Aspirin may also reduce the incidence of venous thrombosis ("Collaborative overview," 1994) [Moderate].

Polycythaemia, essential thrombocytosis, dehydration

In special cases: one large, high

Heart insufficiency and immobilisation

The greatest risk is associated with lower abdominal cancer surgery. Prophylaxis is carried out by administering

Early detection and prevention of venous thrombosis

Side effects of therapy

Previous venous thrombosis

A High risk patients

Dalteparin 5000 IU 12 hours before surgery and then the same amount once daily

Efficacy of prophylactic measures at reducing the risk and rates of deep venous thrombosis and/or pulmonary

Avoid immobilization before and after surgery, avoid general anaesthetics and prefer spinal or epidural

High

Major surgery, age under 40, no risk factors

Further research is likely to have an important impact on confidence in the estimate of effect and may change the

Oral warfarin is contraindicated during pregnancy.

Among the available physical measures the most common and easiest are compression dressings or a surgical

Several high

Early thrombocytopenia is benign and caused by aggregation of thrombocytes.

Major

Major surgery, age under 40, no risk factors

Further research is very unlikely to change our confidence in the estimate of effect.
3. Risk assessment and prophylaxis in internal medicine and neurologic disease patients
4. Risk assessment and prophylaxis during pregnancy including special care units
5. Evaluation and management of heparin-induced thrombocytopenia and thrombosis

**Major Outcomes Considered**
- Efficacy of prophylactic measures at reducing the risk and rates of deep venous thrombosis and/or pulmonary embolism
- Side effects of therapy

**Methods Used to Collect/Select the Evidence**
- Hand-searches of Published Literature (Primary Sources)
- Hand-searches of Published Literature (Secondary Sources)

**Description of Methods Used to Collect/Select the Evidence**
The evidence reviewed was collected from the Cochrane database of systematic reviews and the Database of Abstracts of Reviews of Effectiveness (DARE). In addition, the Cochrane Library and medical journals were searched specifically for original publications.

**Number of Source Documents**
Not stated

**Methods Used to Assess the Quality and Strength of the Evidence**
- Weighting According to a Rating Scheme (Scheme Given)

**Rating Scheme for the Strength of the Evidence**

<table>
<thead>
<tr>
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**Methods Used to Analyze the Evidence**
- Review of Published Meta-Analyses
- Systematic Review

**Description of the Methods Used to Analyze the Evidence**
Not stated

**Methods Used to Formulate the Recommendations**
Not stated

**Rating Scheme for the Strength of the Recommendations**
Not applicable
Pulmonary embolism is a common cause of death of patients with infarction of the brain. The risk can be lowered by prophylactic treatment with anticoagulants. Cancer patients have a higher risk of thrombosis during weeks 1 to 3 of treatment. The laboratory finding is a clear decrease in the thrombocyte count (or a value below 100 in one measurement).

Actions are required if the thrombocyte count falls below 50% from the baseline value, if the thrombocytopenia is more than 50%, or if there are clinical symptoms (e.g., bone pain, fever, or signs of hemorrhage).

Further research is very unlikely to change our confidence in the estimate of effect.

If the patient is under 40 years of age and has a venous thrombosis without any causative factors, consider the possibility of a hereditary coagulation disorder.

In addition to hereditary (intrinsic) factors there are extrinsic factors and conditions that contribute to venous thrombosis:

- Previous venous thrombosis
- Oral contraceptives
- Pregnancy, labour, and puerperium 6 weeks
- Surgery and tissue trauma
- Varicose veins
- Obesity
- Polycythaemia, essential thrombocytosis, dehydration
- Heart insufficiency and immobilisation
- Paralysis, inactivity
- Malignant diseases
- Immobilization (cast, long flights)

