Slovenian Medical Journal

# Venous thromboembolism prophylaxis in neurosurgical patients – Statements of Department of Neurosurgery and the Department of Vascular Diseases at the University Medical Centre Ljubljana

## Preprečevanje venskih trombembolizmov pri nevrokirurških operacijah – Stališča Kliničnega oddelka za nevrokirurgijo in Kliničnega oddelka za žilne bolezni Univerzitetnega kliničnega centra Ljubljana

Andrej Porčnik,[1] Petra Šinigoj,[2] Roman Bošnjak,[1] Borut Prestor,[1] Alenka Mavri[3]

## Abstract

Venous thromboembolism (VTE) is a common and severe complication of neurosurgical operations. The most effective method of VTE prophylaxis is antithrombotic drugs. However, they can increase the risk of bleeding. Moreover, in the case of intracranial or intraspinal haemorrhage, the consequences are often more severe than the benefit of preventing a potential VTE. Neurosurgical operations differ in the risks of VTE and bleeding. Therefore, the most optimal method of VTE prophylaxis should be used for a specific operation. In the article we present an overview of the existing literature and the position statement that has been developed by a working group from the Department of Neurosurgery and the Department of Vascular Diseases at the University Medical Centre Ljubljana.

## Izvleček

Venski trombembolizmi (VTE) so pogost in resen zaplet po nevrokirurških operacijah. Najbolj učinkovita so pri preprečevanju VTE protitrombotična zdravila, ki pa lahko povečajo tveganje za krvavitev. Posledice morebitne intrakranialne ali intraspinalne krvavitve so pogosto hujše kot korist ob preprečitvi VTE. Ker se nevrokirurške operacije razlikujejo glede tveganja za VTE ali za krvavitev, je treba ob vsaki operaciji uporabiti za konkretni poseg optimalno metodo za preprečevanje VTE. V prispevku so po prikazu obstoječe literature prikazana stališča, ki jih je oblikovala delovna skupina s Kliničnega oddelka za nevrokirurgijo in Kliničnega oddelka za žilne bolezni Univerzitetnega kliničnega centra Ljubljana.

[1] Department of Neurosurgery, Division of Surgery, University Medical Centre Ljubljana, Ljubljana, Slovenia
[2] Department of Hypertension, Division of Internal Medicine, University Medical Centre Ljubljana, Ljubljana, Slovenia
[3] Department of Vascular Diseases, Division of Internal Medicine, University Medical Centre Ljubljana, Ljubljana, Slovenia

**Correspondence / Korespondenca:** Andrej Porčnik, e: andrej.porcnik@kclj.si

**Key words:** venous thromboembolism; neurosurgery; antithrombotics prophylaxis

**Ključne besede:** venski trombembolizmi; nevrokirurgija; antitrombotična profilaksa

**Received / Prispelo:** 19. 11. 2019 | **Accepted / Sprejeto:** 21. 7. 2021

**Cite as / Citirajte kot:** Porčnik A, Šinigoj P, Bošnjak R, Prestor B, Mavri A. Venous thromboembolism prophylaxis in neurosurgical patients – Statements of Department of Neurosurgery and the Department of Vascular Diseases at the University Medical Centre Ljubljana. Zdrav Vestn. 2022;91(3–4):108–16. **DOI:** https://doi.org/10.6016/ZdravVestn.3007

## 1 Introduction

Venous thrombosis (VT) and pulmonary embolism (PE), collectively referred to as venous thromboembolism (VTE), is a common and serious complication of neurosurgery. In the early stage, VTE is accompanied by high mortality and PE is one of the most common causes of mortality in patients treated in hospitals. In the later stages, however, VTE leaves lasting consequences, especially pulmonary hypertension and post-thrombotic syndrome with chronic venous ulcers on the limbs, which significantly reduce the patient's quality of life and trigger high treatment costs.

With appropriate measures, the incidence of VTE in surgical patients can be reduced by an average of two-thirds. Antithrombotic drugs are the most effective in preventing VTE, and while they may increase the risk of bleeding, their benefit has been shown in most surgeries. Neurosurgical procedures are unique in this regard, as the consequences of possible bleeding are often more severe than the benefit of preventing VTE. There is very little research that provides us with high-quality data on the feasibility and prevention of VTE in neurosurgical patients, so the level of evidence in the guidelines published so far is low (1,2). It is important, however, that each neurosurgical department develops its own guidelines for the prevention of VTE (3). In this paper, we present the guidelines prepared for the University Medical Centre Ljubljana by a working group of experts from the Department of Neurosurgery and the Department of Vascular Diseases.

