

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

Neurosurgery

Chapter 8

Risk of VTE in Neurosurgery Patients

- **Incidence of DVT in neurosurgery is approximately 23%¹⁻⁹**
 - ▶ Proximal DVT incidence is ~ 5%
- **Risk is increased in patients with glioma¹⁰⁻¹⁵**

1. Skillman JJ, et al. Surgery 1978; 83:354-8.

2. Valladares JB and Hankinson J. Neurosurgery 1980; 6:138-41.

3. Turpie AG, et al. Neurology 1977; 27:435-8.

4. Turpie AG, et al. Arch Intern Med 1989; 149:679-81.

5. Turpie AG, et al. Thromb Res 1985; 39:173-81.

6. Agnelli G. Thromb Haemost 1999; 82:925-30.

7. Chan AT, et al. J Thromb Thrombolysis 1999; 8:139-42.

8. Zelikovski A, et al. J Neurosurg 1981; 54:652-4.

9. Cerrato D, et al. J Neurosurg 1978; 49:378-81.

10. Brandes AA, et al. Eur J Cancer 1997; 33:1592-6.

11. Marras LC, et al. Cancer 2000; 89: 640-6.

12. Ruff RL et al. Ann Neurol 1983; 13: 334-6.

13. Walsh DC, et al. Curr Opin Pulm Med. 2001; 7:326-31.

14. Anderson FA, Et al. Haemost Thromb 2001; 86: OC902

15. Semrand TJ, et al. J Neurosurg 2007; 106: 601-8.

Incidence of DVT * in the Absence of Prophylaxis Neurosurgery

Study	Patients (n)	DVT Incidence	95% CI
Skillman et al, 1978 ¹	48	11	
Cerrato et al, 1978 ²	50	16	
Turpie et al, 1977 ³	63	12	
Turpie et al, 1985 ⁴	68	12	
Turpie et al, 1989 ⁵	81	16	
Zelikovski et al, 1981 ⁶	20	10	
Total	330	77 (23%)	19% to 28%

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

1. Skillman JJ, et al. Surgery 1978; 83:354-8.

2. Cerrato D, et al. J Neurosurg 1978; 49:378-81.

3. Turpie AG, et al. Neurology 1977; 27:435-8.

4. Turpie AG, et al. Thromb Res 1985; 39:173-81.

5. Turpie AG, et al. Arch Intern Med 1989; 149:679-81.

6. Zelikovski A, et al. J Neurosurg 1981; 54:652-4.

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 patients²**
 - ▶ 8.3% vs 25% (RR 0.33; 95% CI 0.11 to 0.94)

1. Turpie AG, et al. Neurology 1977; 27:435-8.

2. Skillman JJ, et al. Surgery 1978; 83:354-8.

VTE Prophylaxis Studies

IPC and GEC Prophylaxis

- **IPC combined with GEC reduced the incidence of silent DVT compared with no prophylaxis¹**
 - ▶ 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 alone²**
 - ▶ 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%

1. Turpie AG, et al. Arch Intern Med 1989; 149:679-81.

2. Sobieraj-Teague M, et al. J Thromb Haemost 2012; 10:229-35.

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**

1. Cerrato D, et al. J Neurosurg 1978; 49:378-81.
2. Constantini S, et al. J Neurosurg 2001; 94:918-21.

VTE Prophylaxis Studies

LMWH and/or GEC Prophylaxis

- **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)

1. Nurmohamed MT, et al. Thromb Haemost 1996; 75:233-8.

2. Agnelli G, et al. N Engl J Med 1998; 339:80-5.

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 groups¹**
 - ▶ 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 prophylaxis¹**
 - ▶ 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)

VTE Prophylaxis

Efficacy of LMWH and IPC Devices

- **A meta-analysis of 18 RCTs published in 2008 showed that LMWH or IPC were effective in reducing DVT¹**
 - ▶ 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

VTE Prophylaxis

Heparin Compared with No Prophylaxis

- **A 2011 meta-analysis of 6 RCTs published in 2011 included 1170 patients undergoing elective cranial neurosurgery¹**
 - ▶ 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**