Prevention of Venous Thrombosis in Surgery

- Low risk (risk of venous thrombosis 2% to 3% [-10%])
  - Minor surgery (<30 min), no risk factors
  - Age <40, no risk factors
- Moderate risk (risk of venous thrombosis 10% to 30%)
  - Minor surgery, risk factors
  - Nonmajor surgery, no risk factors, age 40 to 60
  - Major surgery, age under 40, no risk factors
- High risk (risk of venous thrombosis 50% to 80%)
  - Major surgery, age >40 years, and earlier deep venous thrombosis or pulmonary embolism or cancer
  - Thrombophilia
  - Knee or hip arthroplasty, hip fracture
  - Major trauma, injury of the spinal cord

The estimated risk of venous thrombosis in the above-mentioned risk groups is about 10%, 30%, and 60%, respectively. In classifying patients into risk groups, take into account both the personal predisposing factors and the type of surgery. Give prophylactic medication against thrombosis to patients belonging to the moderate or high-risk groups. Low-molecular-weight heparin (LMWH) is safe and easily administered at home. It should be used more often...
for the low-risk patients and the course of medication should be prolonged in high-risk patients.

- Immobilization increases the risk of thrombosis (e.g., an ankle fracture in a cast involves a 20% risk, and a fractured tibia in a cast a 60% risk).

**How to Prevent Thrombosis in Surgical Patients**

- Avoid immobilization before and after surgery, avoid general anaesthetics and prefer spinal or epidural anaesthetics, optimize the fluid balance.
- Start preventive therapy before the operation, if possible (Hull et al., 1999) [C].
- Among the available physical measures the most common and easiest are compression dressings or a surgical stocking (Amaragiri & Lees, 2000; Wells, Lensing, & Hirsh, 1994; Agu, Hamilton, & Baker, 1999) [A], which in low-risk patients suffice as the only methods of prevention. Their usefulness has been shown in surgical and obstetric patients.
- Early mobilization does not mean that the patient is placed in a sitting position: mere sitting may even increase the risk of thrombosis.
- Warfarin can also be used for prophylaxis, as it is practical and inexpensive, and can be used when long-term prophylaxis is needed (e.g., a fractured pelvis and long immobilization). The use of warfarin involves the risk of bleeding and requires regular monitoring.
- Heparin is effective in reducing the incidence of deep vein thrombosis (Handoll et al., 2002; Palmer et al., 1997; Howard & Aaron, 1998) [A]. LMWHs have displaced ordinary heparin because of their higher efficacy and easy administration (once daily). If the immobilization is prolonged, continue heparin treatment until the patient is able to get up again. Prophylactic treatment with LMWH is safe and often possible to carry out at home. Treatment duration is 4 weeks in hip (Hull et al., 2001) [A] and knee prosthesis surgery and in cancer surgery (Bergqvist et al., 2002) [B], 6 weeks during pregnancy and puerperium. In a high-risk group the treatment can be continued with warfarin for 6 to 12 weeks. A nurse making home visits may help in the administration of LMWH.
- The usual prophylactic treatment scheme with LMWH
  - Moderate risk patients
    - Enoxaparin 20 (–40) mg subcutaneous (s.c.) 2 hours before surgery and then the same amount once daily
    - Dalteparin 2500 IU 2 hours before surgery and then the same amount once daily
  - High risk patients
    - Fondaparinux 2.5 mg s.c. once daily, started 6 hours after surgery. Fondaparinux is an inhibitor of coagulation factor X, that prevents venous thrombosis in association with orthopaedic surgery more efficiently than enoxaparin (Turpie et al., 2004; Agnelli et al., 2005; Garces & Mamdani, 2002; “Fondaparinux,” 2001) [A].
    - Enoxaparin 40 mg s.c. 12 hours before surgery and then the same amount once daily
    - Dalteparin 5000 IU 12 hours before surgery and then the same amount once daily
  - Adverse effects: postoperative and post-traumatic bleeding. The antidote is protamine.