## 2 Neurosurgical procedures and associated risk of bleeding

Neurosurgical procedures are divided into cranial and spinal. The most common cranial neurosurgeries are those on brain tumours, especially gliomas, meningiomas, schwannomas, pituitary adenomas and their metastases. Tumour surgery requires trephination, macroscopic complete resection of the tumour, and very precise haemostasis in its bed. In such procedures, a lot of brain tissue is often exposed, and the tumour is often accessed through the brain parenchyma as well. The same is true for surgeries for intracerebral haematoma. In some, we work mostly in the subarachnoid space; such surgeries are cerebral artery aneurysms (both unruptured and ruptured). All of the described surgeries characteristically take a long time. However, surgeries for epidural and acute subdural haematomas, which also require trephination, take less time and in most cases the brain remains covered by its envelopes. Some surgeries can only be performed with burr hole procedure. Such surgeries are for chronic subdural haematomas, stereotactic needle biopsies for brain lesions, endoscopic procedures to establish communications within the ventricles, insertion of drains into the ventricles and other procedures, as in the case of hydrocephalus, for example. The duration of these surgeries is shorter, and there is less iatrogenic brain injury. The placement of permanent electrodes into the deep brain nuclei (e.g. for the treatment of Parkinson's disease) is also performed with the burr hole procedure; this surgery is performed in the awake state with maintained muscle tone.

The most common spinal neurosurgeries are those on vertebral disk herniation and spinal stenosis, surgeries on spinal tumours, abscesses and haematomas, spinal stabilization, and insertion of a baclofen pump and electrodes for spinal cord stimulation.

Different neurosurgical procedures are associated with different risks of bleeding, depending on the invasiveness of the procedure, type of pathology (risk of bleeding is higher in surgeries on large intraparenchymal tumours), type of approach (approach through the brain parenchyma makes it harder to ensure good haemostasis), and possible patient's increased risk of bleeding. As intracranial and intraspinal space are limited, even minor bleeding can have very serious consequences.

## 3 Risk of venous thromboembolism

Clinical risk factors for VTE are divided into congenital and acquired. Acquired are more common and may be transient or persistent. The most crucial clinical risk factors for VTE include: surgery, injury, immobilization, paresis, cancer and its treatment, previous VTE, age, pregnancy and postpartum period, taking oral contraceptives and hormone replacement therapy, acute illness, heart or respiratory failure, chronic inflammatory bowel disease, nephrotic syndrome, myeloproliferative diseases, paroxysmal nocturnal haemoglobinuria, obesity, smoking, varicose veins, presence of central catheters, dehydration and changes in haemostatic system (e.g. congenital or acquired thrombophilia).

Simultaneous presence of several risk factors increases the chance of developing VTE. Identifying risk factors is important, as they greatly influence the decision on how to prevent VTE, and in the case of VTE, on the choice and duration of treatment.

The occurrence of VTE is crucially influenced by three pathological conditions, which are described as the Virchow's triad: stasis of venous blood flow, changes in blood coagulability, and endothelial injury. These conditions are usually intertwined and thus increase the chance of developing VTE. A single element of the Virchow's triad is present in all clinical risk factors for VTE, and more often, several elements are present at the same time. In neurosurgical patients, blood stasis in the veins occurs during long surgeries, but also due to the development of limb paresis and poor mobility of the patient. In addition, procoagulant factors (e.g. tissue factor) are released from brain tissue during surgery, and in patients with cancer, procoagulant factors are released by cancer cells themselves (1). Tumour tissue growing into the vascular system and tissue damage during surgery lead to endothelial damage. The risk of VTE varies greatly between patients and depends on the clinical characteristics of the patient and the type of surgery. The occurrence of VTE during neurosurgery is most influenced by the presence of malignancy, age of the patient, duration of surgery and the presence of limb paresis (4,5).

## 4 Methods of venous thromboembolism prophylaxis in neurosurgical procedures

Antithrombotic drugs and mechanical methods are available for the prevention of VTE. Regardless of the chosen method of VTE prophylaxis, early patient mobilization as part of early medical rehabilitation and ensuring adequate hydration are crucial.

### 4.1 Antithrombotic drugs

#### 4.1.1 Unfractionated heparin

Preventive dosing of unfractionated heparin at 5,000 units every 8 hours subcutaneously or 5,000 units every 12 hours subcutaneously reduces the incidence of fatal and non-fatal pulmonary embolism by more than 40% (2). However, today, unfractionated heparin has been completely replaced by low-molecular-weight heparins (LMWHs). There are two main reasons: LMWH is dosed only once a day, and the risk of thrombocytopenia is lower than with heparin (6).

#### 4.1.2 Low-molecular-weight heparins

LMWHs are as effective as unfractionated heparin at low prophylactic doses, but at high doses they are more effective than heparin. They reduce the risk of clinical PE and VTE by 70%, but increase the number of complications, mostly bleeding (2).

