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Introduction

Total hip and knee arthroplasty, and hip fracture, are associated with a high risk of deep vein thrombosis (DVT) due to the accompanying vessel trauma, venous stasis, coagulation activation, and older age of most patients. Before thromboprophylaxis was used routinely, DVT, often clinically silent, occurred in 40-60% of these patients. Pulmonary embolism occurred in 5-10%, and fatal embolism, occurring in 1-2% of patients, was the most common cause of death.

Although changes in surgical and anesthetic techniques, and early mobilization, may have reduced the risk of venous thromboembolism, routine thromboprophylaxis remains extremely important and is standard of care. Effective prophylaxis has been shown to reduce the rate of DVT by at least 50%.

Prophylaxis for Hip or Knee Arthroplasty

The following methods of thromboprophylaxis have proven to be effective for total hip or knee arthroplasty:

- a) Low molecular weight heparin (LMWH); simple, once or twice daily SC dosing.
- b) The pentasaccharide, fondaparinux, administered SC once daily, has been shown to be highly efficacious in large trials; simple once daily dosing.
- c) Warfarin in doses to prolong the INR to 2.0 - 3.0; more complex.

The following options are NOT recommended as sole methods of prophylaxis after major orthopedic surgery: low dose unfractionated heparin, aspirin, graduated compression stockings, and intermittent pneumatic compression devices. Intermittent pneumatic compression devices appear to provide some protection, but the evidence is limited, they are probably less effective for proximal than for distal DVT prevention, and are cumbersome, often disliked by patients, and cannot be used after discharge.

Practice Points for Hip and Knee Arthroplasty Thromboprophylaxis

- For both procedures, when venography was used as the end-point in comparative clinical trials, LMWHs were shown to be superior to warfarin.
- Using a venography endpoint, fondaparinux, started 4-8 hours after surgery, was associated with at least 50% fewer asymptomatic DVTs than the LMWH, enoxaparin, started the day after surgery. Some of the improved efficacy with fondaparinux over LMWH may be a result of its earlier initiation.
- Studies using symptomatic thromboembolic endpoints demonstrate that LMWH and warfarin provide similar protection following hip or knee arthroplasty.
- Four meta-analyses have shown a correlation between the prevention of venographic DVT and the prevention of symptomatic DVT.
- Clinically important postoperative bleeding complications are uncommon with both warfarin and low molecular weight heparin; early bleeding may be slightly less with warfarin, presumably because of its delayed onset of action. Fondaparinux appears to have a slightly higher rate of bleeding that is not observed if the initial dose is administered more than 6 hours postoperatively.
- Prophylaxis studies have generally excluded patients with prior DVT and those at high risk of bleeding; therefore, much less is known about the effectiveness and safety of any prophylaxis modality in these patient groups.
- Pre-discharge screening tests for asymptomatic deep vein thrombosis (eg. ultrasound or venography) are not recommended.

Duration of Prophylaxis after Major Orthopedic Surgery

- Prophylaxis should be continued for at least 10 days. Although studies, in which at least 7 days of prophylaxis was used, show a substantial number of asymptomatic thrombi on venography after hospital discharge, studies using clinically important endpoints indicate that few symptomatic thromboembolic events occur.
- Nine randomized trials demonstrate that in-hospital LMWH prophylaxis for approximately 7 days is associated with at least twice as many asymptomatic DVTs, using routine screening venography, as prophylaxis continued for 4–6 weeks. Meta-analyses have also demonstrated a significant reduction in symptomatic thromboembolic events with such post-discharge prophylaxis for about 1 month in hip arthroplasty patients. In smaller numbers of knee arthroplasty patients the reduction in both asymptomatic and symptomatic thromboembolic events with prolonged thromboprophylaxis was of lesser magnitude and not significant.
- At least one study has shown potential benefit with a similar prolongation of warfarin prophylaxis following hip arthroplasty, although another randomized trial found that patients who received oral anticoagulant prophylaxis after discharge from hospital experienced more bleeding than those who received LMWH.
- Therefore, although the optimal duration of post-discharge prophylaxis is not known, most experts now advise continued prophylaxis for 2-6 weeks after hip arthroplasty.

