Enoxaparin reduced venous thromboembolism after elective neurosurgery


Question
For patients who have had neurosurgery, does enoxaparin (a low-molecular-weight heparin [LMWH]) used with compression stockings decrease the rate of venous thromboembolism (VTE) better than compression stockings alone?

Design
Randomized, double-blind, placebo-controlled trial.

Setting
7 Italian neurosurgery centers.

Patients
307 consecutive patients (mean age 56 y, 50% women) who were ≥18 years of age with body weight 40 to 120 kg and who had had elective cranial or spinal surgery. Exclusion criteria were abnormal operative bleeding, bleeding disorders, need for anticoagulants or antiplatelet agents, contrast media allergy, renal failure, expected hospital stay < 7 days, or pregnancy. 84% had venography that was adequate for analysis.

Intervention
All patients wore thigh-length commercial compression stockings from the morning of surgery until discharge. 153 patients received enoxaparin, 40 mg subcutaneously once daily starting the day after surgery. 154 patients were allocated to placebo injections. Prophylaxis duration was 8 days.

Main outcome measures
Symptomatic VTE (deep venous thrombosis [DVT] or pulmonary embolism [PE]) confirmed objectively, DVT confirmed by routine venography, and bleeding.

Main results
Patients who received enoxaparin had lower rates of VTE (all DVT or PE) vs 5 in the placebo group, P = 0.04)

Enoxaparin vs placebo up to 8 days after neurosurgery*  

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Enoxaparin</th>
<th>Placebo</th>
<th>RRR (95% CI)</th>
<th>NNT (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PE or DVT</td>
<td>17%</td>
<td>33%</td>
<td>49% (20 to 68)</td>
<td>7 (4 to 10)</td>
</tr>
<tr>
<td>PE or proximal DVT</td>
<td>5%</td>
<td>14%</td>
<td>61% (13 to 83)</td>
<td>12 (6 to 7)</td>
</tr>
<tr>
<td>Overall DVT</td>
<td>17%</td>
<td>32%</td>
<td>48% (18 to 67)</td>
<td>7 (4 to 10)</td>
</tr>
<tr>
<td>Proximal DVT</td>
<td>5%</td>
<td>13%</td>
<td>59% (7 to 82)</td>
<td>13 (7 to 14)</td>
</tr>
</tbody>
</table>

*PE = pulmonary embolism; DVT = deep venous thrombosis. Other abbreviations as defined in Glossary; RRR, NNT, and CI calculated from data in article.

Commentary
This well-done clinical trial complements a similar study by Nurmohamed and colleagues (1). Both studies show that the combination of LMWH and compression stockings are more efficacious at reducing thrombosis and bleeding than stockings alone. These trials are also important because they have set research standards by including many patients and by using routine contrast venography rather than the less sensitive, noninvasive screening tests used in earlier prophylaxis trials in neurosurgery.

A study by Turpie and colleagues (2) showed that sequential compression devices and stockings provided no more protection than stockings alone in a broad spectrum of neurosurgery patients. These 3 trials, therefore, raise concerns about the efficacy of mechanical thromboprophylaxis as the sole method of prevention in these patients.

The studies by Nurmohamed and Agnelli and their colleagues found trends toward increased bleeding with administration of LMWH. Before the combination of LMWH and stockings becomes routine treatment for neurosurgical patients, many more patients must be studied to provide reassurance that clinically important bleeding is not increased by the use of LMWH, particularly when it is started within 24 hours of surgery.

The role of the various prophylaxis options in neurosurgery (LMWH, low-dose unfractionated heparin, compression stockings, pneumatic compression devices, or combinations of anticoagulant and mechanical prophylaxis) remains unclear. While awaiting further studies, we will continue to individualize the prophylaxis for these patients based on the perceived risks for thrombosis and bleeding. For patients at high risk for bleeding, we use compression stockings and delay the initiation of anticoagulant prophylaxis for several days. For patients with increased thromboembolic risk (surgery for malignancy or motor deficit), we use either low-dose unfractionated heparin or LMWH.

References