitant lower extremity trauma, use of a femoral venous catheter, and/or prolonged immobility

  We recommend that those patients receive thromboprophylaxis, if possible **(Grade 1C+)**.

- If there are no contraindications

  we recommend the use of either LDUH or LMWH, starting as soon as it is considered safe to do so **(Grade 1C+)**.

N.B:

Please refer to the VTE **RAM** "risk Assessment Model", in order to have a better tool to assess the level of risk for your patient, which is a function of exposing (associated with clinical settings) & predisposing (associated with patient) risk factors.

Medical conditions

- In acutely ill medical patients who have been admitted to the hospital
  with congestive heart failure or severe respiratory disease, or who are confined to bed and have one or more additional risk factors, including active cancer, previous VTE, sepsis, acute neurologic disease, or inflammatory bowel disease

  we recommend prophylaxis with LMWH (e.g. Enoxaparin 40 mg, od) **(Grade 1A)** or LDUH **(Grade 1A)**.

- In medical patients with risk factors for VTE, and in whom there is a contraindication to anticoagulant prophylaxis,

  we recommend the use of mechanical prophylaxis with GCS or IPC **(Grade 1C+)**.

N.B:
Please refer to the VTE **RAM** "risk Assessment Model", in order to have a better tool to assess the level of risk for your patient, which is a function of exposing (associated with clinical settings) & predisposing (associated with patient) risk factors.

Cancer patients

- We recommend that cancer patients undergoing surgical procedures receive prophylaxis that is appropriate for their current risk state **(Grade 1A)**

  Refer to the recommendations in the relevant surgical subsections.

- We recommend that hospitalized cancer patients who are bedridden with an acute medical illness receive prophylaxis that is appropriate for their current risk state **(Grade 1A)**.

  Refer to the recommendations in the section dealing with medical patients.

- We suggest that clinicians not routinely use prophylaxis to try to prevent thrombosis related to long term indwelling CVCs in cancer patients **(Grade 2B)**. Specifically, we suggest that clinicians not use LMWH **(Grade 2B)**, and we recommend against the use of fixed-dose warfarin **(Grade 1B)** for this indication.

Critical care

- On admission to a critical care unit

  We recommend that all patients be assessed for their risk of VTE. Accordingly, most patients should receive thromboprophylaxis **(Grade 1A)**.

- For patients who are at high risk for bleeding

  We recommend mechanical prophylaxis with GCS and/or IPC until the bleeding risk decreases **(Grade 1C+)**.

- For ICU patients who are at moderate risk for VTE (eg, medically ill or postoperative patients)

  We recommend using LDUH or LMWH (e.g. Enoxaparin 40 mg, od) prophylaxis **(Grade 1A)**.

- For patients who are at higher risk such as that following major trauma or orthopedic surgery

  We recommend LMWH prophylaxis **(Grade 1A)**.

Long distance travel

- We recommend the following general measures for long-distance travelers (ie, flights of >6 h duration):

  Avoidance of constrictive clothing around the lower extremities or waist; avoidance of dehydration and frequent calf muscle stretching **(Grade 1C)**.

- For long-distance travelers with additional risk factors for VTE

  We recommend the general strategies listed above. If active prophylaxis is considered, because of the perceived increased risk of venous thrombosis, we suggest the use of:
  - Properly fitted, below-knee GCS, providing 15 to 30 mm Hg of pressure at the ankle **(Grade 2B)**.
  - A single prophylactic dose of LMWH, injected prior to departure **(Grade 2B)**.

- We recommend against the use of aspirin for VTE prevention associated with travel **(Grade 1B)**.

Stroke

Antithrombotic therapy for prevention of DVT and PE in AIS

- For acute stroke patients with restricted mobility

  We recommend prophylactic LDUH or LMWH or heparinoids **(Grade 1A)**.

- For patients who have contraindications to anticoagulants

  We recommend use of intermittent pneumatic compression devices or elastic stockings **(Grade 1C)**

DVT/PE Prophylaxis in Patients with Intracerebral Hematoma (ICH)

- In patients with an acute ICH

  We recommend the initial use intermittent pneumatic compression **(Grade 1C+)**. In stable patients, we suggest LDUH may be initiated as soon as the second day after the onset of the hemorrhage **(Grade 2C)**.

Underlying values and preferences:
The recommendation for subcutaneous heparin assumes a relatively low degree of risk aversion.