LMWHs express their anticoagulant effect through inhibition of coagulation factor Xa and factor IIa (thrombin). Inhibition of factor Xa (anti Xa) and factor IIa (anti IIa), and thus the effect of LMWH, depends on the structure and length of heparin chains. The ratio between anti Xa and anti IIa is different for each LMWH and ranges from 2:1 to 4:1 (e.g. for dalteparin: 2.7:1, for enoxaparin: 3.8:1, for nadroparin: 3.5:1). Therefore, individual LMWHs are used for a particular indication only if it has been clinically tested and its efficacy and safety have been demonstrated. The tested and recommended dose must be strictly adhered to. Different LMWHs are not interchangeable (7).

LMWHs are excreted by the kidneys. Impaired renal function may therefore cause LMWH accumulation. Particular care should be taken in elderly patients, patients with diabetes and those at high risk of bleeding (3). In these cases, an anticoagulant drug that is not largely excreted by the kidneys is chosen, or the dose of LMWH is reduced.

#### 4.1.3 Other pharmacological methods

Fondaparinux and direct oral anticoagulants are not used for VTE prophylaxis in neurosurgery because they have not been tested for this purpose. We also do not use aspirin, as it is less effective in preventing VTE than other pharmacological methods, while the risk of bleeding is similar.

### 4.2 Mechanical methods of venous thromboembolism prophylaxis

Mechanical methods of VTE prophylaxis accelerate venous outflow and thus reduce blood stasis in the veins of the lower limbs. Elastic stockings (ES) and intermittent pneumatic compression (IPC) are the most commonly used methods. It is estimated that the use of ES or IPC in surgical patients reduces the risk of developing VT by 50–70%, and their effectiveness in preventing PE has not been unequivocally proven (8-10). In any case, mechanical methods of VTE prophylaxis are less effective than pharmacological ones, but they do not increase the risk of bleeding. Therefore, they are

mainly used immediately after surgery, when the patient is at high risk of bleeding. In patients with significant peripheral arterial disease of the lower limbs, the use of mechanical methods is not recommended due to the possibility of worsening arterial blood flow.

Correct use of mechanical methods is extremely important for their effectiveness. ES should be selected individually and appropriate to the patient's constitution, so as to provide maximum pressure in the ankle area, which gradually decreases up the shin. They should not roll up or slide down as this may cause a clench in individual areas of the leg, increasing the risk of VT. ES may be temporarily removed only for the duration of personal hygiene. An important disadvantage of using ES is the risk of skin changes such as cracks, ulcers and necrosis (8,9).

In order to be effective, the use of IPC must also be constant, at least 22 hours a day (2). Its use can be discontinued for personal hygiene and when standing up during physiotherapy and walking. Some patients tolerate IPC very poorly due to skin irritation and sweating, as well as disturbed sleep with constant buzzing of the air pump.

## 5 Guidelines

### 5.1 Cranial neurosurgical procedures

In large studies, symptomatic VTE occurred in 2–4% of patients after cranial neurosurgery (11-13). The proportion of those who suffered from VTE was significantly higher among patients with primary brain tumours (7.5%) and metastases (19%) (11). Smaller studies have also confirmed the high incidence of VTE in patients with gliomas (3–26%) (14,15). The incidence of asymptomatic VTE was even higher, estimated at 10% using various VTE prevention methods and at more than 20% without prevention (11,16,17). In addition to malignant disease, the occurrence of VTE during cranial neurosurgery is most influenced by the patient's age, duration of surgery and the presence of paresis (4,5,18). Most VTEs appear in the first week after surgery, and their incidence increases with the duration of the procedure (4,19).

Meta-analyses of a small number of mostly older and non-randomized studies have shown that the use of prophylactic doses of unfractionated heparin, LMWH or IPC significantly reduces the incidence of VTE in cranial neurosurgical procedures. At the same time, the combination of pharmacological and mechanical methods of VTE prophylaxis has proven to be more effective compared to the use of solely mechanical methods (20-22). In a small retrospective study, the incidence of VT when using LMWH after neurosurgery was 9.9% and with additional IPC 3.5% (23). A large French retrospective study also confirmed a lower incidence of VT and PE when the use of IPC in the postoperative period was added to the combination of VTE prophylaxis methods (ES and prophylactic dose of LMWH) (24).

The risk of intracranial haemorrhage in patients after cranial neurosurgery without the use of pharmacological methods of VTE prophylaxis was estimated at 1.0–1.5% (12,20,25). The use of prophylactic doses of heparin may increase the risk of intracranial haemorrhage as well as other major haemorrhages. The risk of intracranial haemorrhage was found to have no more than doubled, which was not statistically significant (20-22). In an older meta-analysis, a trend toward higher mortality in patients receiving LMWH after neurosurgical procedure was also observed, but mortality was not due to bleeding and the trend was not statistically significant (22). The occurrence of intracranial haemorrhage is influenced by the time of prophylactic heparin dosing. Taking the medicine before or too early after surgery increases the risk of bleeding (26). Because most intracranial haemorrhages occur within 12 to 24 hours after surgery, the risk of intracranial haemorrhage is lower if prophylactic heparin doses are delayed until satisfactory postoperative haemostasis is established. We must be aware of the fact that the disability of patients significantly increases due to the consequences of intracranial haemorrhage, more than as a result of VTE (2).

