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Thromboembolism

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Deep venous thrombosis (DVT) or pulmonary embolism may occur in almost two in 1,000 persons each year, with up to 25 percent of those having a recurrence.

- About 5 to 15 percent of persons with untreated DVT may die from pulmonary embolism.
- The risk of recurrence of thromboembolism falls over time, but the risk of bleeding from anticoagulation remains constant.

Oral anticoagulants are considered effective in persons with proximal DVT compared with no treatment, although we found few trials.

- In persons with proximal DVT or pulmonary embolism, long-term anticoagulation reduces the risk of recurrence, but high-intensity treatment has shown no benefit. Both approaches increase the risk of major bleeding.
- Low-molecular-weight heparin (LMWH) is more effective than unfractionated heparin, and may be as effective as oral anticoagulants, although all are associated with some adverse effects.
- We do not know how effective tapering of oral anticoagulant agents is compared with stopping abruptly.
- We do not know whether once-daily LMWH is as effective as twice-daily administration at preventing recurrence.
- Home treatment may be more effective than hospital-based treatment at preventing recurrence, and equally effective at reducing mortality.
- Vena cava filters reduce the short-term rate of pulmonary embolism, but they may increase the long-term risk of recurrent DVT.
- Elastic compression stockings reduce the incidence of postthrombotic syndrome after DVT compared with placebo or no treatment.

In persons with isolated calf DVT, anticoagulation with warfarin may reduce the risk of proximal extension, although prolonged treatment seems no more beneficial than short-term treatment.

Anticoagulation may reduce mortality compared with no anticoagulation in persons with a pulmonary embolus, but it increases the risk of bleeding. We found few studies that evaluated treatments for pulmonary embolism.

- LMWH may be as effective and safe as unfractionated heparin.
- Thrombolysis seems as effective as heparin in treating major pulmonary embolism, but it is also associated with adverse effects.
- The use of computerized decision support may increase the time spent in target international normalized ratio range and reduce thromboembolic events or major hemorrhage, compared with manual dosage calculation.

Definition

Venous thromboembolism is any thromboembolic event occurring within the venous system, including DVT and pulmonary embolism. DVT is a radiologically confirmed partial or total thrombotic occlusion of the deep venous system of the legs sufficient to produce symptoms of pain or swelling. Proximal DVT affects the veins above the knee (popliteal, superficial femoral, common femoral, and iliac veins). Isolated calf DVT is confined to the deep veins of the calf and does not affect the veins above the knee. Pulmonary embolism is radiologically confirmed partial or total thromboembolic occlusion of pulmonary arteries, sufficient to cause symptoms of breathlessness, chest pain, or both. Postthrombotic syndrome is edema, ulceration, and impaired viability of

the subcutaneous tissue of the leg occurring after DVT.

Recurrence refers to symptomatic deterioration due to a further (radiologically confirmed) thrombosis, after a previously confirmed thromboembolic event, where there had been an initial partial or total symptomatic improvement. Extension refers to a radiologically confirmed, new, constant, symptomatic intraluminal filling defect extending from an existing thrombosis. Self-testing is where the patient is responsible for testing his or her international normalized ratio at home using capillary sampling and a point-of-care device. Dosing of warfarin and frequency of testing are advised by the health professional clinically responsible for the patient's management. Self-management is where the patient is responsible for testing his or her international normalized ratio at home using capillary sampling and a point-of-care device. Dosing of warfarin and frequency of testing are also managed by the patient, with support from the health professional clinically responsible according to an agreed contract.

