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Deep venous thrombosis and pulmonary embolisms in adult patients undergoing craniotomy for brain tumors

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Abstract

Objective—The development of venothromboembolisms (VTEs), including deep vein thrombosis (DVT) and pulmonary emboli (PE), is common in brain tumor patients. Their development can be catastrophic. Studies evaluating pre-operative clinical factors that predispose patients to the development of VTE are few and limited. An understanding may help risk stratify patients and guide subsequent therapy aimed at reducing the risk of DVTs/PEs.

Methods—All adult patients who underwent surgery for an intracranial tumor at an academic tertiary care institution between 1998 and 2008 were retrospectively reviewed. Stepwise multivariate logistical regression analysis was used to identify pre-operative factors associated with the development of peri-operative (within 30 days of surgery) DVTs/PEs among patients who underwent surgery of their intracranial tumor.

Results—Of the 4293 patients in this study, 126 (3%) patients developed DVT and/or PE in the peri-operative period. The pre-operative factors independently associated with the development of DVTs/PEs were: poorer Karnofsky performance scale (KPS) [odds ratio (OR), 1.040; 95% confidence interval (CI), 1.026–1.052; $P<0.0001$], high grade glioma (OR, 1.702; 95% CI, 1.176–2.465; $P=0.005$), older age (OR, 1.033; 95% CI, 1.020–1.046; $P<0.0001$), hypertension (OR, 1.785; 95% CI, 1.180–2.699; $P=0.006$), and motor deficit (OR, 1.854; 95% CI, 1.244–2.763; $P=0.002$). Eighty six per cent of the patients with DVTs/PEs were treated with either unfractionated or low molecular weight heparin, and 4% of these patients developed intracranial hemorrhage.

Discussion—The present study found that poorer functional status, older age, pre-operative motor deficit, high grade glioma, and hypertension each independently increased the risk of developing peri-operative DVTs/PEs. These findings may provide patients and physicians with prognostic information that may guide therapies aimed at minimizing the development of peri-operative DVTs/PEs.

Keywords

Brain tumor; Deep vein thrombosis; Glioma; Heparin; Pulmonary embolism; Venothromboembolism

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Introduction

Brain tumors have an incidence of about 1 in 10 000 per year, which equates to 20 500 new cases of brain tumors annually in the United States.[1,2] A major complication for brain tumor patients is the development of deep venous thromboses (DVTs) and pulmonary embolisms (PEs).[3–9] The development of DVTs and/or PEs can cause significant problems. These problems range from delaying critical adjuvant therapies including radiation and chemotherapy to catastrophic life threatening complications. An understanding of the clinical risk factors that predispose brain tumor patients to developing DVTs/PEs is poorly understood. This understanding, however, would help risk stratify patients with respect to risk and subsequently guide peri-operative therapy for patients undergoing craniotomy for tumor.

Venous thromboembolisms (VTEs) remain one of the leading causes of death among cancer patients.[10] Patients with brain tumors in particular seem to be at higher risk of developing VTEs.[11] Large-scale studies attempting to identify risk factors that predispose brain tumor patients to developing perioperative VTEs are few and limited. The aims of this study were: (1) to ascertain the incidence of peri-operative DVTs/PEs among patients undergoing craniotomy for brain tumors; (2) to identify risk factors for developing DVTs/PEs among these patients; and (3) to evaluate the incidence of treatment-related complications for patients with newly diagnosed DVTs/PEs.

Methods

Patient selection

Institutional Review Board approval was obtained prior to conducting this study (No. 5299). All adult patients (age >18 years) who underwent surgery (craniotomy or needle biopsy) for tumor at a single academic tertiary-care institution from 1998 to 2008 were recorded. Pathology was determined by a senior neuropathologist in all cases, and the grading criteria were based on the World Health Organization (WHO) classification system.[12,13] Patients with incomplete medical records lacking clinical presentation, magnetic resonance imaging (MRI), and/or hospital course were excluded. Patients who were unable to receive fractionated heparin were also excluded. Additionally, patients with a prior history of DVT and/or PE were excluded. This was carried out to create a more uniform patient population to understand the incidence of DVT/ PE among patients undergoing surgery for tumor.

