Does anticoagulation prevent thrombosis for persons with fractures distal to the hip?

- Evidence-Based Answer
Low-molecular-weight heparin (LMWH) prophylaxis significantly reduces the total incidence of deep venous thrombosis (DVT) for patients with lower-limb fractures managed with surgical fixation and cast immobilization (strength of recommendation [SOR]: A, based on multiple randomized controlled studies [RCTs]). Evidence is insufficient to show whether LMWH specifically reduces the risk of clinically significant DVTs, and recommendations on its use are conflicting (SOR: C, based on expert opinion). Evidence is insufficient to recommend for or against warfarin prophylaxis for DVT in fractures distal to the hip (SOR: C, based on expert opinion).

- Evidence Summary
Thrombotic complications are common in lower-limb fractures. In 1968, a prospective observational study evaluated the natural history of DVT and pulmonary embolism (PE) in tibial fractures treated with open reduction and internal fixation with early mobilization. Seventy-six consecutive patients with 79 tibial fractures were evaluated with venograms, most within 1 month of injury. The overall incidence of thrombosis was 45%. Half were minor, involving 1 to 3 of the paired deep venous trunks of the lower leg without clinical signs of embolism. Twelve patients (16%) had extensive thrombosis, involving 4 to 6 of the deep venous trunks. Three of these had nonfatal PE diagnosed clinically, and 1 had a fatal PE confirmed at autopsy. The mean age of those with extensive thrombosis or PE was 54 years, and these events were uncommon below age 25 years.1

Incidence of DVT and PE was also evaluated in a cohort of 102 unselected patients who underwent operative fixation for lower-limb fractures, excluding patella, ankle, and foot fractures. All underwent venography approximately 9 days after fixation and were followed clinically for 6 weeks. The overall incidence of DVT was 28% (40% with femoral shaft, 43% with tibial plateau, 22% with tibial shaft, and 12% with tibial plateau [distal articular tibia]). Four developed clinical evidence of PE during hospitalization but only 1 had objective confirmation. None of the patients showed clinical evidence of PE as outpatients.2

LMWH prophylaxis significantly reduced thrombosis in patients with lower-limb fractures in 3 out of 4 RCTs. The first RCT evaluated 253 patients with lower-limb fractures immobilized in plaster casts after surgical fixation. Half the patients received subcutaneous LMWH (nadroparin [Fraxiparin], a European LMWH similar to enoxaparin), and half received no thrombosis prophylaxis. Based on compression ultrasound at the time of cast removal (17 days postinjury, on average), the overall DVT incidence was 11%. Six patients (5%) receiving LMWH had DVTs vs 21 (17%) in the control group (number needed to treat [NNT]=8 to prevent 1 DVT detectible by compression ultrasound). Two thirds of patients with DVT were asymptomatic. One third had clinical signs of DVT, including 1 patient diagnosed with PE on clinical grounds. There was no difference in bleeding complications between the treatment groups.3

A second RCT evaluated LMWH (MonoEmbolex, a European LMWH) prophylaxis in 328 outpatients with lower limb injuries, which included fractures, severe contusions, and ligamentous injuries. All were treated nonsurgically with cast immobilization (mean=18.8 days, range=2–72 days) and 176 patients used daily LMWH injections. All underwent Doppler evaluation for leg thromboses after cast removal, and positive results were confirmed with venograms. Overall, there were no DVTs among the LMWH prophylaxis group and 7 DVTs (4.3%) in the group without LMWH prophylaxis (P<.006). Among those with fractures, the untreated DVT rate was 5.9% (vs 0% with LMWH prophylaxis). Those over age 40 who did not use LMWH had a DVT rate of 11.4% (vs 1.7% in younger patients). Without LMWH prophylaxis, casting for more than 10 days approximately doubled the risk of DVT compared with less than 10 days (6.1% vs 3.1%). This study did not report on the anatomic location of DVTs or if they were clinically evident.4

The third RCT evaluated reviparin (another European LMWH) vs placebo in 440 outpatients with lower limb injuries, of whom 293 had fractures. About half had surgical management and all
were treated with a plaster cast or brace for an average of 44 days. Most were ambulatory with crutches. All underwent venography within a week of cast removal. The DVT rate for fracture patients using reviparin was 10.4%, vs 18.2% among those without LMWH prophylaxis (absolute risk reduction=7.8%; NNT=12.8). Three fourths of the DVTs were in distal veins, and 21% of the DVTs in the LMWH patients occurred in deep veins compared with 34% in patients without. Two pulmonary emboli occurred, both in patients without LMWH prophylaxis. The final RCT evaluated tinzaparin (yet another European LMWH) in 300 adult outpatients immobilized in plaster for at least 3 weeks. Most patients (205 out of 300) underwent venography, and the overall DVT rate was 10% (tinzaparin) vs 17% (controls). Among the 150 fracture patients who underwent venography, the DVT rate was 11% (tinzaparin) vs 13% (controls). This difference was not significant, probably due to insufficient numbers. None of the DVTs was clinically detectable. In hip fracture and hip arthroplasty, warfarin and LMWH are both effective in preventing thrombosis. No studies have specifically evaluated warfarin prophylaxis in lower extremity fractures or compared it with LMWH.

- **Clinical Commentary**

**Although LMWH costs more than daily warfarin, it has fewer complications**

LMWH has largely replaced warfarin for DVT prevention in lower extremity fractures in our clinic. Subsequently, screening for warfarin’s drug-drug interactions and measuring the PT/INR levels to adjust patient doses are no longer needed. LMWH provides effective DVT prevention without laboratory monitoring. Even though LMWH costs significantly more than daily warfarin, the complications associated with warfarin use, or no prophylaxis therapy at all, could be substantially greater. We do not typically use prophylactic anticoagulation on ankle fractures, but we do routinely put high-risk patients with tibia, fibula, and femur fractures on aspirin and LMWH. In our experience, we have not had a patient develop a DVT while on LMWH prophylaxis.

**Recommendations from Others**

The American College of Chest Physicians (ACCP) says that LMWH prophylaxis reduces the risk of asymptomatic DVTs and is standard of care in Europe. The ACCP does not recommend thromboprophylaxis for isolated lower extremity fractures in the US because of cost and insufficient evidence of clinically important reduction in venous thromboembolism (VTE). However, ACCP lists unspecified “lower extremity or pelvic fracture” as a risk factor for VTE, and does recommend that trauma patients with at least 1 risk factor for VTE receive thromboprophylaxis. They make no recommendation about the use of warfarin.

**REFERENCES**