Anticoagulation for cerebral venous sinus Thrombosis

- In patients with venous sinus thrombosis

  We recommend that clinicians use :
  - Unfractionated heparin **(Grade 1B)**
  - Low molecular weight heparin **(Grade 1B)**

  Over no anticoagulant therapy during the acute phase, even in the presence of hemorrhagic infarction. In these patients.

  We recommend oral anticoagulation for 3 to 6 months (target INR, 2.5; range, 2.0 to 3.0) **[Grade 1C]**.

VTE prophylaxis during pregnancy and postpartum

When describing the various regimens of UFH and LMWH, we will use the following short forms:

- Minidose UFH:
  UFH 5,000 U SC q12h
- Moderate-dose UFH:
  UFH SC q12h in doses adjusted to target an anti-Xa level of 0.1 to 0.3 U/mL.
- Adjusted-dose UFH:
  UFH SC q12h in doses adjusted to target a mid-interval aPTT into the therapeutic range.
- Prophylactic LMWH:
  e.g. Enoxaparin 40 mg SC q24 h
  dalteparin 5,000 U SC q24h, (although at extremes of body weight modification of dose may be required).
- Intermediate-dose LMWH:
  e.g. Enoxaparin 40 mg SC q12h or
  dalteparin 5,000 U SC q12h.

Δ Adjusted-dose LMWH:
Weight-adjusted, full-treatment doses of LMWH administered once or twice daily (e.g. Enoxaparin 1mg/kg q12h, dalteparin 100 U/kg q12h, Tinzaparin 175 U/kg od or dalteparin 200 U/kg od).

As the half-life of LMWH is shorter in pregnancy, twice daily dosing is preferable, at least in the initial treatment phase.

Δ Postpartum anticoagulants:

warfarin for 4 to 6 weeks with a target INR of 2.0 to 3.0, with initial UFH or LMWH overlap until the INR is ≥ 2.0.

Δ In addition, the term surveillance

Refers to clinical vigilance and aggressive investigation of women with symptoms suspicious of DVT or PE.

Risk factors for venous thromboembolism in pregnancy

- Age over 35 years
- Immobility
- Obesity
- Operative delivery
- Pre-eclampsia
- Parity greater then 4
- Surgical procedure in pregnancy or puerperium, e.g. postpartum sterilization
- Previous DVT
- Thrombophilia

- congenital: antithrombin deficiency
  protein C deficiency
  protein S deficiency
  factor V Leiden
  prothrombin gene variant
- acquired: lupus anticoagulant
  anticardiolipin antibodies

- Excessive blood loss
- Paraplegia
- Sickle cell disease
- Inflammatory disorders and infection, e.g. inflammatory bowel disease and urinary tract infection
- Dehydration

New onset or transient

- Surgical procedure in pregnancy or puerperium, e.g. evacuation of retained products of conception, postpartum sterilization.
- Ovarian hyperstimulation syndrome
- Severe infection, e.g. pyelonephritis
- Midcavity instrumental delivery
- Immobility (> 4 days bed rest)
- Immobility after delivery
- Excessive blood loss
- Prolonged labour
- long-haul travel
- pre-eclampsia
- Hyperemesis
- dehydration

General recommendation

- All women should undergo an assessment of risk factors for VTE in early pregnancy or before pregnancy. This assessment should be repeated if the women is admitted to hospital or develop other intercurrent problems.

- Women with previous VTE should be screened for inherited and acquired Thrombophilia, ideally before pregnancy.

- Regardless of their risk of VTE, immobilization of women during pregnancy, labour and the puerperium should be minimized and dehydration should be avoided.

No prior VTE or thrombophilia

- Women with three or more persisting risk factors

  Should be considered for thromboprophylaxis with LMWH antenatally and for three to five days postpartum.

- Women should be assessed before or during labour for risk factors for VTE
  Age over 35 years and BMI greater than 30 kg/cm2, body weight greater than 90 kg are important independent risk factor for postpartum VTE even after vaginal delivery. The combination of either of these risk factors with any other risk factor for VTE (such as pre-eclampsia or immobility) or the presence of two other persisting risk factors

  Should lead the clinicians to consider the use of LMWH for three to five days.

Prior VTE

- In patients with a single episode of VTE associated with transient risk factor that is no longer present.

  Clinical surveillance and postpartum anticoagulants are recommended.

