VENOUS THROMBOEMBOLIC DISEASE: EVIDENCE BASED PRACTICE GUIDELINES

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Rationale for DVT prophylaxis

- High prevalence of VTE: Almost all hospitalized patients have one or more risk factors for VTE.
- DVT is common in many hospitalized patient groups.
- Hospital-acquired DVT and PE are usually clinically silent. It is difficult to predict which at-risk patients will develop symptomatic thromboembolic complications. Screening at-risk patients using physical examination or noninvasive testing is neither cost-effective nor effective.
- Adverse consequences of unprevented VTE: Symptomatic DVT and PE. Fatal PE. Costs of investigating symptomatic patients. Risks and costs of treating unprevented VTE. Increased future risk of recurrent VTE. Chronic postthrombotic 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 thromboprophylaxis has repeatedly been demonstrated.
Figure 4. Estimated Numbers of DVT, PE, and Attributable Deaths Over a 30-day Period Among a Hypothetical Cohort of 10 000 Acutely Ill Medical Inpatients, by Method of Prophylaxis

Attributable deaths are those due to pulmonary embolism or to adverse reactions to drugs used in prophylaxis or treatment.
For every general hospital, we recommend that a formal, active strategy that addresses the prevention of VTE be developed (Grade 1A).

We recommend that the local thromboprophylaxis strategy be in the form of a written, institution-wide thromboprophylaxis policy (Grade 1C).

We recommend the use of strategies shown to increase thromboprophylaxis adherence, including the use of computer decision support systems (Grade 1A), preprinted orders (Grade 1B), and periodic audit and feedback (Grade 1C).
Risk factors for VTE

- Surgery
  - Trauma (major or lower extremity)
  - Immobility, paresis
- Malignancy
  - Cancer therapy (hormonal, chemotherapy, or radiotherapy)
  - Previous Venous Thromboembolism
- Increasing age
- Pregnancy and the postpartum period
- Estrogen-containing oral contraception or hormone replacement therapy
- Selective estrogen receptor modulators
- Acute medical illness
  - Heart or respiratory failure
  - Inflammatory bowel disease
  - Nephrotic syndrome
- Myeloproliferative disorders
- Paroxysmal nocturnal hemoglobinuria
- Obesity
- Smoking
- Varicose veins
- Central venous catheterization
- Inherited or acquired thrombophilia
Approximate risk of DVT in hospitalized patients

- **Patient Group DVT Prevalence %**
  - Medical patients: 10–20
  - General surgery: 15–40
  - Major gynecologic surgery: 15–40
  - Major urologic surgery: 15–40
  - Neurosurgery: 15–40
  - Stroke: 20–50
  - Hip or knee arthroplasty: 40–60
  - Major trauma: 40–80
  - SCI: 60–80
  - Critical care patients: 10–80
**RISK STRATIFICATION**

- **Low Risk:** Minor surgery in patients <40 years with no additional risk factors.

- **Moderate Risk:** Minor surgery in patients with additional risk factors. Surgery in patients aged 40-60 years with no additional risk factors.

- **High Risk:** Surgery in patients >60 years. Surgery in patients aged 40-60 years with additional risk factors (prior venous thromboembolism, cancer, hypercoagulable state).

- **Highest Risk:** Surgery in patients with multiple risk factors (age >40 years, cancer, prior venous thromboembolism).
For low-risk general surgery patients who are undergoing minor procedures and have no additional thromboembolic risk factors, we recommend against the use of specific thromboprophylaxis other than early and frequent ambulation (Grade 1A).

For moderate-risk general surgery patients who are undergoing a major procedure for benign disease, we recommend thromboprophylaxis with LMWH, LDUH, or fondaparinux (each Grade 1A).

For higher-risk general surgery patients who are undergoing a major procedure for cancer, we recommend thromboprophylaxis with LMWH, LDUH three times daily, or fondaparinux (each Grade 1A).
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- For general surgery patients with multiple risk factors for VTE who are thought to be at particularly high risk, we recommend that a pharmacologic method (ie, LMWH, LDUH three times daily, or fondaparinux) be combined with the optimal use of a mechanical method (ie, graduated compression stockings [GCS] and/or IPC) [Grade 1C].