Recorded variables

The clinical, operative, and hospital course records of the patients who met the inclusion criteria were retrospectively reviewed. The information collected from neurosurgery and neuro-oncology clinical notes included patient demographics, comorbidities, presenting symptoms, neuro-imaging, neurological function, and adjuvant therapy. The Karnofsky performance scale (KPS) index was used to classify patients' pre-operative functional status.[14] A motor deficit was defined as decreased strength, while sensory loss was decreased sensation to light touch as identified by a clinician during a physical exam. A language deficit was defined as any combination of receptive and/or expressive aphasia. The

characteristics that were recorded from MRI included the lesion's size (largest diameter based on T1-weighted images with contrast for enhancing tumors or Fluid Attenuated Inversion Recovery (FLAIR) for non-enhancing tumors), specific lobe involvement, and whether the tumor was supra- or infratentorial.

Goals of surgery

The general aim of surgery in these cases was to achieve gross total resection of the tumor when possible. Subtotal resection was achieved primarily when the tumor involved eloquent brain as confirmed by intra-operative mapping and/or monitoring (awake/speech language mapping, direct cortical motor stimulation, and motor evoked or somatosensory evoked potentials). Biopsy was pursued typically when patients were not considered medically stable for surgical resection. Motor and somatosensory evoked potentials were routinely used in the majority of cases, while surgical navigation (CT and/or MRI wand) was used in all cases after 2001. The surgical time was not available in the charts.

DVT/PE prophylaxis, detection, and treatment

Patients routinely have thigh-high anti-embolism stockings placed on their bilateral lower extremities upon entering the operating room. In addition, sequential compression devices are also placed. These anti-DVT modalities are used throughout their hospital stay, where the thigh-high anti-embolism stockings are on at all times and the sequential compression devices are used while in bed. Subcutaneous heparin (5000 units every eight or 12 hours) is started 24 hours after surgery, and continued while the patients remain in the hospital. Our hospital typically does not administer low molecular weight heparin in the post-operative period for neurosurgical patients. All patients who undergo surgery receive daily physical therapy and are encouraged to mobilize the morning after surgery if they are able to do so.

DVTs and PEs were detected with the use of Doppler ultrasound and CT PE protocol, respectively. Doppler ultrasound was performed when patients had symptoms of swelling, pain, and/or temperature changes in one or both legs. Venography and MRI were not routinely performed. CT PE protocols were used when patient developed signs of shortness of breath, chest pain, tachycardia, tachypnea, and/or oxygen desaturation. These protocol involved use of a spiral or helical CT, with administration of intravenous contrast. In rare circumstances, ventilation-perfusion scans were used when the patient was unable to tolerate contrast usually secondary to contrast allergies or had significantly impaired renal function. Pulmonary angiograms were not routinely used. Patients were followed for 30 days following surgery to detect VTE events.

The majority of patients with DVT/PE were started on intravenous unfractionated heparin after obtaining a head CT without contrast to evaluate for intracranial hemorrhage (ICH). If there was no ICH, intravenous unfractionated heparin was started with an aPTT goal of 50–80 seconds. After heparin levels were therapeutic for 24 hours, coumadin was started and titrated for a goal international normalized ration of 2.0–2.5. Another head CT was performed 24 hours after starting heparin to evaluate for new ICH. In a minority of patients, patients were started on enoxaparin at a weight-based dose of 1 mg/kg every 12 hours, and transitioned to coumadin for an goal international normalized ration of 2.0–2.5.

Statistical analysis

Summary data were presented as mean±standard deviation for parametric data and as median (inter-quartile range) for non-parametric data. For intergroup comparison, Student's *t*-test was used for continuous data and Mann–Whitney *U* test for categorical data. Logistical regression analysis was used to identify pre-operative factors associated with the development of DVT/PE. In this analysis, all variables associated with the development of DVT/ PE in univariate analysis ($P<0.10$) were included into a stepwise multivariate logistical regression analysis. Values with $P<0.05$ were considered statistically significant. All analyses were performed using JMP 9 (SAS Institute, Carey, NC, USA).

