Fixed-dose, Subcutaneous, Unfractionated Heparin Effective for VTE

■ **CLINICAL QUESTION:** How safe and effective is fixed-dose subcutaneous unfractionated heparin in the treatment of venous thromboembolism?

■ **BOTTOM LINE:** In this study, fixed-dose weight-adjusted unfractionated heparin (UFH) administered subcutaneously was as safe and effective as low-molecular-weight heparin (LMWH) in the treatment of venous thromboembolism (VTE). Estimated drug costs for a 6-day course are $712 for LMWH and $37 for UFH. Most clinicians will want to see similar results from at least 1 additional well-done clinical trial, including more patients with symptomatic pulmonary embolism, before routinely treating VTE with subcutaneous UFH. (LOE = 1b)

■ **REFERENCE:** Kearon C, Ginsberg JS, Julian JA, et al, for the Fixed-Dose Heparin (FIDO) Investigators. Comparison of fixed-dose weight-adjusted unfractionated heparin and low-molecular-weight heparin for acute treatment of venous thromboembolism. JAMA 2006;296:935-942.

■ **STUDY DESIGN:** Randomized controlled trial (single-blinded)

■ **FUNDING:** Foundation

■ **SETTING:** Outpatient (any)

■ **ALLOCATION:** Concealed

■ **SYNOPSIS:** These investigators randomly assigned (concealed allocation assignment) 708 patients, 18 years or older, with acute VTE to subcutaneous UFH (initial dose of 333 U/kg, followed by a fixed dose of 250 U/kg every 12 hours) or LMWH (dalteparin or enoxaparin, 100 IU/kg every 12 hours). The dose of subcutaneous UFH remained fixed for individual patients and was not changed during treatment as a result of anticoagulation profiles. The diagnosis of VTE included patients with acute deep vein thrombosis of the legs (81%) or symptomatic pulmonary embolism (19%). Oral warfarin was usually started on the same day as heparin in both groups and continued for a minimum of 3 months with doses adjusted to achieve an international normalized ratio (INR) of between 2.0 and 3.0. Heparin was continued for at least 5 days and until the INR was 2.0 or higher for 2 consecutive days. Individuals unaware of treatment group assignment assessed all outcomes, including study eligibility criteria. Follow-up occurred for more than 98% of subjects for 3 months. All eligible and consenting patients underwent final data analysis. The risk of recurrent VTE in the first 3 months after treatment was not significantly different between patients in the UFH group (3.8%) and those in the LMWH group (3.4%). The risk of major bleeding during the first 10 days of treatment was also similar between the UFH group (1.1%) and LMWH group (1.4%). Approximately 70% of patients in both groups received treatment entirely out of hospital. Overall, there were 18 deaths in the UFH group and 22 deaths in the LMWH group (difference not significant). Adverse events were unrelated to whether subjects were subtherapeutic or supratherapeutic.

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