**Prevention of Venous Thrombosis in Internal Medicine and in Neurological Diseases**

**Risk Factors for Venous Thrombosis**

- Heart failure and other non-surgical high-risk patients
- Heart failure and myocardial infarction
- Pulmonary embolism is a common cause of death of patients with infarction of the brain. The risk can be lowered with early mobilisation, antiembolism stockings, and LMWH. Haemorrhage complications diminish the benefits.
- Cancer
- Severe infection

**Implementation**

- LMWH therapy should be considered for all patients who are at bed rest for more than 3 days and who have one or more of the above-mentioned risk factors. The treatment is often continued with warfarin if the need for prophylaxis is prolonged.

**Prevention of Venous Thrombosis in Neoplastic Diseases**

- Active, and especially metastatic, cancer elevates the risk of venous thrombosis. Thromboembolism that appears without apparent reason may be the first sign of a latent malignant disease.
- Even if thrombosis prophylaxis in indicated, it is still underused: the reason for this is that the disease itself and its treatment usually raise the risk of haemorrhaging. Prophylaxis is started on an individual basis after careful consideration of indications and contraindications.
- Warfarin often interacts with treatments used in cancer patients and for this reason LMWH is considered a safer and more effective alternative for these patients.
- The greatest risk is associated with lower abdominal cancer surgery. Prophylaxis is carried out by administering LMWH for one month: enoxaparin 40 mg × 1 or dalteparin 5000 IU × 1.
- The risk is also elevated in patients who have a history of venous thrombosis during earlier immobilization or infection, or who have additional risk factors for venous thrombosis. Prophylaxis is usually indicated at least during bedrest.

**Prevention of Venous Thrombosis During Pregnancy**

- Carried out in special care units
High Risk of Thromboembolism

- A venous thrombus above the knee, or pulmonary embolism during an earlier pregnancy.
- Patients with a hereditary or acquired blood coagulation disorder and a previous venous thrombosis. (In antithrombin III deficiency the risk is so high that prophylactic treatment must always be given, even if the patient has no history of thrombosis).
- Acquired coagulation disorders include (e.g., lupus anticoagulant and myeloproliferative diseases [e.g., polycythaemia vera, essential thrombocytosis]).

Treatment in Special Care Units

- Start prophylactic treatment with LMWH after confirming the pregnancy, or at the latest on weeks 16-18. Mini-heparin treatment is not sufficient! Continue antithrombotic therapy for 6 weeks after parturition; however, at the time of delivery the drug can be changed to oral warfarin, which is contraindicated during pregnancy. The risk of thrombosis is highest at the end of the pregnancy, and higher doses of LMWH are often used.
- The initiation of heparin treatment depends on the risk: in women who have had thromboembolism during an earlier pregnancy or on oral contraceptives the treatment should always be started on week 24 at the latest.
- Prophylactic treatment in patients with activated protein C (APC) resistance due to genetic defect of factor V (see the Finnish Medical Society Duodecim guideline on "Inherited Thrombophilia"):
  - Heterozygotes who have not had a thrombosis: prophylactic treatment is recommended only in cases of caesarean section or immobilization.
  - Heterozygotes who have had a thrombosis: prophylactic treatment is recommended during pregnancy and puerperium.
  - Homozygotes: prophylactic treatment is recommended regardless of whether the patient has had a thrombosis or not.

Thrombocytopenia and Thrombosis as Complications of Heparin Treatment

- Early thrombocytopenia is benign and caused by aggregation of thrombocytes.
- Severe immunologically mediated thrombocytopenia leads to activation of thrombocytes and endothelial damage, causing arterial thrombi.
- Symptoms are caused by arterial or venous thrombosis during weeks 1-3 of the treatment. The onset is typically on the fifth or the tenth day from the beginning of the treatment.
- The laboratory finding is a clear decrease in the thrombocyte count (or a value below 100 in one measurement). Thrombocytopenia occurs in approximately 1% of LMWH users (Prandoni et al., 2005)
- In the follow-up of heparin treatment, haemoglobin and thrombocyte values should be taken at 1-week intervals for 4 weeks.
- Actions are required if the thrombocyte count falls below 50% from the baseline value, if the thrombocytopenia is progressing, or if the antithrombotic treatment proves ineffective.
- Do not start warfarin treatment before the thrombocyte count is normalized.
- Platelet transfusions are contraindicated. Consult a haematologist.
- Alternative anticoagulants: fondaparinux, danaparoid, lepirudin

Related Resources

Refer to the original guideline document for related evidence, including Cochrane reviews and other evidence summaries.

