Therapeutic Anticoagulation After Craniotomies: Is the Risk for Secondary Hemorrhage Overestimated?

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Abstract

Objective  Deep venous thrombosis (DVT) and pulmonary embolism (PE) are major causes of postoperative morbidity and mortality in surgery. However, there is neither a standardized protocol for perioperative prevention of DVT or PE in neurosurgery nor a consensus concerning the management of postoperative DVT or PE after craniotomy in the early postoperative course.

Methods  We retrospectively analyzed management and complications in a group of patients with postoperative DVT or PE after craniotomy between 2006 and 2011 to estimate the risk of secondary hemorrhage under therapeutic anticoagulation. The interval between time of craniotomy and diagnosis of PE or DVT, administered anticoagulation, and the appearance of a clinically relevant secondary hemorrhage were analyzed.

Results  Forty-two patients met the given criteria. Indications for surgery were intracranial tumors (n = 33), aneurysms (n = 5), and hematomas (n = 4). PE or DVT was observed between the first and the 28th postoperative day (median, fifth postoperative day). Therapeutic anticoagulation was performed with enoxaparin or heparin (according to partial thromboplastin time levels). Full heparinization was applied in 30 patients between the second and the 30th postoperative day (median, 12th postoperative day). None of these patients developed a secondary hemorrhage.

Conclusion  The documented differences in the anticoagulative drug used, the drug’s dosage, and the start of medication reflect the lack of a standardized protocol concerning the treatment of postoperative PE or DVT after craniotomy. A more aggressive management regarding the application of anticoagulative drugs after craniotomy may be justified considering the absence of clinically relevant hemorrhages in this study and the life-threatening potential of perioperative DVT or PE.

Introduction

After neurosurgical procedures with long general anesthesia, deep venous thrombosis (DVT) and pulmonary embolism (PE) are major causes of postoperative morbidity and mortality. In untreated control groups of randomized studies after craniotomies, DVT rates exceed 25%.¹ In such patients, clinically evident DVT occurs in 2% to 4%.² PE rates vary between 0.8% and 2%.³,⁴ The efficiency, cost effectiveness, and safety of prophylactically administered anticoagulative drugs after general surgical and neurosurgical procedures have been demonstrated in clinical studies.⁵⁻¹⁰ Furthermore, the
Methods
A consecutive series of patients undergoing craniotomies between 2006 and 2011 with postoperative PE or DVT was retrospectively analyzed regarding demographic attributes, diagnosis, method of perioperative thrombosis prevention, and interval between surgery and PE or DVT. PE and DVT were detected by elevated d-dimer levels, ultrasonography, and lung computed tomography (CT). In addition, the administered anticoagulative medication and its dosage were examined as well as patients’ weight and kidney and liver functions. Secondary hemorrhage was excluded either by uneventful course or by cranial CT. Routine postoperative CT was not performed. The decision for postoperative CT was made individually and after consultation with the surgeon. The surgeon decided on the dosage of the applied anticoagulative drugs depending on the assumed risk for a secondary hemorrhage in each individual case. Subtherapeutic anticoagulation was defined as a dosage higher than prophylactic in contrast to therapeutic heparinization as the standard dosage for treatment of PE or DVT in a nonsurgical setting.

Results
A consecutive series of 42 patients was retrospectively analyzed. Indications for surgery were meningiomas (n = 17), vestibular schwannomas (n = 8), aneurysms (n = 5), gliomas (n = 4), subdural hematomas (n = 3), ependymoma (n = 1), hemangioblastoma (n = 1), brain metastases (n = 1), prolap tinoma (n = 1), and intracerebral hemorrhage (n = 1). A total of 26 patients were female, and 16 were male. Patients’ age ranged from 17 to 80 years (mean, 55 years). None of the patients had a severe impairment of kidney or liver function.

