

## Journal Watch

### **Comparison of Low-Molecular-Weight Heparin and Warfarin for the Secondary Prevention of Venous Thromboembolism in Patients With Cancer: A Randomized Controlled Study.**

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#### **Abstract:**

Background The use of warfarin sodium for treating venous thromboembolism in patients with cancer is associated with a significant risk of recurrence and bleeding. The use of low-molecular-weight heparin sodium for secondary prevention of venous thromboembolism in cancer patients may reduce the complication rate.

Objective To determine whether a fixed dose of subcutaneous low-molecular-weight heparin is superior to oral warfarin for the secondary prophylaxis of venous thromboembolism in patients with cancer and venous thromboembolism.

Methods In a randomized, open-label multicenter trial performed between April 1995 and March 1999, we compared subcutaneous enoxaparin sodium (1.5 mg/kg once a day) with warfarin given for 3 months in 146 patients with venous thromboembolism and cancer.

Main Outcome Measure A combined outcome event defined as major bleeding or recurrent venous thromboembolism within 3 months.

Results Of the 71 evaluable patients assigned to receive warfarin, 15 (21.1%; 95% confidence interval [CI], 12.3%-32.4%) experienced one major outcome event compared with 7 (10.5%) of the 67 evaluable patients assigned to receive enoxaparin (95% CI, 4.3%-20.3%;  $P = .09$ ). There were 6 deaths owing to hemorrhage in the warfarin group compared with none in the enoxaparin group. In the warfarin group, 17 patients (22.7%) died (95% CI, 13.8%-33.8%) compared with 8 (11.3%) in the enoxaparin group (95% CI, 5.0%-21.0%;  $P = .07$ ). No difference was observed regarding the progression of the underlying cancer or cancer-related death.

Conclusions These results confirm that warfarin is associated with a high bleeding rate in patients with venous thromboembolism and cancer. Prolonged treatment with low-molecular-weight heparin may be as effective as oral anticoagulants and may be safer in these cancer patients.

#### **Comments:**

Strengths/uniqueness: This is the first published trial directly comparing warfarin and low molecular weight heparin for treatment of thromboembolism in cancer patients. Study strengths include randomization, intention-to-treat analysis, well-balanced groups, and completeness of follow-up. Although physicians and patients were not blinded to treatment assignment, the outcome assessors were unaware of group allocation, reducing the risk of bias.

Weaknesses: Unfortunately, the trial was terminated prematurely due to a slow rate of patient accrual. Although a trend towards fewer major bleeding episodes was observed in the enoxaparin arm, the study had inadequate power to demonstrate a statistically significant difference.

Relevance to Palliative Care: Thromboembolism is a common occurrence in palliative patients, associated with significant morbidity and mortality. As the study was conducted in patients with a life expectancy of greater than three months, some of whom were in remission, the results are not generalizable to patients in the terminal phase of illness. Ultimately, the results of this study are inconclusive, and trials with larger numbers of patients are required. Economic implications must also be considered.