Definitions:

Classification of the Quality of Evidence

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GRADE (Grading of Recommendations Assessment, Development and Evaluation) Working Group 2007 (modified by the EBM Guidelines)
Even if thrombosis prophylaxis is indicated, it is still underused: the reason for this is that the disease itself and
very low risk of thrombosis in healthy, non-immobilized patients is often underestimated. Several high-quality
studies in cancer surgery (Bergqvist et al., 2002) and knee prosthesis surgery and in cancer surgery (Bergqvist et al., 2002)
demonstrated that prophylaxis with heparin was more effective than no prophylaxis. In non-surgical patients,
Adverse effects of heparin therapy include bleeding, and thrombocytopenia and thrombosis. Low Molecular
Weight Heparin (LMWH) is the most commonly used prophylactic anticoagulant, with a more predictable
and more effective alternative for these patients.


Thrombophilia Symptoms are caused by arterial or venous thrombosis during weeks 1

An adverse effects of warfarin therapy is bleeding

Several studies with some limitations

Paralysis, inactivity

Surgery and tissue trauma

High

The usual prophylactic treatment scheme with LMWH

Low

Expert opinion

Further research is very likely to have an important impact on confidence in the estimate of effect and is likely to change

Start prophylactic treatment with LMWH after confirming the pregnancy, or at the latest on weeks 16

Obesity

If the patient is under 40 years of age and has a venous thrombosis without any causative factors, consider the

Moderate

Fondaparinux

Appropriate use of prophylactic measures for prevention of venous thrombosis

In special cases: one large, high

Pregnancy, labour, and puerperium 6 weeks

Early thrombocytopenia is benign and caused by aggregation of thrombocytes.

Warfarin can also be used for prophylaxis, as it is practical and inexpensive, and can be used when long

Several high

Further research is likely to have an important impact on confidence in the estimate and may change the

Heterozygotes who have not had a thrombosis: prophylactic treatment is recommended only in cases of

One or more studies with very severe limitations

Heterozygotes who have had a thrombosis: prophylactic treatment is recommended during pregnancy and

The risk is also elevated in patients who have a history of venous thrombosis during earlier immobilization or have had pulmonary embolism. Further research is very likely to have an important impact on confidence in the estimate of effect and is likely to change our confidence in the estimate of effect.

LMWH may also be used if the patient has known thrombophilia or a history of thromboembolism and is not on anticoagulants. In special cases: one large, high quality study with one severe limitation.

Venous thrombosis is a common and dangerous disease that can, however, be treated and often prevented. Thrombophilia is a condition in which the blood is more likely to clot, and it can cause venous thrombosis. Knee or hip arthroplasty, hip fracture, obesity, heart failure, and other non-cardiovascular disease are risk factors for venous thrombosis. Appropriate use of prophylactic measures for prevention of venous thrombosis is recommended. Carried out in special care units.

High risk patients include major surgery, age >40 years, and earlier deep venous thrombosis or pulmonary embolism or cancer. Low risk patients include risk of venous thrombosis 2% to 3% [Major surgery, obesity, cancer].

The usual prophylactic treatment scheme with LMWH is initiated 2 hours before surgery and then the same amount once daily. For example, Dalteparin 2500 IU 2 hours before surgery and then the same amount once daily. In special cases: one large, high quality study with one severe limitation.

Adverse effects of heparin therapy include bleeding, and thrombocytopenia and thrombosis. However, the risk of bleeding can be minimized by careful monitoring of the patient's response to therapy.

In addition to hereditary (intrinsic) factors there are extrinsic factors and conditions that contribute to venous thrombosis. Severe immunologically mediated thrombocytopenia leads to activation of thrombocytes and endothelial damage, which can contribute to the formation of blood clots.

Further research is very unlikely to change our confidence in the estimate of effect.