

# 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%<sup>1-9</sup>**
  - ▶ Proximal DVT incidence is ~ 5%
- **Risk is increased in patients with glioma<sup>10-15</sup>**

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 <sup>1</sup>	48	11	
Cerrato et al, 1978 <sup>2</sup>	50	16	
Turpie et al, 1977 <sup>3</sup>	63	12	
Turpie et al, 1985 <sup>4</sup>	68	12	
Turpie et al, 1989 <sup>5</sup>	81	16	
Zelikovski et al, 1981 <sup>6</sup>	20	10	
<b>Total</b>	<b>330</b>	<b>77 (23%)</b>	<b>19% to 28%</b>

\*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 <sup>1</sup>**
  - ▶ 1.5% vs 23.5% (RR 0.07; 95% CI 0.009 to 0.49)
- **Confirmed in a second RCT of 95 patients<sup>2</sup>**
  - ▶ 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 prophylaxis<sup>1</sup>**
  - ▶ 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<sup>2</sup>**
  - ▶ 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 safety<sup>2</sup>**

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<sup>1,2</sup>**
  - ▶ 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 groups<sup>1</sup>**
  - ▶ 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<sup>1</sup>**
  - ▶ 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 DVT<sup>1</sup>**
  - ▶ 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 neurosurgery<sup>1</sup>**
  - ▶ 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**