INFOGRAPHIC

GUIDELINES

European guidelines on peri-operative venous thromboembolism prophylaxis: first update.

Chapter 6: Neurosurgery

Lidia Mora, John G. Gaudet, Federico Bilotta and Nicolas Bruder

European Journal of Anaesthesiology 2024, 41:594-597

Rationale

The reported incidence of venous thromboembolic events (VTE) in neurosurgery is widely variable, due to the high heterogeneity of study designs,^{1,2} and a wide range of surgical procedures and patient risk profiles. Therefore VTE prevention should be individualised, wherever feasible, in patients scheduled for spine or intracranial surgery. Unfortunately, validated risk stratification scales are lacking, and it is not possible to provide general recommendations for this peri-operative risk specifically.³ Moreover, attempts to demonstrate the effectiveness of peri-operative VTE screening strategies in improving outcomes have mainly proved inconclusive.⁴ The risk of permanent neurological sequelae and the need for urgent decompression of a postoperative haematoma generally discourages chemoprophylaxis in the absence of major thromboembolic risk factors.

Spine surgery

Although the reported incidence rates of deep vein thrombosis (DVT) and pulmonary embolism are significantly higher in prospective than in retrospective studies, the diagnostic strategy, the type and timing of thrombo-prophylaxis, the spinal segment involved (cervical or lumbosacral) as well as the invasiveness (minimally invasive vs. open surgery) and the indication for surgery (degenerative vs. oncologic), all seem to affect the perioperative thromboembolic risk.^{1,5,6} Overall, reported incidence rates range between 0 and 11%,^{1,5} but very high rates (up to 36%) are described in patients undergoing

spinal tumour/vertebral metastasis resections or following major spinal procedures such as adult deformity corrections or multiple level decompressions.⁷ Specific patient risk factors include advanced age, active cancer, disability, diabetes mellitus, history of DVT or elevated pre-operative D-dimers, and those arising from surgery include major intra-operative bleeding, long and/or extensive interventions, involving cervical or thoracic levels, spinal trauma, or spinal cancer.^{5,7,8}

Whenever possible, early mobilisation is recommended for all patients.⁹ Whereas the use of mechanical thromboprophylaxis, including graduated compression stockings (GCS) and intermittent pneumatic compression (IPC) does not increase the haemorrhagic risk,^{1,10} optimal dosing and timing (initiation and duration) of chemoprophylaxis remain difficult to establish.^{3,6,7} In the absence of robust evidence and given the implied comorbidity of haemorrhagic complications, especially in the epidural canal, there is no widely accepted consensus on the use of anticoagulants in spinal surgery. In patients at high thromboembolic risk, combined thromboprophylaxis seems beneficial, with IPC initiated pre-operatively and drug-induced preventive anticoagulation started within 24 to 48 h after surgery once correct haemostasis is achieved.^{6,7,10-12} In the absence of renal failure, lowmolecular-weight heparin (LMWH) should be preferred to unfractionated heparin (UFH)¹³ as the latter appears to increase the risk of postoperative bleeding. Neither inferior vena cava filters nor acetylsalicylic acid¹⁴ appear to reduce the risk of VTE.

From the Department of Anaesthesiology, Intensive Care and Pain Clinic, Vall d'Hebron Trauma, Rehabilitation and Burns Hospital, Autonomous University of Barcelona, Barcelona, Spain (LM), CHUV, Lausanne University Hospital (JGG), 'Sapienza' University of Rome, Rome, Italy (FB) and Aix-Marseille University, APHM, Marseille, France (NB)

Correspondence to Lidia Mora, MD, Department of Anaesthesiology, Intensive Care and Pain Clinic, Vall d'Hebron Trauma, Rehabilitation and Burns Hospital, Autonomous University of Barcelona, Barcelona, Spain. E-mail: lidiamoramiquel@gmail.com

0265-0215 Copyright © 2024 European Society of Anaesthesiology and Intensive Care. Unauthorized reproduction of this article is prohibited.

DOI:10.1097/EJA.000000000002009

Intracranial surgery

The risk of VTE following intracranial surgery and nontraumatic haemorrhage is high, and has been repeatedly associated with worse long-term clinical outcomes.¹⁵ Symptomatic DVT occurs with a frequency of 1.2 to 6% and 0.5 to 1.5% for pulmonary embolism but may be higher in patients with specific risk factors such as older age, previous history of VTE, obesity, motor deficit, malignant tumour (glioblastoma) or meningioma,^{2,16} low Karnofsky performance status (KPS < 80), long duration of surgery and length of hospital stay.