Prevention of postoperative thromboembolism was performed with elastic graduated compression stockings or pneumatic compression boots has been shown to reduce the incidence of DVT after surgical procedures.\(^{11}\) However, a standardized protocol in the perioperative prevention of DVT for neurosurgical procedures is still missing.\(^{12}\) For one, this is because of the fear of secondary hemorrhage, which is supposed to be increased when applying anticoagulative drugs early in the postoperative course. Furthermore, the available literature does not yield a consensus concerning the management of postoperative DVT or PE with therapeutic anticoagulation after craniotomies.
double-blind study, there was no significant postoperative hemorrhage. In a prospective, randomized, double-blind clinical trial revealed the efficacy and safety of enoxaparin and UFH for prophylaxis of venous thromboembolism after brain tumor surgery. However, heparin-induced thrombocytopenia is a potential adverse drug effect of heparin medication with a reported frequency of 0.2% to 5%. A recently published study reviewed the current practice of perioperative prevention of DVT in German neurosurgical departments. There was no homogenous practice in the administration of heparin (UFH, LMWH, or both) and even compression stockings. In general, the risk for secondary hemorrhage under heparin was estimated higher after cranial versus spinal interventions. Heparin application after craniotomy starting during the first 5 days after surgery is assumed to be associated with a high or very high risk for relevant secondary hemorrhage up to 20% of German neurosurgical departments.

Although a retrospective study cannot provide sufficient evidence of higher than prophylactic dosages of anticoagulative drugs being a safe treatment of PE or DVT after craniotomies, our results suggest that the rate of secondary hemorrhages under these circumstances may be overestimated. As studies dealing with prophylactically administered low-dose heparin, no significant postoperative hemorrhages were observed in the present study analyzing therapeutic anticoagulation after craniotomies. Taking into consideration the potential risk for postoperative secondary hemorrhages, the risk-to-benefit ratio for using anticoagulative drugs in therapeutic dosages in patients with PE or DVT after craniotomy may be still favorable for the patient.

Our review of the literature and MEDLINE research revealed no further studies concerning therapeutic anticoagulation in cases of PE or DVT after craniotomies. In general, neurosurgeons hesitate to administer higher than prophylactic dosages of anticoagulative drugs in the early postoperative course after craniotomies. The reasons might be fear of secondary hemorrhages, the lack of clinical studies and accepted protocols in the postoperative management of PE and DVT after craniotomies and medicolegal considerations because LMWH and heparin are not approved after neurosurgical procedures.

The presented study is the first published clinical series of patients with LE or DVT after craniotomy receiving LMWH. The old data of Swann et al. about management of LE or DVT lacks comparability because of the administered anticoagulative substances and the inclusion of patients with spinal disorders. The patient number in this study with DVT or LE after craniotomy was 10, and the delay between surgery and beginning of anticoagulative medication was 8 to 54 days (mean, 26 days). Rebleeding was only observed in a patient.

**Fig. 2** Dosage distribution in the 20 patients receiving higher than prophylactic dosages before postoperative day 7.
without surgery. Ruff et al included more patients but used the same anticoagulative regimen as Swann et al but no LMWH. The prospective study of Gerlach et al reporting on 2823 patients undergoing major and minor intracranial procedures dealt with the prophylaxis of thromboembolic events. The safety of therapeutic heparin administration in patients diagnosed with DVT or PE in the course was not addressed, as in the study of Goldhaber et al and the review article of Epstein.

In 14 patients in the present study, no postoperative CT scans were performed. These patients might have developed secondary hemorrhages. Yet without clinical signs, the radiologic finding of a small secondary hemorrhage would not have had any effects on treatment. Additionally, although limited by the variety of applied substances and their dosages, our data suggest no differences between the used anticoagulative drugs concerning the risk for rebleeding. Consequently, systematic studies are needed to estimate the risk for secondary hemorrhages under therapeutic anticoagulation after craniotomy.

**Conclusion**

The documented differences in the used anticoagulative substance, the start of medication, and the dosage reflect the need for a standardized protocol concerning the treatment of postoperative PE or DVT after craniotomy. Considering there was no secondary hemorrhage in this study and that PE and DVT are potentially life-threatening complications, it may be justified to be more aggressive in the application of anticoagulative drugs after craniotomy. Our observations do not support the assumption of a very high risk for rebleeding with application of heparin in the early days after craniotomy.

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**Conflict of Interest**

None

**References**


