Deep Vein Thrombosis Prophylaxis in Orthopaedic Surgery

a report by

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Despite a huge literature base, thromboprophylaxis in orthopaedics remains controversial. The scale of the problem is disputed and the cost–benefit and risk–benefit ratios, and the practicality of any particular protocol, are uncertain.

What Is the Scale of the Problem?
Some orthopaedic procedures, such as upper limb surgery, probably carry minimal risk of thrombosis, while others, such as revision hip surgery or complex lower limb trauma reconstruction, probably carry a particularly high risk. Asymptomatic deep vein thrombosis (DVT) occurs in 58% of major trauma patients, 3–18% of knee arthroscopy patients and 10–35% of patients with isolated lower limb injuries. Without prophylaxis, the death rate from pulmonary embolism (PE) after hip replacement or knee replacement is probably around 0.4%, and perhaps slightly higher after hip fracture. With 1.2 million arthroplasties per year in Europe, that equates to 4,800 deaths – a huge problem. About 3–4% will develop a symptomatic DVT or PE requiring treatment, which is the most common avoidable complication and the most common reason for re-admission. The frequency of chronic venous insufficiency, an important longer-term outcome, is unknown.

Does Prophylaxis Work?
The event rates listed above can be reduced with careful prophylaxis. Historically, almost all prophylaxis studies relied on radiological surrogates; more recently, a reduction in radiological thrombosis using extended-duration chemical prophylaxis has been shown to correlate with a reduction in symptomatic events. No study could be large enough to directly show a reduction in fatal PE, but it is biologically plausible that a reduced DVT frequency translates to a reduced fatal PE rate. Most studies refer to hip and knee arthroplasty patients; there are far fewer data on other orthopaedic procedures.

What Prophylaxis Should Be Used?
There are three categories of prophylaxis: general, mechanical and chemical.

General Measures

Early Mobilisation
There is a good physiological premise, although only weak circumstantial evidence, that early mobilisation reduces thromboembolism.

Neuraxial Anaesthesia
This reduces mortality and enhances peri-operative analgesia. The DVT rate is reduced by about one-third. There are concerns about concomitant use of chemical prophylaxis and neuraxial anaesthesia, lest a spinal haematoma develop. It is prudent to avoid giving neuraxial anaesthesia and low-molecular-weight heparin (LMWH) within at least six hours of each other. The interval for pentasaccharides, with their longer half-life, is likely to be much longer.

Surgical Technique
A rough surgical technique may potentiate thromboplastin release. Prolonged torsion of the dislocated hip while reaming, or aggressive dorsal retraction of the tibia, causes two problems: first, the adjacent deep veins may be damaged; and second, by blocking venous return, the calf veins are distended, exposing subendothelial collagen and thus initiating thrombosis.

Tourniquet
There is no evidence that tourniquet use aggravates thrombogenesis. The accumulation of clotting factors while the tourniquet is inflated is probably balanced by the fibrinolytic and valve-flushing hyperaemia on tourniquet deflation.

Mechanical Prophylaxis

Graduated Compression Stockings
These are commonly used. To work, they must be properly woven and well-fitted and remain in place. The evidence on their efficacy after orthopaedic surgery is weak, but a meta-analysis of other surgical studies suggests a modest benefit.

Intermittent Pneumatic Compression Devices
These devices enhance both deep venous flow and fibrinolysis. The peak venous flow varies with different devices depending on the frequency of contractions, the number of compartments, above- or below-knee design and inflation pressure. The ideal parameters have not been established; however, in general these devices are effective.

Foot Pumps
These rhythmically empty the venous plexus in the sole of the foot, flushing out the deep leg veins and providing prophylaxis that is probably equivalent to LMWH in hip arthroplasty. The evidence after knee arthroplasty is less convincing. The efficacy of foot pumps depends on factors such as the pressure and frequency of the impulses and the ability of the leg to produce pre-load.

Advantages of Mechanical Prophylaxis
These methods do not carry a risk of bleeding, which is intrinsic to chemical methods. This is enticing to surgeons and anaesthetists, who have to balance risk and benefit, particularly in the peri-operative period.

Drawbacks of Mechanical Prophylaxis
All mechanical methods have the disadvantages of expense and
compliance. Furthermore, they are not practical for, nor is there evidence for, extended-duration prophylaxis.

**Chemical Prophylaxis**

**Aspirin**

Aspirin is only weakly antithrombotic. It risks alternative complications (e.g. wound bleeding, transfusion, gastrointestinal bleeding). If chosen as the sole prophylactic method, patients are deprived of safer and more effective alternative mechanical and chemical methods. The two largest evidence-based consensus groups and the National Institute for Health and Clinical Excellence (NICE) recommend against its use. It is not even licensed for thromboprophylaxis in the UK.41–44

**Low-molecular-weight Heparins**

There are several different types of LMWH. These drugs are readily bioavailable with a wide window of safety; monitoring is therefore not required. The drugs are relatively cheap and easy to administer by injection once or twice daily, depending on half-life. LMWHs have been very widely studied and are at least as effective as warfarin, compression devices and foot pumps. They are more effective than unfractionated heparin and far more effective than placebo.45

**Warfarin**

Used carefully, warfarin is as effective as LMWHs in reducing venographic DVT, and death is exceedingly rare. It can be given for an extended duration. Warfarin is used widely in North America, but for compelling reasons it is generally regarded as obsolete in Europe:

- regular monitoring is required, which is expensive and time-consuming;
- if started too close to surgery or at too high a dose, there is a risk of bleeding;
- if started judiciously – later and at a lower dose – there is an interval of several days during which the patient will be unprotected at his or her most thrombogenic time; and
- it interacts with many drugs, as well as with alcohol.