Mechanical thromboprophylaxis with or without LMWH or UFH has proved beneficial in patients undergoing intracranial surgery.^{12,13,17} IPC alone may reduce the incidence of DVT by 60%.^{10,12} Although UFH appears to be as effective as LMWH in reducing the risk of thrombosis by 50% (number needed to treat, 6 to 8), it may increase the risk of intracranial haemorrhage which occurs in 1 to 2% postoperatively.¹³ Anti-Xa assays should be used to monitor anticoagulant therapy, as supra-prophylactic levels have been associated with major bleeding in neurosurgical patients.¹⁸ The timing of chemoprophylaxis may also affect the risk of intracranial bleeding, which is the highest within 24 h after surgery. At least one-third of VTE are identified in the first week after surgery.¹⁹ Chemoprophylaxis started 24 to 48 h after intracranial surgery seems to be the best compromise to balance the haemorrhagic and thrombotic risks.

Following nontraumatic intracerebral haemorrhage, the effectiveness of IPC is comparable with other neurosurgical patients (reduction in VTE of 60%). Retrospective studies show that pharmacologic prophylaxis may be safely started within 4 days after haemorrhage to reduce the incidence of VTE without promoting haematoma expansion or rebleeding.²⁰ The prospective CLEAR III trial showed that delayed chemoprophylaxis is associated with an increased risk of VTE events in patients with intraventricular haemorrhage.²¹

Recommendations

- We recommend the peri-operative use of IPC from the beginning of surgery, in patients undergoing moderate-to-high complexity spinal procedures, craniotomy and in patients at risk of bleeding complications (GRADE 1C).
- In patients at high risk of thrombosis, a combination of mechanical and pharmacological prophylaxis is suggested, starting LMWH or UFH in the first 24 h postoperatively and no later than 72 h, provided that the risk of bleeding is ruled out and haemostasis is correct (**GRADE 2B**).
- After nontraumatic intracerebral haemorrhage, provided the volume of intracranial blood is not expanding and haemostasis is correct, it is suggested to start pharmacological prophylaxis 2 to 4 days after the bleeding (**GRADE 2C**).

Five supplementary tables (Appendix 1, http://links.lww. com/EJA/A965; Appendix 2, http://links.lww.com/EJA/ A966; Appendix 3, http://links.lww.com/EJA/A967; Appendix 4, http://links.lww.com/EJA/A968 and Appendix 5, http://links.lww.com/EJA/A969) providing a summary of the literature review and updates since the last edition of the ESAIC Guidelines on Thromboprophylaxis in Neurosurgery section²² are provided. These tables also show the extraction of the most relevant quality assessment data, the level of evidence (LoE), and the SIGN global checklist for the literature citations included in this chapter.

References

- 1 Colomina MJ, Bago J, Perez-Bracchiglione J, *et al.* Thromboprophylaxis in elective spinal surgery: a protocol for systematic review. *Medicine* (*Baltimore*) 2020; **99**:e20127.
- 2 Fluss R, Kobets AJ, Inocencio JF, et al. The incidence of venous thromboembolism following surgical resection of intracranial and intraspinal meningioma. A systematic review and retrospective study. Clin Neurol Neurosurg 2021; 201:106460.
- 3 Douketis JD, Spyropoulos AC, Murad MH, et al. Perioperative management of antithrombotic therapy: an American College of Chest Physicians Clinical Practice Guideline. Chest 2022; 162:e207– e243.
- 4 Dickerson JC, Harriel KL, Dambrino RJ, et al. Screening duplex ultrasonography in neurosurgery patients does not correlate with a reduction in pulmonary embolism rate or decreased mortality. J Neurosurg 2019; **132**:1589–1597.
- 5 Bouyer B, Rudnichi A, Dray-Spira R, *et al.* Thromboembolic risk after lumbar spine surgery: a cohort study on 325 000 French patients. *J Thromb Haemost* 2018; **16**:1537–1545.
- 6 Ellenbogen Y, Power RG, Martyniuk A, et al. Pharmacoprophylaxis for venous thromboembolism in spinal surgery: a systematic review and metaanalysis. World Neurosurg 2021; 150:e144-e154.
- 7 De la Garza Ramos R, Longo M, Gelfand Y, et al. Timing of prophylactic anticoagulation and its effect on thromboembolic events after surgery for metastatic tumors of the spine. Spine (Phila Pa 1976) 2019; 44:E650– E655.
- 8 Zhang L, Cao H, Chen Y, et al. Risk factors for venous thromboembolism following spinal surgery: a meta-analysis. *Medicine (Baltimore)* 2020; 99: e20954.
- 9 Zakaria HM, Bazydlo M, Schultz L, et al. Ambulation on postoperative day #0 is associated with decreased morbidity and adverse events after elective lumbar spine surgery: analysis from the Michigan Spine Surgery Improvement Collaborative (MSSIC). *Neurosurgery* 2020; 87:320–328.
- 10 Pranata R, Deka H, Yonas E, et al. The use of intermittent pneumatic compression to prevent venous thromboembolism in neurosurgical patients-a systematic review and meta-analysis. *Clin Neurol Neurosurg* 2020; **191**:105694.
- 11 Yepes-Nunez JJ, Rajasekhar A, Rahman M, *et al.* Pharmacologic thromboprophylaxis in adult patients undergoing neurosurgical interventions for preventing venous thromboembolism. *Blood Adv* 2020; 4:2798–2809.
- 12 Wang X, Zhang Y, Fang F, et al. Comparative efficacy and safety of pharmacological prophylaxis and intermittent pneumatic compression for prevention of venous thromboembolism in adult undergoing neurosurgery: a systematic review and network meta-analysis. *Neurosurg Rev* 2021; 44:721-729.
- 13 Macki M, Fakih M, Anand SK, et al. A direct comparison of prophylactic lowmolecular-weight heparin versus unfractionated heparin in neurosurgery: a meta-analysis. Surg Neurol Int 2019; 10:202.
- 14 Fiasconaro M, Poeran J, Liu J, et al. Venous thromboembolism and prophylaxis therapy after elective spine surgery: a population-based study. Can J Anaesth 2021; 68:345–357.
- 15 Li J, Wang D, Wang W, et al. In-hospital venous thromboembolism is associated with poor outcome in patients with spontaneous intracerebral hemorrhage: a multicenter, prospective study. J Stroke Cerebrovasc Dis 2020; 29:104958.
- 16 Rizzo SM, Tavakol S, Bi WL, et al. Meningioma resection and venous thromboembolism incidence, management, and outcomes. Res Pract Thromb Haemost 2023; 7:100121.