There is very little research that provides us with quality data on the feasibility and prevention of VTE in neurosurgical procedures, so the existing foreign recommendations are not entirely uniform either (1,2,27,28). In patients who need neurosurgery for malignant disease, the use of IPC is recommended, and with the establishment of appropriate haemostasis, the introduction of pharmacological prevention of VTE as well. In the case of a shorter cranial neurosurgical procedure for non-malignant disease, the use of only IPC is mostly advised. The use of antithrombotic drugs is not recommended to avoid bleeding (2). In the recommendations for the treatment of critically ill patients, for example, the introduction of prophylactic doses of LMWH is suggested also in patients with stable unoperated intracerebral haematomas, 48 hours after the onset of bleeding, when it is assumed that adequate haemostasis in the haematoma bed is already established (29). These recommendations also advise the introduction of prophylactic doses of LMWH at least 24 hours after treatment of a ruptured aneurysm that caused subarachnoid haemorrhage.

### 5.2 Spinal neurosurgical procedures

Compared to the incidence of VTE in cranial neurosurgical procedures, its incidence is lower in most spinal neurosurgeries. According to a larger US database and meta-analysis of 14 studies, the incidence of VTE within 30 days after spinal surgery and without the use of any method of VTE prophylaxis is about 1.1–1.2% (of which VT 0.7% and PE 0.4 %) (30,31). Active malignancies, long and complicated spinal surgeries (e.g. combined anterior and posterior approach, multi-segment surgeries), previous VTE, age, and poor mobility before and after surgery have been identified as important risk factors that increase the likelihood of VTE after spinal neurosurgical procedure (31-35). In patients requiring spinal surgery due to malignancy, the incidence of VTE was 2.0% and in patients requiring spinal surgery for non-malignant disease, it was 0.5% (32).

The use of mechanical and pharmacological methods has been shown to be effective in preventing VTE (21,31,36). A retrospective study found symptoms of venous thrombosis in only 0.05% of patients after spinal surgery who received LMWH (34). A meta-analysis of studies that involved both the patients after spinal neurosurgery as well as those after cranial neurosurgery showed that the use of IPC was similarly effective as the use of prophylactic doses of LMWH in the prevention of VTE (21).

The incidence of intraspinal haemorrhage when using LMWH has been poorly studied. The data available suggest a low incidence (0.2–0.7%) (34,36,37). However, when bleeding occurs, reoperation may be required or even persistent severe neurological impairments (i.e. neurological deficits) may be expected.

In patients requiring spinal neurosurgery for non-malignant disease, existing foreign recommendations assess the risk of VTE as low (2). Due to the risk of bleeding into the spinal canal when using LMWH, mechanical methods of VTE prevention bring the patient the greatest benefit. It should be borne in mind that IPC, as a mechanical method of VTE prophylaxis, restricts patients in free verticalization. In patients who require spinal neurosurgery due to malignancy or surgery with a combined anterior and posterior surgical approach, the risk of VTE is assessed as moderate and the use of IPC in the postoperative period is recommended. However, when the risk of bleeding into the spinal canal disappears, a prophylactic dose of LMWH is added (2). Early mobilization of the patient after each operation is extremely important.

## 6 The position of the working group of the Department of Neurosurgery and the Department of Vascular Diseases of the University Medical Centre Ljubljana on venous thromboembolism prophylaxis in neurosurgical patients

The risk of VTE was determined according to the type of neurosurgical procedure (neurosurgical procedure with low, moderate or high risk for VTE) and according to the presence of patient characteristics that in themselves increase the risk of VTE (active cancer, including central nervous system tumour, previous VTE, poor mobility before or after surgery, severe limb paresis or plegia). Measures to prevent VTE are presented depending on the degree of the risk of VTE posed by the neurosurgical procedure and taking into account the risk of bleeding into the central nervous system, which, regardless of frequency, may cause severe physical impairment or even death of the patient (Table 1).

### 6.1 Neurosurgical procedures with a low risk for venous thromboembolism

Neurosurgical procedures with a low risk for VTE include non-extensive, non-cancerous spinal neurosurgical procedures (Table 1): lumbar or cervical discectomy, lumbar or cervical laminectomy without stabilization, baclofen pump insertion (despite the presence of spastic para- or tetraplegia), and insertion of electrodes for spinal cord stimulation. These procedures are short, usually lasting from one to two hours and rarely more than three hours. Electrodes for spinal cord stimulation are inserted in the awake state with maintained muscle tone. Most patients who need such surgeries have no mobility problems at the time of admission, they walk independently, and early mobilization is feasible after the surgery. If there are no complications, these patients are fully mobile on the first day after surgery. The leg muscle pump is therefore activated quickly and the venous stasis time is short.