**Pentasaccharides**

Pentasaccharides are synthetic antithrombotic agents that are designed to inhibit precisely Factor Xa. The first of this class to be widely studied and commercially available is fondaparinux (Arixtra). It has 100% bioavailability and is renally excreted rather than metabolised. As it has a long half-life (15 hours), it can be administered daily. A systematic and thorough comparison with a particular LMWH (enoxaparin) in over 7,300 total hip replacement and total knee replacement patients showed an impressive odds reduction of 55.2% (95% confidence interval 45.8–63.1; p=10) in favour of the pentasaccharide for venographic prevalence of DVT.46

**Factor Xa Inhibitors and Antithrombin Inhibitors**

These relatively new classes of drugs are being enthusiastically developed as an alternative to warfarin. They can be given orally, which would allow simple extended-duration use. With a suitable therapeutic window, monitoring would not be required. Interactions would be less likely, although reversibility could be a problem. The first to reach the formulary, Melagatran (Exanta), has been withdrawn because of liver toxicity, but other drugs are now reaching the licensing stage.

**Advantages of Chemical Prophylaxis**

Chemical methods can be effective, especially LMWH, pentasaccharides and, now, direct thrombin inhibitors and Factor Xa inhibitors. They are generally easy to administer (tablet or injection format) and can be used for an extended duration. Relative to the overall cost of surgery, they are fairly inexpensive.

**Bleeding with Chemical Prophylaxis**

Like most medical interventions, thromboprophylaxis involves a balance of risk and benefit. Chemical prophylaxis will inevitably cause bleeding unless the proximity to surgery is respected: if an effective dose of chemical is administered too close to surgery, bleeding will occur. In general, it is European practice to give LMWHs prior to operation, thus providing an anticoagulant remedy to the pre-operative thrombogenic factors (tissue thromboplastins and venous stasis). However, if the drug is given too long before surgery, the serum levels will be too low for any prophylactic effect; if given too close to surgery, surgical bleeding can be expected. In general, it is North American practice to give LMWHs after surgery at a higher dose and more frequently. This may reduce the risk of surgical bleeding, but the thrombogenic process will be well-established before the drug can act. The drug now has to function as a therapeutic rather than as a prophylactic.47

**Duration of Use**

If prophylaxis is used, it should be given for an appropriate duration of time. The risk of thrombosis may depend on many factors, such as the particular procedure performed, the likelihood of post-operative immobility, the physiological return of fibrinolysis, thrombogenesis to usual equilibrium and individual inherited propensity to thrombosis. Thromboprophylaxis in the latter part of the 20th century was usually studied academically and administered clinically only while the patient was still in hospital. This was for pragmatic rather than scientific reasons. However, it is now clear that the risk of thrombosis in hip or knee arthroplasty and hip fracture persists for much longer. Several sources show that half of symptomatic venous thromboembolism cases after knee replacement and two-thirds of cases after hip replacement occur beyond the second week, usually when the patient has been discharged from hospital. Furthermore, it has been established that the risk of late thrombosis (both radiological and symptomatic) can be reduced substantially by continuing the administration of prophylaxis for longer.48,49 The precise period depends on many factors, but current evidence would support 14 days for knee replacement and four to five weeks for hip replacement and hip fracture. As patients are discharged from hospital earlier and earlier, the proportion (and indeed importance) of prophylaxis to be given after discharge increases. This is likely to be a cost-effective approach.

**Combined Use of Mechanical and Chemical Methods**

In the late 20th century, there tended to be a conflict between chemical methods and mechanical methods. This dichotomy was inappropriate, as each has advantages and disadvantages.50 Furthermore, the obsession with evidence-based medicine tended to allow recommendations only if supported by a particular randomised trial or meta-analysis. However, the
randomised trial is only as reliable as the unitary hypothesis studied and the exclusion criteria applied to the studied sample. In this author’s view, clinicians should regard randomised trials and meta-analysis as showing the general direction rather than being the constraining basis of practice. The combined literature, as well as a pragmatic view, would support a combination of mechanical and chemical methods.5,52

**Particularly High Risk of Thromboembolism**

For those patients with particularly high risk of bleeding, a mechanical method should be used until the bleeding risk is lessened; an effective chemical can be safely started and continued for as long as there is a risk of thrombosis.

**Uncertain Delay to Surgery**

If the time of surgery is uncertain, such as for hip fracture and trauma patients, the mechanical method can be started as close to the moment of trauma as possible and continued until such time after surgery as the clinician feels that a chemical can be commenced.

**Neuraxial Anesthesia**

The risk of a spinal haematoma can be minimised by delaying the administration of a chemical for at least eight hours after the catheter is removed; the interim can be safely covered with a mechanical method.