Low Molecular Weight Heparins and Fondaparinux

Dalteparin, enoxaparin, nadroparin, tinzaparin, and fondaparinux have been approved for the prevention of deep vein thrombosis following total hip and/or knee arthroplasty. (The approved indications and dosing for each agent may be found in the CPS. Each also has precautions for usage outlined.)

- Low molecular weight heparins are often initiated preoperatively in Europe. In North America, because of perceived risk of hemorrhage and convenience, they are commonly commenced postoperatively, usually not until the morning following surgery. Initiation of LMWH with half the usual dosage 4 hours or more postoperatively is efficacious after hip arthroplasty without increased bleeding. This regimen showed a significant reduction in distal and proximal DVT compared with warfarin.
- Fondaparinux is commenced at least 6 hours after surgery.
- Heparin-induced thrombocytopenia (HIT) is less common with low molecular weight heparins than with unfractionated heparin. A need for platelet monitoring in patients receiving LMWH, and its frequency, is controversial. Fondaparinux has not been associated with HIT.
- Low molecular weight heparin should be avoided in patients with a prior history of HIT.
- Perispinal hematoma is a rare but serious complication of epidural and spinal anesthesia/analgesia. Its risk may be increased when any anticoagulant thromboprophylaxis is used concurrently. Extreme caution or avoidance of low molecular weight heparin and other antithrombotic agents is recommended shortly after patients have had a traumatic epidural or spinal intervention. For patients receiving ongoing epidural analgesia, antithrombotic agents should be used cautiously. If epidural or spinal analgesia/anesthesia is to be used concurrently with prophylactic doses of a low molecular weight heparin it is recommended:
 1. That introduction of the catheter or needle occur before the patient receives any LMWH;
 2. That the catheter be removed at the nadir of the LMWH anticoagulant effect (just before a dose or at least 10 hours after a BID LMWH dose or at least 20 hours after a once daily LMWH dose); and
 3. That any subsequent LMWH dose be given 2 hours or more after catheter removal.
- Fondaparinux presumptively also carries risks of perispinal hematoma.

Warfarin Prophylaxis

- Give first dose of 5-7.5 mg on the night of surgery (depending on the patient's age and size).
- Elderly patients may be very sensitive to warfarin. Lower initial doses should be considered.
- Warfarin dose should be adjusted daily to achieve, and maintain, an INR of 2.0 - 3.0, preferably within four-days.
- If an epidural catheter is to be removed this should be done when the INR is < 1.2.

Prophylaxis for Hip Fracture

The risk of venous thromboembolism following hip fracture is also very high.

- Thromboprophylaxis recommendations related to hip and knee arthroplasty generally apply to hip fracture as well.
- If surgery is to be delayed, preoperative prophylaxis during this delay is recommended.
- Recommended thromboprophylaxis options for hip fracture patients include: fondaparinux, low molecular weight heparin, and adjusted dose warfarin (INR 2.0-3.0).
- There are few randomized trials of prophylaxis in hip fracture patients. A recent large trial, comparing the LMWH, enoxaparin, with fondaparinux demonstrated 79% fewer proximal and 55% fewer distal DVTs with fondaparinux. As in the elective hip and knee arthroplasty studies, in this trial, the fondaparinux was started earlier (4-8 hours postop) (recommended time 6-8 hours postop) than the LMWH (12-24 hours postop).
- Fondaparinux continued for 28 days after hip fracture reduces the incidence of both venographically demonstrated thrombosis and of symptomatic thrombosis to very low levels. By inference, LMWH and warfarin for a similar period are assumed to be of benefit.
- Prophylaxis is recommended for a minimum of 10 days and until mobilization. Most experts now recommend extended prophylaxis for up to 4 weeks after hip fracture surgery.

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