Pharmacological VTE prophylaxis is not recommended in neurosurgical procedures with low risk for VTE and in the absence of patient's characteristics that significantly increase the risk of VTE, as possible bleeding could have serious consequences (Table 1). Early mobilization and physiotherapy are crucial for the patient. As they are hindered by the use of IPC, this method of VTE prophylaxis is not recommended. However,

**Table 1:** Measures taken for venous thromboembolism prophylaxis (VTE) in neurosurgical procedures.

| Neurosurgical procedures | Mechanical VTE prophylaxis | Pharmacological VTE prophylaxis* | Mobilization |
|---|---|---|---|
| **Surgeries with a low risk of VTE:**<br>• lumbar discectomy,<br>• lumbar laminectomy,<br>• discectomy, laminectomy or other uncomplicated cervical spine surgery<br>• insertion of a baclofen pump,<br>• insertion of electrodes for spinal cord stimulation. | • ES after surgery | Not required, except in patients at high risk for VTE**. | zgodnja |
| **Surgeries with a moderate risk of VTE:**<br>• VP shunt insertion or other hydrocephalus surgery,<br>• insertion of electrodes for deep brain stimulation,<br>• chronic subdural haematoma surgery,<br>• acute subdural or epidural haematoma surgery,<br>• thoracic vertebral hernia surgery with transthoracic approach,<br>• cervical or lumbar spine stabilization,<br>• surgery for trigeminal neuralgia,<br>• surgery for spinal abscess or haematoma,<br>• cranioplasty. | • IPC: during and after surgery until mobilization with walking<br>• ES: when the patient does not tolerate IPC | Not required, except in patients at high risk for VTE**. | zgodnja |
| **Surgeries with a high risk of VTE**:<br>• intracranial tumour or abscess surgery,<br>• intracerebral haematoma surgery,<br>• cerebral artery aneurysm surgery,<br>• spine tumour surgery,<br>• extensive cervical or lumbar spine surgery (e.g. with a combined anterior and posterior approach). | • IPC: during and after surgery until mobilization with walking<br>• ES: when the patient does not tolerate IPC | LMWH at a low prophylactic dose ≥ 24 h after surgery*** until discharge. | zgodnja |

Legenda: ES – elastic stockings; IPC – intermittent pneumatic compression; LMWH – low-molecular-weight heparin; VP – ventriculoperitoneal; s.c. – subcutaneous.
* LMWH in a low prophylactic dose: dalteparin (Fragmin) 2.500 IU/24 h s.c., enoxaparin (Clexane) 20 mg/24 h s.c., nadroparin (Fraxiparine) 0,3 ml/24 h s.c., not earlier than 25 hours after surgery.
** High risk for VTE: active malignancy, previous VTE, severe paresis or plegia of the limbs, very limited mobility.
*** LMWH in a low prophylactic dose ≥ 24 hours after surgery, if there are no clinical or imaging evidence of bleeding. Restoration of adequate haemostasis can be expected at least 24 hours after surgery, CT/MRI follow-up examination is desirable, which should not show significant bleeding.

the use of ES after surgery is recommended. Patients with other significant associated risk factors for VTE need pharmacological VTE prophylaxis; the treatment of these patients is the same as in neurosurgical procedures with a high risk for VTE.

## 6.2 Neurosurgical procedures with a moderate risk for venous thromboembolism

These include shorter, non-cancerous and less invasive cranial neurosurgeries and some spinal neurosurgeries (Table 1). Cranial neurosurgical procedures included in this group are: ventricular drain insertion and other hydrocephalus surgeries, surgeries for trigeminal neuralgia, placement of electrodes for deep brain stimulation, chronic and acute subdural haematoma surgeries, and surgeries for epidural haematomas. In such surgeries, the exposure of brain tissue is minimal, and the release of procoagulant factors is therefore small. Most surgeries usually take less than three hours. Only the insertion of electrodes for deep brain stimulation, which mostly takes place in the

awake state with maintained muscle tone, takes longer. Mobilization after surgery is relatively quick. Among the spinal neurosurgical procedures, this group includes surgeries in which it is necessary to stabilize the lumbar or cervical spine, surgeries for thoracic vertebral hernias with access through the chest, and operations for haematoma or spinal cord abscess. These surgeries are longer than most spinal surgeries, and mobilization after spinal haematoma or abscess surgery takes longer than in other spinal surgeries.

In neurosurgical procedures with a moderate risk for VTE and in the absence of patient's characteristics that significantly increase the risk of VTE, the use of IPC without pharmacological prophylaxis is recommended (Table 1). IPC is placed before the start of the procedure and is used until the beginning of the mobilization with walking. If the patient poorly tolerates or rejects IPC, ES is prescribed after surgery. If the patient does not tolerate ES or if it irritates the skin, the use of ES should be discontinued. When inserting electrodes for deep brain stimulation, IPC is placed only after the surgery, as during the surgery the device would interfere with testing the functional status of the patient and monitoring the signals of the basal ganglia.