Results

Pre-operative characteristics

A total of 4293 out 4537 patients met the inclusion criteria (Table 1). The average age was 51.6±14.7 years at the time of surgery. The median (interquartile range) pre-operative KPS was 80 (80–90), and the major presenting symptoms were headaches in 1251 (29%), motor deficits in 874 (20%), vision deficits in 832 (19%), seizures in 782 (18%), and cognitive deficits in 778 (18%). The average size of the tumor was 3.5±1.8 cm, where the majority of these tumors was located in the supratentorial compartment (88%) and was intra-axial (62%). Pathologically, the majority of these tumors were gliomas (37%), where 948 (22%) were glioblastoma (WHO Grade IV), 283 (7%) were anaplastic (WHO Grade III), and 281 (7%) were WHO Grade II. Additionally, 536 (12%) patients had metastatic tumors, 826 (19%) meningiomas, and 237 (6%) had schwannomas. The majority of patients were positioned supine (82%), while a small number were positioned prone (13%) and park bench (5%). Gross total resection was achieved in 88% of patients. Two hundred and eighty-four (7%) patients underwent needle biopsy.

Incidence of peri-operative DVT/PE

DVT/PEs were detected in 126 (3%) patients within 30 days following surgery. Among these 126 patients, 67% had DVT, 25% had PEs, and 8% had both DVT/ PE. Eighty-one (64%) were treated with heparin, 28 (22%) were treated with enoxaparin, and 92 (73%) patients were transitioned to coumadin, and 17 (13%) had Greenfield filters placed. Five (4%) of the patients with DVT/PE developed an ICH, where four patients were on heparin infusions and one on enoxaparin ($P=0.99$).

Factors associated with the development of peri-operative DVT/PE

In univariate analysis, the factors associated with DVT/PEs were: gliomas, high grade gliomas, intra-axial tumors, frontal tumor location, increasing age, coronary artery disease, diabetes, hypertension, decreased KPS, headaches, motor deficits, language deficit, cognitive deficit, increasing tumor size, and needle biopsy. Some of the factors that were not significantly associated with the development of DVTs/PEs included surgical positioning, pre-operative coronary artery disease, and extent of resection.

In stepwise multivariate analysis, the factors significantly associated with the development of peri-operative DVT/PE were: decreasing KPS [odds ratio (OR), 1.040; 95% confidence

interval (CI), 1.026–1.052; *P*<0.0001], high grade glioma (OR, 1.702; 95% CI, 1.176–2.465; *P*=0.005), older age (OR, 1.033; 95% CI, 1.020–1.046; *P*<0.0001), hypertension (OR, 1.785; 95% CI, 1.180–2.699; *P*=0.006), and pre-operative motor deficit (OR, 1.854; 95% CI, 1.244–2.763; *P*=0.002) (Table 2). Furthermore, KPS and age were subdivided to find which KPS and age had the greatest statistical association in the multivariate model. Among different KPS, KPS≤70 (OR, 1.721; 95% CI, 1.161–2.549; *P*=0.007) had the greatest statistical association with the development of DVT/PE. Among age, ages older than 65 (OR, 1.854; 95% CI, 1.252–2.745; *P*=0.002) had the greatest statistical association with survival.

Discussion

In this study of 4293 patients who underwent intracranial tumor surgery, 126 (3%) patients developed DVT/PEs in the peri-operative period. Patients with poorer pre-operative functional status, high grade gliomas, older age, hypertension, and pre-operative motor deficits were more likely to develop peri-operative DVTs/PEs. Each of these factors increased the risk by almost twofold for developing VTEs. The majority of these patients were treated with unfractionated heparin, and only a small percentage (4%) developed intracranial hemorrhages.

The association between VTE and cancer has been recognized for over 100 years, and currently represents the second leading cause of death in cancer patients.[15] The risk of VTE in cancer patients is frequently multifactorial including inducing vascular endothelial cell damage[16] and releasing pro-coagulants that activate the clotting cascade.[17] Furthermore, the hypercoagulable state is frequently exacerbated by chemotherapeutic drugs, placement of central venous catheters, and patient inactivity.[16] Patients undergoing craniotomy by itself has also been suggested to increase the risk of VTEs.[9,18,19]