- If the previous event is pregnancy or estrogen - related or there are additional risk factors (such as (obesity)

  Antenatal anticoagulant prophylaxis is recommended

- In patients with a single idiopathic episode of VTE who are not receiving long – term anticoagulants

  One of the following regimens is recommended:
  - Prophylactic LMWH
  - Minidose UFH
  - Moderate- dose UFH
  - Or Clinical surveillance plus postpartum anticoagulant

- In patients with a single episode of VTE and Thrombophilia (confirmed laboratory abnormality) or a strong family history of thrombosis and not receiving long – term anticoagulants

  One of the following regimens is recommended:
  - prophylactic or intermediate dose LMWH
  - Minidose or moderate-dose UFH, plus postpartum anticoagulant

- In antithrombin-deficient women, compound heterozygotes for prothrombin G20210A and factor V Leiden and homozygotes for these condition with a history of VTE

  We recommend:
  - Intermediate – dose LMWH prophylaxis
  - Or moderate – dose UFH

- In patients with multiple (two or more) episodes of VTE and/or women receiving long-term anticoagulants

  The recommended prophylaxis regimen is:
  - Adjusted-dose UFH
  - or adjusted-dose LMWH
  Followed by resumption of long-term anticoagulants after delivery

- In all women with pervious DVT

  Antenatally and postpartum, the added use of graduated elastic compression stocking is recommended.

Inherited thrombophilia with no previous venous thromboembolism

- In antithrombin-deficient women, compound heterozygotes for prothrombin G20210A and factor V Leiden, and homozygotes for these condition with no prior VTE

  Active prophylaxis is recommended.

- In all other patients with no prior VTE and Thrombophilia (confirmed laboratory abnormatity)

  Surveillance or prophylactic LMWH or minidose unfractionated heparin (UH), plus postpartum anticoagulant is recommended.

Neuroaxial anesthesia/analgesia In patients receiving VTE prophylaxis

Patients receiving subcutaneous LDUH or LMWH

- Needle insertion should be delayed at least 8 - 12 hours after the subcutaneous dose of LDUH or the twice-daily prophylactic dose of LMWH, or at least 18 hours after a once daily LMWH injection.

- Anticoagulant prophylaxis should be delayed if a hemorrhagic aspirate (i.e bloody tap) is encountered during the initial spinal needle insertion.

- Removal of an epidural catheter should be done when the anticoagulant effect is at minimum (usually just before the next schedules dose).

- Anticoagulant prophylaxis should be delayed at least 2 hours after spinal needle or epidural catheter removal

- Indwelling catheters can successfully be maintained while on LDUH or LMWH prophylaxis.

Patients on VKA (oral anticoagulant)

- In patients on chronic Warfarin therapy, anticoagulant should be stopped (ideally 4-5 days) prior to the neuroaxial anaesthesia and INR should be measured.

- In patients receiving an initial dose of Warfarin prior to surgery, INR should be checked prior to the procedure if the first dose was given more than 24 hours earlier.

- In patients receiving low-dose Warfarin (≤ 5mg daily) therapy during epidural analgesia, INR should be checked on a daily basis and checked before catheter removal.

- Before removal of the epidural catheter, INR must be documented to be < 1.5.

- Neurologic testing of sensory and motor function should be performed routinely for patients on Warfarin therapy and at least for 24 hours after catheter removal if the INR was > 1.5 at the time of removal.

- Warfarin should be stopped if INR > 3 in a patient with an indwelling epidural catheter.

-It is recommended that epidural analgesia should not be used for longer than 1 or 2 days because of the unpredictable anticoagulant effect of the anticoagulant.

Patient on fondaparinux

Current ACCP guideline recommended that Fondapairnux should not be administered along with continuous epidural anesthesia because of lack of data on its safety.

Because of the unpredictable anticoagulant effect of the anticoagulant.

All patients should be monitored carefully and frequently for the symptoms and signs of cord compression.

These symptoms include progression of lower extremity numbness or weakness, bowel or bladder dysfunction, and new onset of back pain. If spinal hematoma is suspected, diagnostic imaging and definitive surgical therapy must be performed rapidly to reduce the risk of permanent paresis.

Referances

1-These guidelines are based for most part on the recommendations of the 7th ACCP Conference on Anti-thrrombotic and thrombolytic therapy.

Geerts WH , Pineo GF, Heit JA, Bergqvist D, Lassen MR, Colwell CW , Ray JG. Pervention of Venous Thromboembolism (VTE) : the Seventh ACCP Conference on Antithromotic and Thrombolytic Therapy. Chest. 2004 Sep; 126(3 Suppl): 338S-400S.

2-The guidelines for VTE prophylaxis with neuroaxial anesthesia are based on the above document in addition to The Second ASRA Consensus Conference on Neuroaxial Anesthesia and anticoagulation.