However, if patients have other significant risk factors for VTE, they need pharmacological VTE prophylaxis. The treatment of these patients is the same as in neurosurgical procedures with a high risk for VTE.

### 6.3 Neurosurgical procedures with a high risk for venous thromboembolism

Cranial neurosurgical procedures with a high risk of VTE include surgeries on intracranial tumours and abscesses, intracerebral haematomas, and cerebral artery aneurysms. Spinal neurosurgeries with a high risk of VTE include spine tumour surgeries and extensive cervical and lumbar spine surgeries (e.g. combined anterior and posterior approaches). These surgeries are characterized by long duration, high level of exposure of brain tissue during surgery, and the hypercoagulable state further caused by procoagulation factors released by cancer cells in the case of malignancy. Mobilization after surgery is also slower in these cases.

In neurosurgical procedures with a high risk of VTE, the use of IPC and LMWH in a lower prophylactic dose (enoxaparin (Clexane), 20 mg/24 hours subcutaneously, or dalteparin (Fragmin), 2,500 IU/24 hours subcutaneously, or nadroparin (Fraxiparine), 2,850 IU (0.3 ml)/24 hours subcutaneously) is recommended. IPC is placed before the surgery. LMWH is introduced after the procedure when proper haemostasis is expected to be established and the risk of bleeding is already reduced, at least 24 hours after surgery. With patients after cranial neurosurgery, it is recommended that a follow-up CT or MRI of the head be performed the day after the surgery. If the examination shows no signs of significant bleeding, LMWH may be administered at a low prophylactic dose and continued until discharge to home care. After the introduction of LMWH, IPC therapy can be stopped when patient's mobilization with walking begins. If LMWH was not introduced during hospitalization (e.g. due to significant bleeding demonstrated by CT or MRI), IPC is continued until complete mobilization or discharge to home care.

### 6.4 Patients already receiving anticoagulant therapy

Patients receiving anticoagulant therapy prior to scheduled neurosurgery should visit a competent anticoagulant clinic at least one week before the procedure. They should have the date of the surgery and a description of the type of procedure with them, so that they can receive instructions for safe discontinuation of anticoagulant therapy and its reintroduction.

## 7 Conclusion

The positions on VTE prophylaxis after neurosurgical procedures were defined in order to ensure the safest and most effective treatment of our patients. In November 2019, the positions were adopted by the Board of Neurosurgery (UMC Ljubljana) and introduced into clinical practice. In the coming years, we plan to carefully assess the effectiveness, safety and consistency of their use. Such an analysis will allow further improvements and an even higher-quality management of patients after neurosurgery.

### Conflict of interest

None declared.