Despite the inherent risk of developing VTEs for patients undergoing craniotomy for tumors, studies on the risk of developing VTEs remain few and limited. Prior studies have primarily focused on evaluating the effectiveness of various forms of VTE prophylaxis in patients with brain tumors, including unfractionated and low molecular weight heparin,[20,21] compression devices,[22] and invasive filters.[23] Studies trying to ascertain risk factors for patients undergoing craniotomy for tumor remain unclear. Quevedo *et al.*[4] studied 64 patients with high grade gliomas, and found that patients with paretic arm or leg, or prior history of VTE were more susceptible to developing VTE. Sughrue *et al.*[7] studied 854 patients who underwent meningioma resection, and found serious medical complication in 7% of patients. The risk of any medical complication, where DVT/PE comprised 11% of the complications, was increased in patients older than 65, worsened neurological deficit, hypertension, and/or increased number of cardiac medications.[7] Semrad and colleagues evaluated 9489 patients diagnosed with malignant glioma using the California Cancer Registry, and found that an associated diagnosis of DVT/PE was found in 7.5% of patients.[24] The risks of developing VTE were older age, GBM diagnosis, three or more chronic comorbidities, and neurosur-gery within 61 days.[24] These studies, however, are limited to specific intracranial pathology, do not evaluate the perioperative period, include patients prior history of DVT/PE, and not all patients underwent craniotomy.[4,7,9,24] These

features make it difficult to ascertain risk factors of peri-operative DVT/PE for patients undergoing brain tumor surgery.

In the present study, patients with poorer pre-operative KPS were almost twofold more likely to develop peri-operative VTEs as compared with higher functioning patients. Likewise, patients who presented with pre-operative motor deficit were also more likely to develop VTE.

A lower KPS and pre-operative deficit may make it more difficult for these patients to ambulate, thus predisposing them to developing VTE.[4,16,25] These studies, however, evaluated patients with intracranial and extracranial cancer,[16] only high grade gliomas,[4] and/or examined patients in the post-operative period (months after surgery) during the administration of adjuvant therapy.[25] Nonetheless, patients who present with poor KPS and/or motor deficit should be mobilized early in the post-operative period to minimize their increased risk of VTE.

As with poor pre-operative status, older patients had an increased risk of developing peri-operative VTE. Patients who were older than 65 had an almost twofold increased risk of VTE. This has been documented in all hospitalized patients,[24,26] patients undergoing major surgery,[26] and patients with high grade gliomas.[19,24] Older patients typically are less mobile and have more comorbidities, making them prone to developing VTE. Besides age, patients with hypertension had a twofold increased likelihood of developing VTE.[24,26] Hypertension has been reported previously as an independent predictor of VTE in the general population, although a causal relationship has not been clearly established.[27] Of note, pre-operative heart disease was not identified as an independent risk factor for VTE, suggesting that the increased risk associated with hypertension may be secondary to vascular damage rather than hypertension-induced cardiac disease. Few studies, however, have evaluated the risk of VTE in the peri-operative period for patients with any type of intracranial tumor.

Patients with high-grade gliomas were more likely to develop VTE as compared to the other types of intracranial tumors. Prior studies have studied patients with high-grade glioma in isolation.[4,24] The present study shows that patients harboring high-grade gliomas have an almost twofold increased risk of incurring a peri-operative DVT/PE. Some studies have speculated that malignant gliomas induce hypercoagulability secondary to secretion of pro-thrombotic factors from tumor cells.[28] Patients who are suspected of having high-grade gliomas should undergo early mobilization, post-operative prophylaxis, and/or compression devices to minimize their risk of peri-operative VTEs.

Strengths and limitations

We believe this study provides several useful insights. First, large-scale studies attempting to identify the incidence of peri-operative DVTs/PEs among patients undergoing craniotomy for all types of tumors is limited. Second, an understanding of independent pre-operative factors that predispose to VTEs has yet to be clearly elucidated. Most studies only study certain intracranial pathology, evaluate the risk of VTE in the delayed post-operative period where there are an increased number of confounding variables including adjuvant therapy, steroid therapy, etc., and include patients who did not undergo surgery or tumor resection.

Lastly, this study may provide useful information that may help guide treatment strategies aimed at minimizing VTE for patients harboring brain tumors.

