PREVENTION AND TREATMENT OF VENOUS THROMBOEMBOLISM

International Consensus Statement 2013
Guidelines According to Scientific Evidence

Developed under the auspices of the:

Cardiovascular Disease Educational and Research Trust (UK)
European Venous Forum
North American Thrombosis Forum
International Union of Angiology and
Union Internationale du Phlebologie
Risk of VTE in Neurosurgery Patients

- Incidence of DVT in neurosurgery is approximately 23%\textsuperscript{1-9}
  - Proximal DVT incidence is ~ 5%
- Risk is increased in patients with glioma\textsuperscript{10-15}

### Incidence of DVT * in the Absence of Prophylaxis Neurosurgery

<table>
<thead>
<tr>
<th>Study</th>
<th>Patients (n)</th>
<th>DVT Incidence</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skillman et al, 1978¹</td>
<td>48</td>
<td>11</td>
<td></td>
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<tr>
<td>Cerrato et al, 1978²</td>
<td>50</td>
<td>16</td>
<td></td>
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<tr>
<td>Turpie et al, 1977³</td>
<td>63</td>
<td>12</td>
<td></td>
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<tr>
<td>Turpie et al, 1985⁴</td>
<td>68</td>
<td>12</td>
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<tr>
<td>Turpie et al, 1989⁵</td>
<td>81</td>
<td>16</td>
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<tr>
<td>Zelikovski et al, 1981⁶</td>
<td>20</td>
<td>10</td>
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<tr>
<td><strong>Total</strong></td>
<td><strong>330</strong></td>
<td><strong>77 (23%)</strong></td>
<td><strong>19% to 28%</strong></td>
</tr>
</tbody>
</table>

*Diagnosed by surveillance with objective methods: phlebography, FUT or DUS

VTE Prophylaxis Studies
IPC Compared with No Prophylaxis

- In a RCT which included 161 patients, IPC reduced the incidence of silent DVT compared with no prophylaxis \(^1\)
  - 1.5% vs 23.5% (RR 0.07; 95% CI 0.009 to 0.49)

- Confirmed in a second RCT of 95 patients\(^2\)
  - 8.3% vs 25% (RR 0.33; 95% CI 0.11 to 0.94)

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VTE Prophylaxis Studies
IPC and GEC Prophylaxis

- IPC combined with GEC reduced the incidence of silent DVT compared with no prophylaxis\(^1\)
  - 9% vs 20% (RR 0.45; 95% CI 0.20 to 1.04)

- In a RCT which included 150 patients, calf compression (new mechanical device) + GEC reduced the incidence of DVT compared with GEC alone\(^2\)
  - Asymptomatic DVT: 4% vs. 18.7% (RR 0.21; 95% CI 0.05 to 0.75)
  - Proximal DVT: 2.7% vs. 8.0%
  - Symptomatic DVT: 0% vs. 2.7%

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VTE Prophylaxis Studies
LDUH Versus No Prophylaxis

- A RCT which included 100 patients compared LDUH with no prophylaxis
  - 6% for LDUH vs 34% (RR 0.18; 95% CI 0.05 to 0.56)
  - No increase in hemorrhagic complications

- In a more recent trial Constantini et al failed to show efficacy, but confirmed safety²

Two large RCTs with 604 evaluable patients compared LMWH + GEC with GEC alone$^{1,2}$

- LMWH + GEC was more effective than GEC alone
  - Venographic DVT: 17.9% vs 28.9% (RR 0.62; 95% CI 0.46 to 0.84)
  - Proximal DVT/PE: 5.7% vs 12.0% (RR 0.48; 95% CI 0.27 to 0.83)

- Non-significant trend of increased incidence of major hemorrhage in the LMWH + GEC group
  - 3.4% vs 2.0% (RR 1.73; 95% CI 0.64 to 4.71)

VTE Prophylaxis Studies
LDUH Compared with LMWH

- 150 patients undergoing craniotomy for brain tumor were randomized to LDUH or LMWH in addition to GEC and IPC in both groups\(^1\)
  - 9.3% asymptomatic DVT in both groups
  - Majority of thrombi were confined to the calf

VTE Prophylaxis
LMWH or LDUH Compared with No Prophylaxis

- Meta-analysis of 4 RCTs (827 patients): 3 with LMWH and 1 with LDUH vs. no prophylaxis

  - LMWH or LDUH demonstrated a reduction in the incidence of all DVT:
    - 15.6% vs. 29.0% (RR 0.54; 95% CI 0.41 to 0.70)
    - Reduction in proximal DVT (2 studies; 616 patients): 6.2% vs. 12.5% (RR 0.50; 95% CI 0.30 to 0.84)

  - Safety:
    - Non-significant trend of increased incidence of major hemorrhage from 2.5% to 3.1% (RR 1.23; 95% CI 0.60 to 2.53)
    - Overall bleeding increased from 2.9% to 5.9% (RR 2.0; 95% CI 1.09 to 3.67)

A meta-analysis of 18 RCTs published in 2008 showed that LMWH or IPC were effective in reducing DVT

- LMWH: RR 0.60; 95% CI 0.44 to 0.81
- IPC: RR 0.41; 95% CI 0.21 to 0.78

Pooled rates of intracranial hemorrhage and minor bleeding were higher with LMWH therapy

- 2.1% with LMWH vs. 1.1% with mechanical methods

A 2011 meta-analysis of 6 RCTs published in 2011 included 1170 patients undergoing elective cranial neurosurgery\(^1\)

- Pooled RR was 0.58 (95% CI 0.45 to 0.75)
- Intracranial hemorrhage was more common in heparin cohort, but not statistically significant
- For every 1000 patients who received heparin prophylaxis, 91 VTE events were prevented
- Whereas, 7 intracranial hemorrhages and 28 more minor bleeds occurred

**Author’s Conclusion:** “Heparin prophylaxis for patients undergoing elective cranial neurosurgery reduces the risk of VTE, but may also increase bleeding risks with a ratio of serious or symptomatic VTE relative to serious bleeding that is only slightly favorable”

VTE Prophylaxis Recommendations
Neurosurgery

- IPC in all patients with or without GEC stockings
  - Level of evidence: High

- Addition of LMWH is associated with an increase of efficacy
  - Level of evidence: High

- The use and timing of LMWH administration should be individualized because of increased bleeding risk