## References


1. Faraoni D, Comes R, Geerts W, Wiles M. ESA VTE Guidelines Task Force. European guidelines on perioperative venous thromboembolism prophylaxis. Eur J Anaesthesiol. 2018;35(2):90-5. DOI: 10.1097/EJA.0000000000000710 PMID: 29112542
2. Gould MK, Garcia DA, Wren SM, Karanicolas PJ, Arcelus JI, Heit JA, et al. Prevention of VTE in nonorthopedic surgical patients: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest. 2012;141(2):e227S-77S. DOI: 10.1378/chest.11-2297 PMID: 22315263
3. Geerts WH, Bergqvist D, Pineo GF, Heit JA, Samama CM, Lassen MR, et al. Prevention of venous thromboembolism: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines (8th Edition). Chest. 2008;133:381S-458S. DOI: 10.1378/chest.08-0656 PMID: 18574271
4. Khaldi A, Helo N, Schneck MJ, Origitano TC. Venous thromboembolism: deep venous thrombosis and pulmonary embolism in a neurosurgical population. J Neurosurg. 2011;114(1):40-6. DOI: 10.3171/2010.8.JNS10332 PMID: 20815694
5. Simanek R, Vormittag R, Hassler M, Roessler K, Schwarz M, Zielinski C, et al. Venous thromboembolism and survival in patients with high-grade glioma. Neuro-oncol. 2007;9(2):89-95. DOI: 10.1215/15228517-2006-035 PMID: 17327573
6. Warkentin TE, Levine MN, Hirsh J, Horsewood P, Roberts RS, Gent M, et al. Heparin-induced thrombocytopenia in patients treated with low-molecular-weight heparin or unfractionated heparin. N Engl J Med. 1995;332(20):1330-5. DOI: 10.1056/NEJM199505183322003 PMID: 7715641
7. Hirsh J, Raschke R. Heparin and low-molecular-weight heparin: the Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy. Chest. 2004;126(3):188S-203S. DOI: 10.1378/chest.126.3_suppl.188S PMID: 15383472
8. Dennis M, Sandercock PA, Reid J, Graham C, Murray G, Venables G, et al.; CLOTS Trials Collaboration. Effectiveness of thigh-length graduated compression stockings to reduce the risk of deep vein thrombosis after stroke (CLOTS trial 1): a multicentre, randomised controlled trial. Lancet. 2009;373(9679):1958-65. DOI: 10.1016/S0140-6736(09)60941-7 PMID: 19477503
9. Roderick P, Ferris G, Wilson K, Halls H, Jackson D, Collins R, et al. Towards evidence-based guidelines for the prevention of venous thromboembolism: systematic reviews of mechanical methods, oral anticoagulation, dextran and regional anaesthesia as thromboprophylaxis. Health Technol Asses. 2005;9(49):iii-iv,ix-x,1-78. DOI: 10.3310/hta9490 PMID: 16336844
10. Urbankova J, Quiroz R, Kucher N, Goldhaber SZ. Intermittent pneumatic compression and deep vein thrombosis prevention. A meta-analysis in postoperative patients. Thromb Haemost. 2005;94(6):1181-5. DOI: 10.1160/TH05-04-0222 PMID: 16411391
11. Chan AT, Atiemo A, Diran LK, Licholai GP, McLaren Black P, Creager MA, et al. Venous thromboembolism occurs frequently in patients undergoing brain tumor surgery despite prophylaxis. J Thromb Thrombolysis. 1999;8(2):139-42. DOI: 10.1023/A:1008915202859 PMID: 10436144
12. Danish SF, Burnett MG, Ong JG, Sonnad SS, Maloney-Wilensky E, Stein SC. Prophylaxis for deep venous thrombosis in craniotomy patients: a decision analysis. Neurosurgery. 2005;56(6):1286-92. DOI: 10.1227/01.NEU.0000159882.11635.EA PMID: 15918945
13. Algattas H, Kimmell KT, Vates GE, Jahromi BS. Analysis of Venous Thromboembolism Risk in Patients Undergoing Craniotomy. World Neurosurg. 2015;84(5):1372-9. DOI: 10.1016/j.wneu.2015.06.033 PMID: 26117085
14. Wong JM, Panchmatia JR, Ziewacz JE, Bader AM, Dunn IF, Laws ER, et al. Patterns in neurosurgical adverse events: intracranial neoplasm surgery. Neurosurg Focus. 2012;33(5):E16. DOI: 10.3171/2012.7.FOCUS12183 PMID: 23116096
15. Marras LC, Geerts WH, Perry JR. The risk of venous thromboembolism is increased throughout the course of malignant glioma: an evidence-based review. Cancer. 2000;89(3):640-6. DOI: 10.1002/1097-0142(20000801)89:3<640::AID-CNCR20>3.0.CO;2-E PMID: 10931464
16. Valladares JB, Hankinson J. Incidence of lower extremity deep vein thrombosis in neurosurgical patients. Neurosurgery. 1980;6(2):138-41. DOI: 10.1227/00006123-198002000-00004 PMID: 7366805
17. Henwood PC, Kennedy TM, Thomson L, Galanis T, Tzanis GL, Merli GJ, et al. The incidence of deep vein thrombosis detected by routine surveillance ultrasound in neurosurgery patients receiving dual modality prophylaxis. J Thromb Thrombolysis. 2011;32(2):209-14. DOI: 10.1007/s11239-011-0583-8 PMID: 21505787
18. Ruff RL, Posner JB. Incidence and treatment of peripheral venous thrombosis in patients with glioma. Ann Neurol. 1983;13(3):334-6. DOI: 10.1002/ana.410130320 PMID: 6303201
19. Ganau M, Prisco L, Cebula H, Todeschi J, Abid H, Ligarotti G, et al. Risk of Deep vein thrombosis in neurosurgery: state of the art on prophylaxis protocols and best clinical practices. J Clin Neurosci. 2017;45:60-6. DOI: 10.1016/j.jocn.2017.08.008 PMID: 28890040
20. Hamilton MG, Yee WH, Hull RD, Ghali WA. Venous thromboembolism prophylaxis in patients undergoing cranial neurosurgery: a systematic review and meta-analysis. Neurosurgery. 2011;68(3):571-81. DOI: 10.1227/NEU.0b013e3182093145 PMID: 21311292
21. Collen JF, Jackson JL, Shorr AF, Moores LK. Prevention of venous thromboembolism in neurosurgery: a metaanalysis. Chest. 2008;134(2):237-49. DOI: 10.1378/chest.08-0023 PMID: 18641095
22. Iorio A, Agnelli G. Low-molecular-weight and unfractionated heparin for prevention of venous thromboembolism in neurosurgery: a meta-analysis. Arch Intern Med. 2000;160(15):2327-32. DOI: 10.1001/archinte.160.15.2327 PMID: 10927730
23. Frisius J, Ebeling M, Karst M, Fahlbusch R, Schedel I, Gerganov V, et al. Prevention of venous thromboembolic complications with and without intermittent pneumatic compression in neurosurgical cranial procedures using intraoperative magnetic resonance imaging. A retrospective analysis. Clin Neurol Neurosurg. 2015;133:46-54. DOI: 10.1016/j.clineuro.2015.03.005 PMID: 25837574
24. Chibbaro S, Cebula H, Todeschi J, Fricia M, Vigouroux D, Abid H, et al. Evolution of Prophylaxis Protocols for Venous Thromboembolism in Neurosurgery: Results from a Prospective Comparative Study on Low-Molecular-Weight Heparin, Elastic Stockings, and Intermittent Pneumatic Compression Devices. World Neurosurg. 2018;109:e510-6. DOI: 10.1016/j.wneu.2017.10.012 PMID: 29033376
25. Hacker RI, Ritter G, Nelson C, Knobel D, Gupta R, Hopkins K, et al. Subcutaneous heparin does not increase postoperative complications in neurosurgical patients: an institutional experience. J Crit Care. 2012;27(3):250-4. DOI: 10.1016/j.jcrc.2011.09.005 PMID: 22226424
26. Dickinson LD, Miller LD, Patel CP, Gupta SK. Enoxaparin increases the incidence of postoperative intracranial hemorrhage when initiated preoperatively for deep venous thrombosis prophylaxis in patients with brain tumors. Neurosurgery. 1998;43(5):1074-81. DOI: 10.1097/00006123-199811000-00039 PMID: 9802851
27. Shaikhouni A, Baum J, Lonser RR. Deep Vein Thrombosis Prophylaxis in the Neurosurgical Patient. Neurosurg Clin N Am. 2018;29(4):567-74. DOI: 10.1016/j.nec.2018.06.010 PMID: 30223969
28. Hansrani V, Khanbhai M, McCollum C. The Prevention of Venous Thromboembolism in Surgical Patient. In: Islam M, ed. Thrombosis and Embolism: from Research to Clinical Practice. Berlin: Springer; 2016.