Horlocker TT, Wedel DJ, Benzon H, Brown DL, Enneking FK, Heit JA, MF, Rosenquist RW, Rowlingson J, Tryba M, Yuan CS. Regional anesthesia in the anticoagulated patient: defining the risks (the second ASRA Consensus Conference on Neuraxial Anesthesia and Anticoagulation). Reg Anesth Pain Med.2003 May-Jun: 28(3): 172-97

3-The guidelines for VTE prophylaxis during pregnancy and postpartum is based on:

3.1 The recommendations of the Royal College of Obstetricians and Gynecologists Thromboprophylaxis During Pregnancy, Labor, and After Vaginal Delivery.

Nelson-Percy C, Bewley S, De-Swiet M, Greer IA, Hnt BJ, Oakland M, RCOG Consumer's Form, Reynolds FJM, Thompson PJ, Voke J.
Thromboprophylaxis During Pregnancy, Labour, and After Vaginal Delivery: The Royal College of Obstetricians and Gynaecologists. RCOG Guidelines No. 37. 2004 Jan ; 1-13.

3.2 The recommendations of the 7th ACCP conference on Antithrombotic and thrombolytic therapy.

Bates SM, Greer IA, Hirsh J, Ginsberg JS. Use of Antithrombotic Agents During Pregnancy: the Seventh ACCP conference on Antithrombotic and Thrombolytic Therapy. Chest. 2004 Sep; 126: 627S-644S.

Enoxaparin dosing in patients with severe renal impairment

Recommended dosage regimens for patients with severe renal impairment (creatinine clearance <30 mL/min)

Indication	Dosage regimen
DVT prophylaxis in: ▶ Abdominal surgery ▶ Hip or knee-replacement surgery ▶ Medical patients during acute illness	**30 mg SC once a day**
Prophylaxis of ischemic complications of UA/NSTEMI*	**1 mg/kg SC once a day** (when concurrently administered with aspirin)
Inpatients with acute DVT with or without PE	**1 mg/kg SC once a day** (in conjunction with warfar in sodium therapy)
Outpatients with acute DVT without PE	**1 mg/kg SC once a day** (in conjunction with warfar in sodium therapy)

*UA/NSTEMI=Unstable Angina and non-0-wave myocardial infarction.

Cockcroft-Gault equation for estimating creatinine clearance†

In men:

$$\text{Creatinine clearance} = \frac{(140 - \text{age}) \times \text{weight (kg)}}{72 \times \text{serum creatinine (mg/100 mL)}}$$

In women:

$$\text{Creatinine clearance} = \frac{(140 - \text{age}) \times \text{weight (kg}}{72 \times \text{serum creatinine (mg/100 mL)}} \times 0.85$$

Reference: 1.Cockcroft DW, Gault MH. Prediction of creatinine clearance from serum creatinine, *Nophron*,1976;16:31-41
Use of this equston and others like it may not always be as accurate as the actual measurement of crealinine clearance.

Enoxaparin dosing in special populations

For moderate and mild renal impairment*

- Moderate renal impairment: creatinine clearance 30-50 mL/min
- Mild renal impairment: creatinine clearance 50-80 mL/min

* No dose adjustment is recommended for these populations: however, all such patients should be observed carefully for signs and symptoms of bleeding.

For low-weight or obese patients†

- Low-weight women (<45 kg)
- Low-weight men (<57 kg)
- Obese men and women

† There are no recommendations for dose adjustments for these populations: however, low-weight patients should be observed carefully for signs and symptoms of bleeding.

Clinical pharmacology information

- Anti-Xa exposure after a non-weight-adjusted (prophylaxis) dose is 52% higher in low-weight women (<45 kg) and 27% higher in low-weight men (<57 kg)
- In obese men and women (BMI 30-48 kg/m2), anti-Xa exposure after weight-adjusted doses is marginally higher at steady state, while Amax is not increased.

Abbreviations

AIS	Acute Ischemic Stroke
DUS	Doppler Ultrasound
DVT	Deep Venous Thrombosis
GCS	Gradual Compression Stocking
HFS	Hip Fracture Surgery
ICH	Intra Cerebral Hematoma
IPC	Intermittent Pneumatic Compression
LDUH	Low Dose Unfractionated Heparin
LMWH	Low Molecular Weight Heparin
PE	Pulmonary Embolism
RCT	Randomized Clinical Trials
SCI	Spinal Cord Injury
TKA	Total Knee Arthroplasty
THA	Total Hip Arthroplasty
THR	Total Hip Replacement
VKA	Vitamin K Antagonist
VTE	Venous Thrombo-Embolism
VFP	Venous Foot Pump

Instructions for use
Enoxaparin administration

1 Pick an area on the right or left side of the abdomen in a laying or sitting position, at least 2 inches from the navel and out toward the waist. Clean the injection site with sterile alcohol swab and let dry. Alternate injection sites between left and right sides.