Eur J Anaesthesiol 2024; 41:594-597



- 17 Agnelli G, Piovella F, Buoncristiani P, et al. Enoxaparin plus compression stockings compared with compression stockings alone in the prevention of venous thromboembolism after elective neurosurgery. N Engl J Med 1998; 339:80-85.
- 18 May CC, Cua S, Smetana KS, et al. Supraprophylactic anti-factor Xa levels are associated with major bleeding in neurosurgery patients receiving prophylactic enoxaparin. World Neurosurg 2022; 157:e357-e363.
- 19 Briggs RG, Lin YH, Dadario NB, *et al.* Optimal timing of postoperative enoxaparin after neurosurgery: a single institution experience. *Clin Neurol Neurosurg* 2021; **207**:106792.
- 20 Chi G, Lee JJ, Sheng S, et al. Systematic review and meta-analysis of thromboprophylaxis with heparins following intracerebral hemorrhage. *Thromb Haemost* 2022; **122**:1159– 1168.
- 21 Investigators CIT. Venous thromboembolism after intraventricular hemorrhage: results from the CLEAR III Trial. *Neurosurgery* 2019; 84:709-716.
- 22 Faraoni D, Comes RF, Geerts W, et al. European guidelines on perioperative venous thromboembolism prophylaxis: neurosurgery. *Eur J Anaesthesiol* 2018; **35**:90–95.

Eur J Anaesthesiol 2024; **41:**594–597

GRAPHICAL ABSTRACT

EUROPEAN GUIDELINES ON PERIOPERATIVE VENOUS THROMBOEMBOLISM PROPHYLAXIS Chapter 6 **FIRST UPDATE** Neurosurgery **Rationale** Incidence of venous thromboembolic events (VTE) in Neurosurgery is variable because of the wide range of surgical procedures and patient risk profiles VTE prevention should be individualised in patients scheduled for spine or intracranial surgery **Spine Surgery Risk Factors Intracranial Surgery Risk Factors** Age • Age · Active cance · Previous history of VTE · Disability · Obesity Diabetes mellitus Motor deficit History of deep venous thrombosis (DVT) Malignant tumour (glioblastoma) or meningioma · Elevated preoperative D-dimers Low Karnofsky Performance Status (KPS < 80) · Major intraoperative bleeding · Long duration of surgery · Long and/or extensive interventions involving cervical or thoracic · Length of hospital stay levels, spinal trauma, or spinal cancer **Becommendations** Perioperative use of Intermittent Pneumatic Compression (IPC) Combination of mechanical and pharmacological prophylaxis is suggested is recommended Moderate to high complexity spine procedures In patients at high risk of thrombosis Craniotomy ┥┥╸ LMWH or UFH Patients at risk of bleeding complications the risk of bleeding is ruled out and haemostasis is correct From the beginning of surgery Grade 1C Start pharmacological prophylaxis in the first 24h post-operatively and no later than 72 \mbox{h} Pharmacological prophylaxis is suggested After nontraumatic intracerebral haemorrhage Grade 2B ES provided the volume of intracranial blood is not expanding and (A) IC haemostasis is correct Start pharmacological prophylaxis 2-4 days after the bleeding Whenever possible, early mobilization is recommended for all patients Grade 2C

Eur J Anaesthesiol 2024; 41:594-597