- For general surgery patients with a high risk of bleeding, we recommend the optimal use of mechanical thromboprophylaxis with properly fitted GCS or IPC (Grade 1A). When the high bleeding risk decreases, we recommend that pharmacologic thromboprophylaxis be substituted for or added to the mechanical thromboprophylaxis (Grade 1C).

- For patients undergoing major general surgical procedures, we recommend that thromboprophylaxis continue until discharge from hospital (Grade 1A). For selected high-risk general surgery patients, including some of those who have undergone major cancer surgery or have previously had VTE, we suggest that continuing thromboprophylaxis after hospital discharge with LMWH for up to 28 days be considered.
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- For patients undergoing entirely laparoscopic procedures who do not have additional thromboembolic risk factors, we recommend against the routine use of thromboprophylaxis, other than early and frequent ambulation (Grade 1B).

- For patients undergoing laparoscopic procedures in whom additional VTE risk factors are present, we recommend the use of thromboprophylaxis with one or more of LMWH, LDUH, fondaparinux, IPC, or GCS (all Grade 1C).
For patients undergoing major thoracic surgery, we recommend routine thromboprophylaxis with LMWH, LDUH, or fondaparinux (each Grade 1C).

For thoracic surgery patients with a high risk of bleeding, we recommend the optimal use of mechanical thromboprophylaxis with properly fitted GCS and/or IPC (Grade 1C).
For cancer patients undergoing surgical procedures, we recommend routine thromboprophylaxis that is appropriate for the type of surgery (Grade 1A).

For cancer patients with indwelling CVCs, we recommend that clinicians not use either prophylactic doses of LMWH (Grade 1B) or minidose warfarin (Grade 1B) to try to prevent catheter-related thrombosis.

For cancer patients receiving chemotherapy or hormonal therapy, we recommend against the routine use of thromboprophylaxis for the primary prevention of VTE (Grade 1C).
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- For all major trauma patients, we recommend routine thromboprophylaxis if possible (Grade 1A).
- For major trauma patients, in the absence of a major contraindication, we recommend that clinicians use LMWH thromboprophylaxis starting as soon as it is considered safe to do so (Grade 1A). An acceptable alternative is the combination of LMWH and the optimal use of a mechanical method of thromboprophylaxis (Grade 1B).
For major trauma patients, if LMWH thromboprophylaxis is contraindicated due to active bleeding or high risk for clinically important bleeding, we recommend that mechanical thromboprophylaxis with IPC or possibly with GCS alone be used (Grade 1B). When the high bleeding risk decreases, we recommend that pharmacologic thromboprophylaxis be substituted for or added to the mechanical thromboprophylaxis (Grade 1C).

In trauma patients, we recommend against routine DUS screening for asymptomatic deep vein thrombosis (DVT) (Grade 1B). We do recommend DUS screening in patients who are at high risk for VTE (eg, in the presence of a spinal cord injury [SCI], lower-extremity or pelvic fracture, or major head injury), and who have received suboptimal thromboprophylaxis or no thromboprophylaxis.
For trauma patients, we recommend against the use of an inferior vena cava (IVC) filter as thromboprophylaxis (Grade 1C).

For major trauma patients, we recommend the continuation of thromboprophylaxis until hospital discharge (Grade 1C). For trauma patients with impaired mobility who undergo inpatient rehabilitation, we suggest continuing thromboprophylaxis with LMWH or a VKA (target INR, 2.5; range, 2.0 to 3.0) (Grade 2C)
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- For patients with acute SCI, we recommend the optimal use of IPC and/or GCS if anticoagulant thromboprophylaxis is contraindicated because of high bleeding risk early after injury (Grade 1A). When the high bleeding risk decreases, we recommend that pharmacologic thromboprophylaxis be substituted for or added to the mechanical thromboprophylaxis (Grade 1C).

- Following acute SCI, we recommend against the use of LDUH alone (Grade 1A).

- For patients with SCI, we recommend against the use of an IVC filter as thromboprophylaxis (Grade 1C).