2 Carefully remove the needle cap by firmly pulling it straight off the syringe and discard. If required, dose adjustment must be done prior to injection. Do not expel the air bubble from the syringe before the injection.

3 Gently pinch the cleansed area of the abdomen between your thumb and index finger to make a fold in the skin. Insert the full length of the needle at a 90˚ angle into the fold of the skin. Inject using standard technique, pushing the plunger to the bottom of the syringe.

4 Remove the needle from the injection site, keeping your finger on the plunger. To minimize bruising do not rub the injection site after completion of the injection.

5 Immediately dispose off the syringe in the nearest sharps collector.

Risk Assesment Model

Proposed VTE RAM for surgical and medical patients

Step 1 : Exposing risk factors associated with clinical setting

Assign 1 Factor	Assign 2 Factors	Assign 3 Factors	Assign 4 Factors
☐ Minor Surgery*	☐ Major Surgery*	☐ Myocardial infarction	☐ Elective major lower extremity arthroplasty
	☐ Immobilizing plaster cast	☐ Congestive heart failure	☐ Hip, pelvis or leg fracture
	☐ Medical or surgical patients confined to bed > 72 hours	☐ Severe sepsis/infection	☐ Stroke
	☐ Central venous access		☐ Multiple trauma
			☐ Acute spinal cord injury

* Operations in which the dissection is important or that last longer than 45 minutes, including laparoscopic procedures.

Baseline risk factor score (if score = 5, go to step 4):-

Step 2 : Predisposing risk factors associated with patient

Assign 1 Factor unless otherwise noted

CLINICAL SITTING	CLINICAL SITTING	MOLECULAR CLINICAL SITTING
☐ Age 40 to 60 years (1 factor)	☐ Factor V Leiden/activated protein C resistance (3 factors)	☐ Lupus anticoagulant (3 factors)
☐ Age over 60 years (2 factors)	☐ Antithrombin III deficiency (3 factors)	☐ Antiphospholipid antibodies (3 factors)
☐ History of DVT/PE (3 factors)	☐ Proteins C and S deficiency (3 factors)	☐ Myeloproliferative disorders (3 factors)
☐ Pregnancy or postpartum (< 1 month)	☐ Dysfibrinogenemia (3 factors)	☐ Disorders of plasminogen and plasmin activation (3 factors)
☐ Malignancy (2 factors)	☐ Homocysteinemia (3 factors)	☐ Heparin-induced thrombocytopenia (3 factors)
☐ Varicose veins	☐ 20210A prothrombin mutation (3 factor)	☐ Hyperviscosity syndromes (3 factors)
☐ Inflammatory bowel disease		☐ Homocysteinemia (3 factors)
☐ Obesity (>20% ideal body weight)		
☐ Combined oral contraceptive/hormonal replacement therapy		

Total additional predisposing risk factors score: .....

Step 3 : Total risk factors (exposing + predisposing):
Step 4 : Recommended prophylactic regimens for each risk group

Low risk (1 Factor)	Moderate risk (2 Factor)	High risk (3-4 Factors)	Highest risk (5 or more Factors)
No specific measures	LDUFH (every 12 h), LMWH. IPC and GCS†	LDUFH (every 8h), LMWH, and IPC	LMWH, oral anticoagulants, IPC‡ (+LDUFH or LMWH), GCS† (+LDUFH or LMWH)
Early ambulation		GCS† (+LDUFH or LMWH)	Adjusted-dose heparin

Abbreviations: LDUFH, low-dose unfrationated heparin; IPC, intermittent pneumatic compression; GCS, graduated compression stockings.

† Combining GCS with other prophylactic methods (LDUFH, LMWH, or IPC) may give better protection.

‡ Date show benefit of plantar pneumatic compression in orthopedic total arthroplasty and leg trauma and can be used with IPC is not feasible or tolerated.

Capri et al: effective risk stratification of surgical & non-surgical Patients for VTE. Seminar in hematology Vol 38. NO2, suppl 5, April 2001