29. Nyquist P, Jichici D, Bautista C, Burns J, Chhangani S, DeFilippis M, et al. Prophylaxis of Venous Thrombosis in Neurocritical Care Patients: An Executive Summary of Evidence-Based Guidelines: A Statement for Healthcare Professionals From the Neurocritical Care Society and Society of Critical Care Medicine. Crit Care Med. 2017;45(3):476-9. DOI: 10.1097/CCM.0000000000002247 PMID: 28085682

30. Schoenfeld AJ, Herzog JP, Dunn JC, Bader JO, Belmont PJ. Patient-based and surgical characteristics associated with the acute development of deep venous thrombosis and pulmonary embolism after spine surgery. Spine. 2013;38(21):1892-8. DOI: 10.1097/BRS.0b013e31829fc3a0 PMID: 23778367

31. Sansone JM, del Rio AM, Anderson PA. The prevalence of and specific risk factors for venous thromboembolic disease following elective spine surgery. J Bone Joint Surg Am. 2010;92(2):304-13. DOI: 10.2106/JBJS.H.01815 PMID: 20124056

32. White RH, Zhou H, Romano PS. Incidence of symptomatic venous thromboembolism after different elective or urgent surgical procedures. Thromb Haemost. 2003;90(3):446-55. PMID: 12958614

33. Gephart MG, Zygourakis CC, Arrigo RT, Kalanithi PS, Lad SP, Boakye M. Venous thromboembolism after thoracic/thoracolumbar spinal fusion. World Neurosurg. 2012;78(5):545-52. DOI: 10.1016/j.wneu.2011.12.089 PMID: 22381270

34. Gerlach R, Raabe A, Beck J, Woszczyk A, Seifert V. Postoperative nadroparin administration for prophylaxis of thromboembolic events is not associated with an increased risk of hemorrhage after spinal surgery. Eur Spine J. 2004;13(1):9-13. DOI: 10.1007/s00586-003-0642-8 PMID: 14615928

35. Senders ZJ, Zussman BM, Maltenfort MG, Sharan AD, Ratliff JK, Harrop JS. The incidence of pulmonary embolism (PE) after spinal fusions. Clin Neurol Neurosurg. 2012;114(7):897-901. DOI: 10.1016/j.clineuro.2012.01.044 PMID: 22386262

36. Cox JB, Weaver KJ, Neal DW, Jacob RP, Hoh DJ. Decreased incidence of venous thromboembolism after spine surgery with early multimodal prophylaxis: clinical article. J Neurosurg Spine. 2014;21(4):677-84. DOI: 10.3171/2014.6.SPINE13447 PMID: 25105337

37. Strom RG, Frempong-Boadu AK. Low-molecular-weight heparin prophylaxis 24 to 36 hours after degenerative spine surgery: risk of hemorrhage and venous thromboembolism. Spine. 2013;38(23):E1498-502. DOI: 10.1097/BRS.0b013e3182a4408d PMID: 23873245