- For patients undergoing rehabilitation following acute SCI, we recommend the continuation of LMWH thromboprophylaxis or conversion to an oral VKA (INR target, 2.5; range, 2.0 to 3.0) (Grade 1C).
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- For patients admitted to a critical care unit, we recommend routine assessment for VTE risk and routine thromboprophylaxis in most (Grade 1A).

- For critical care patients who are at moderate risk for VTE (eg, medically ill or postoperative general surgery patients), we recommend using LMWH or LDUH thromboprophylaxis (Grade 1A).

- For critical care patients who are at higher risk (eg, following major trauma or orthopedic surgery), we recommend LMWH thromboprophylaxis (Grade 1A).

- For critical care patients who are at high risk for bleeding, we recommend the optimal use of mechanical thromboprophylaxis with GCS and/or IPC at least until the bleeding risk decreases (Grade 1A). When the high bleeding risk decreases, we recommend that pharmacologic thromboprophylaxis be substituted for or added to the mechanical thromboprophylaxis (Grade 1C).
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- We recommend that mechanical methods of thromboprophylaxis be used primarily in patients at high risk of bleeding (Grade 1A), or possibly as an adjunct to anticoagulant-based thromboprophylaxis (Grade 2A).

- For patients receiving mechanical methods of thromboprophylaxis, we recommend that careful attention be directed toward ensuring the proper use of, and optimal adherence with, these methods (Grade 1A).
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- We recommend against the use of aspirin alone as thromboprophylaxis against VTE for any patient group (Grade 1A)
In patients with acute DVT, we recommend initial treatment with LMWH SC once or twice daily, as an outpatient if possible (Grade 1C), or as an inpatient if necessary (Grade 1A), rather than treatment with IV UFH.

In patients with acute DVT treated with LMWH, we recommend against routine monitoring with anti-factor Xa level measurements (Grade 1A).

In patients with acute DVT and severe renal failure, we suggest UFH over LMWH (Grade 2C).
For patients with DVT secondary to a transient (reversible) risk factor, we recommend treatment with a VKA for 3 months over treatment for shorter periods (Grade 1A).

For patients with unprovoked DVT, we recommend treatment with a VKA for at least 3 months (Grade 1A). We recommend that after 3 months of anticoagulant therapy, all patients with unprovoked DVT should be evaluated for the risk-benefit ratio of long-term therapy (Grade 1C). For patients with a first unprovoked VTE that is a proximal DVT, and in whom risk factors for bleeding are absent and for whom good anticoagulant monitoring is achievable, we recommend long-term treatment (Grade 1A).
For patients with DVT and cancer, we recommend LMWH for the first 3 to 6 months of long-term anticoagulant therapy (Grade 1A). For these patients, we recommend subsequent anticoagulant therapy with VKA or LMWH indefinitely or until the cancer is resolved (also, see Section 2.4) [Grade 1C].
For a patient who has had a symptomatic proximal DVT, we recommend the use of an elastic compression stocking with an ankle pressure gradient of 30 to 40 mm Hg if feasible (Grade 1A). Compression therapy, which may include use of bandages acutely, should be started as soon as feasible after starting anticoagulant therapy and should be continued for a minimum of 2 years, and longer if patients have symptoms of PTS. (Note: feasibility, both short and long term, refers to ability of patients and their caregivers to apply and remove stockings.)
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- For patients with acute UEDVT, we recommend treatment with a VKA for ≥ 3 months (Grade 1C).
- For most patients with UEDVT in association with an indwelling central venous catheter, we suggest that the catheter not be removed if it is functional and there is an ongoing need for the catheter (Grade 2C).
- For patients who have UEDVT in association with an indwelling central venous catheter that is removed, we do not recommend that the duration of long-term anticoagulant treatment be shortened to < 3 months (Grade 2C).
We recommend that renal function be considered when making decisions about the use and/or the dose of LMWH, fondaparinux, and other antithrombotic drugs that are cleared by the kidneys, particularly in elderly patients, patients with diabetes mellitus, and those at high risk for bleeding (Grade 1A). Depending on the circumstances, we recommend one of the following options in this situation: avoiding the use of an anticoagulant that bioaccumulates in the presence of renal impairment, using a lower dose of the agent, or monitoring the drug level or its anticoagulant effect (Grade 1B).