Incidence and Prevalence

We found no reliable study of the incidence or prevalence of DVT or pulmonary embolism in the United Kingdom. A prospective Scandinavian study found an annual incidence of 1.6 to 1.8 per 1,000 persons in the general population. A more recently published retrospective study from Norway found the incidence of DVT between 1995 and 2001 to be 0.93 per 1,000 person-years (95% confidence interval [CI], 0.85 to 1.02 per 1,000 person-years), and of pulmonary embolism to be 0.50 per 1,000 person-years (95% CI, 0.44 to 0.56 per 1,000 person-years). A further Australian study found a standardized annual incidence per 1,000 residents of 0.57 (95% CI, 0.47 to 0.67) for all venous thromboembolism, 0.35 (95% CI, 0.26 to 0.44) for DVT, and 0.21 (95% CI, 0.14 to 0.28) for pulmonary embolism. Ethnic origin may affect incidence, with one study reporting increased incidence in black persons. One postmortem study estimated that 600,000 persons develop pulmonary embolism each year in the United States, of whom 60,000 die as a result.

Clinical Questions

What are the effects of treatments for proximal DVT?	
Beneficial	Compression stockings
	LMWH (reduced mortality, recurrence, and risk of major hemorrhage compared with unfractionated heparin)
Likely to be beneficial	Home treatment with short-term LMWH
	Oral anticoagulants
Trade-off between benefits and harms	Long-term LMWH vs. long-term anticoagulation (both showed similar levels of benefits but with important adverse effects)
	Long-term vs. short-term oral anticoagulation
	Vena cava filters (reduce short-term rate of pulmonary embolism, but may increase the long-term risk of recurrent DVT)
Unknown effectiveness	Abrupt discontinuation of oral anticoagulation
	Once-daily vs. twice-daily LMWH
Unlikely to be beneficial	High-intensity oral anticoagulation
What are the effects of treatments for isolated calf DVT?	
Likely to be beneficial	Warfarin (reduced rate of proximal extension compared with no further treatment in persons who had received initial heparin and wore compression stockings)
Unlikely to be beneficial	Prolonged duration of anticoagulation
What are the effects of treatments for pulmonary embolism?	
Likely to be beneficial	Anticoagulants (warfarin and heparin)*
	Thrombolysis
Trade-off between benefits and harms	Prolonged duration of anticoagulation
Unknown effectiveness	LMWH (no clear evidence of a difference in mortality, new episodes of thromboembolism, or in risk of major hemorrhage compared with unfractionated heparin)
Unlikely to be beneficial	High-intensity anticoagulation (extrapolated data from persons with proximal DVT)
What are the effects of interventions on oral anticoagulation management in persons with thromboembolism?	
Unknown effectiveness	Computerized decision support in oral anticoagulation (increased time spent in target international normalized ratio range)
	Self-testing and self-management of oral anticoagulation

DVT = deep venous thrombosis; LMWH = low-molecular-weight heparin.

**—Clinical consensus based on observational data.*

Etiology and Risk Factors

Risk factors for DVT include immobility, surgery (particularly orthopedic surgery), malignancy, pregnancy, older age, and inherited or acquired prothrombotic clotting disorders.

The oral contraceptive pill is associated with increased risk of death from venous thromboembolism (absolute risk increase with any combined oral contraceptive: one to three deaths per 1 million women per year). The principal cause of pulmonary embolism is DVT.

Prognosis

The annual recurrence rate of symptomatic calf DVT in persons without recent surgery is more than 25 percent. The rate of fatal recurrent venous thromboembolism after anticoagulation has been estimated at 0.3 per 100 patient-years. Proximal extension develops in 40 to 50 percent of persons with symptomatic calf DVT. Proximal DVT may cause fatal or nonfatal pulmonary embolism, recurrent venous thrombosis, and postthrombotic syndrome. One case series (462 persons) published in 1946 found 5.8 percent mortality from pulmonary emboli in persons with untreated DVT in a maternity hospital. More recent cohorts of treated persons have reported mortality of 4.4 percent at 15 days and 10 percent at 30 days. One nonsystematic review of observational studies found that after recent surgery in persons who have an asymptomatic calf DVT, the rate of fatal pulmonary embolism was 13 to 15 percent. The incidence of other complications without treatment is not known. The risk of recurrent venous thrombosis and complications is increased by thrombotic risk factors and is more common in men.

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