Prophylaxis of venous thromboembolism in orthopaedic surgery

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Introduction

Factors that promote venous stasis, result in vascular endothelial damage, or promote hypercoagulability contribute to the risk of venous thromboembolism (VTE). In orthopaedic patients not receiving postoperative VTE prophylaxis, deep vein thrombosis (DVT) and pulmonary embolism (PE) occur at a rate of 40–84% and 0.7–30%, respectively [1]. In patients undergoing major orthopaedic surgery (total hip replacement, total knee replacement, hip fracture surgery), prevention is therefore a necessity. The American College of Chest Physicians (ACCP) recommends the use of thromboprophylaxis in patients undergoing major orthopaedic surgery [2] (Table 1).

Thromboprophylaxis with low molecular weight heparins: the outstanding issues

Although LMWHs are highly effective and generally safe in the prevention of VTE in patients undergoing major orthopaedic surgery, there is no general agreement on the optimal dosing schedule. In North America the initial LMWH dose is generally administered 12–24 hours after surgery, but in Europe it is usually administered in the evening (10–12 hours) before surgery. A meta-analysis concluded that preoperative-initiated LMWH was significantly more effective than postoperative-initiated LMWH [3]. In a recent clinical trial, the total and proximal DVT rates among the preoperative (10.7% and

Table 1. ACCP Consensus Conference on antithrombotic prophylaxis in major orthopaedic surgery [2] Number of points
Probability of diagnosis

Recommended prophylaxis

Elective total hip replacement

- LMWH therapy (started 12 h before surgery, or 12 to 24 h after surgery; or half the usual high-risk dose 4 to 6 h after surgery, followed by the usual high-risk dose the following day); or adjusted-dose warfarin therapy (goal INR 2.5; range, 2.0 to 3.0), started preoperatively or immediately postoperatively (all grade 1A)
- Alternative, more complex option: adjusted-dose heparin therapy, started preoperatively (grade 2A)
- Adjuvant prophylaxis with ES or IPC device may improve efficacy (grade 2C)
- Not recommend sole therapy with LDUH, aspirin, dextran, or IPC device)

Elective total knee replacement

- LMWH or adjusted-dose warfarin (goal INR 2.5; range, 2.0 to 3.0) (grade 1A)
- Alternative: optimal use of IPC device (grade 1B)
- Not recommended LDUH (grade 1C+)

Hip fracture surgery

LMWH or adjusted-dose warfarin (goal INR 2.5; range, 2.0 to 3.0) (grade 1B)

- Possible alternative: LDUH (grade 2B)
- Not recommend sole therapy with aspirin (grade 2A)

LMWH=Low molecular weight heparin; INR= international normalized ratio; ES=elastic stockings; IPC=intermittent pneumatic compression; LDUH=low dose unfractionated heparin

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0.8%, respectively) and postoperative (13.1% and 0.8%, respectively) LMWH groups did not differ significantly [4]. Geerts et al. concluded that for most patients receiving LMWH prophylaxis, the initial dose can be administered either before or after surgery but for patients at high risk for bleeding, the initial LMWH dose should be delayed until 12–24 hours after surgery [1]. Regardless of the timing of the initial LMWH dose, the first postoperative dose should be delayed until haemostasis is assured [1].

Likewise, the duration of postoperative prophylaxis after orthopaedic surgery is the subject of much debate. In early trials, thromboprophylaxis was continued for the duration of postoperative hospitalisation (7–14 days) but as the duration of hospitalisation is now much less (often 5 days), this may not provide adequate prophylaxis. Additional work is required to establish the optimal prophylactic regimen.

Clinical experience with bemiparin thromboprophylaxis

As part of the ongoing clinical trial programme the safety and efficacy of different bemiparin regimens in the prevention of VTE have been studied in patients undergoing major orthopaedic surgery. In a large-scale randomised, double-blind trial in 298 high-risk patients scheduled to undergo elective hip arthroplasty, 149 patients received bemiparin (3500 anti-Xa IU) plus a placebo injection and 149 received UFH (5000 IU) twice a day [3]. During the postoperative period, significantly more patients treated with UFH developed symptoms of VTE than in the bemiparin group (7.2 versus 18.7%, $p=0.01$). There were no significant differences in the frequency of bleeding complications and both agents were well tolerated. Antithrombin concentrations, anti-Xa activity and TFPI levels were significantly higher in the bemiparin group postoperatively compared with preoperative levels. Similar levels of DVT (7.0%) were reported in a study in 57 patients undergoing orthopaedic surgery treated with 3500 IU anti-Xa (40 mg) daily starting 6 hours after surgery [3]. No episodes of major bleeding were observed and the incidence of wound haematoma was low. The authors concluded that thromboprophylaxis with bemiparin started 6 hours post-operatively appears to be safe and effective.

Most orthopaedic surgery is now carried out using local or regional anaesthesia and, although these methods offer many advantages, there have been isolated reports of a very small increased risk of haemorrhagic complications associated with epidural and intradural punctures (1:150 000 and 1:220 000, respectively) in patients treated with LMWHs. The risk is so small that medical societies and consensus discussion groups worldwide continue to recommend the use of prophylaxis with LMWHs in patients undergoing epidural/spinal anaesthesia. In order to compare the effects of different thromboprophylactic

regimens, the effects of bemiparin and enoxaparin given pre- and postoperatively were studied in a double-blind, multicentre trial in 381 patients undergoing primary total knee replacement. Patients were randomised to receive subcutaneous injections of either 3500 IU anti-Xa bemiparin in the first 6 hours after surgery or 40 mg of enoxaparin given 12 hours before surgery followed by daily administration for 10 ± 2 days [Editorial note: insert reference for Bemiparin Study group in knee arthroplasty study]. VTE occurred in 53/165 (32.1%) of patients treated with bemiparin and in 62/168 (36.9%) patients receiving enoxaparin. The absolute risk difference was 4.8% in favour of bemiparin (95% CI, -15.1–5.6%, $p=0.02$). The incidence of proximal DVT was 1.8% (3/165) in the bemiparin group and 4.2% (7/168) in the enoxaparin group. Both treatments were well tolerated and the number of major haemorrhagic events was low (3 patients in each group) (Figure 1).

Fig. 1. Incidence of deep vein thrombosis and proximal deep vein thrombosis in patients undergoing total knee replacement treated with bemiparin or enoxaparin

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