This study, however, has some limitations. One limitation is that these findings only apply to patients undergoing craniotomy for surgery. These findings are not necessarily applicable to patients undergoing needle biopsies of their lesion or those undergoing conservative management of their tumors. This study also only evaluates the development of DVTs/PEs in the perioperative period (within 30 days of surgery) and those without prior history of DVTs/PEs. This was carried out to evaluate the role surgery has on the development of symptomatic VTE, and does not necessarily apply to the prolonged post-operative period, patients with asymptomatic VTE, or those already known to be predisposed to developing DVTs/PEs. It is not the protocol of our institution to conduct surveillance VTE examinations, so the true incidence of peri-operative DVTs/PEs (both symptomatic and asymptomatic) is probably higher. Additionally, this study is not aimed to evaluate the efficacy of different modalities of VTE prophylaxis or treatment. All of the patients in this study received similar multimodality VTE prophylaxis, and the overwhelming majority underwent unfractionated heparin with coumadin therapy. This is, however, not the standard of care everywhere where other treatments include low molecular weight heparin and other agents. Finally, this study is inherently limited by its retrospective design, and, as a result, it is not appropriate to infer direct causal relationships. However, we tried to create a uniform patient population by utilizing a strict inclusion and exclusion criteria, thus providing more relevant information for patients undergoing craniotomy for tumor. We included only patients who underwent surgical procedures of their intracranial tumors, as well as were administered fractionated heparin. In addition, we excluded patients with incomplete medical records, prior history of DVTs/PEs, and pediatric patients. Furthermore, we performed multivariate analyses to control for potential confounding variables. Given these statistical controls and a relatively precise outcome measure, we believe our findings offer useful insights into the development of VTE for patients undergoing surgery of brain tumors. However, prospective studies are needed to provide better data to guide clinical decision-making.

Conclusion

With the rise of incidentally discovered brain tumors as a result of widespread availability of neuroimaging modalities, there will be an expected increase in the number of patients undergoing craniotomy for tumors. Patients harboring brain tumors are known to have an increased risk of developing VTEs. The development of these VTEs can be catastrophic. The findings of this study may help risk stratify patients for developing peri-operative VTEs, and may subsequently guide therapy at minimizing these potentially fatal complications.

References

1. DeAngelis LM. Brain tumors. N Engl J Med. 2001; 344:114–23. [PubMed: 11150363]
2. Jemal A, Murray T, Ward E, Samuels A, Tiwari RC, Ghafoor A, et al. Cancer statistics, 2005. CA Cancer J Clin. 2005; 55:10–30. [PubMed: 15661684]

3. Nates JL, Aravindan N, Hirsch-Ginsberg C, Sizer KC, Kee S, Nguyen AT, et al. Critically ill cancer patients are not consistently hypercoagulable after craniotomy. Neurocrit Care. 2007; 7:211–6. [PubMed: 17968522]
4. Quevedo JF, Buckner JC, Schmidt JL, Dinapoli RP, O'Fallon JR. Thromboembolism in patients with high-grade glioma. Mayo Clinic proceedings. Mayo Clinic. 1994; 69:329–32.
5. Sallah S, Wan JY, Nguyen NP. Venous thrombosis in patients with solid tumors: determination of frequency and characteristics. Thromb Haemostasis. 2002; 87:575–9. [PubMed: 12008937]
6. Schiff D, DeAngelis LM. Therapy of venous thromboembolism in patients with brain metastases. Cancer. 1994; 73:493–8. [PubMed: 8293418]
7. Sughrue ME, Rutkowski MJ, Shangari G, Chang HQ, Parsa AT, Berger MS, et al. Risk factors for the development of serious medical complications after resection of meningiomas. Clinical article. J Neurosurg. 2011; 114:697–704. [PubMed: 20653395]
8. Turpie AG, Gallus A, Beattie WS, Hirsh J. Prevention of venous thrombosis in patients with intracranial disease by intermittent pneumatic compression of the calf. Neurology. 1977; 27:435–8. [PubMed: 558547]
9. 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; 8:139–42. [PubMed: 10436144]
10. Sawaya RE, Ligon BL. Thromboembolic complications associated with brain tumors. J Neurooncol. 1994; 22:173–81. [PubMed: 7745469]
11. Iberti TJ, Miller M, Abalos A, Cavenee WK, Burger PC, Jouvet A, et al. Abnormal coagulation profile in brain tumor patients during surgery. Neurosurgery. 1994; 34:389–94. discussion 394–85. [PubMed: 8190212]
12. Louis DN, Ohgaki H, Wiestler OD, et al. The 2007 WHO Classification of Tumours of the Central Nervous System. Acta Neuropathol (Berl). 2007; 114:97–109. [PubMed: 17618441]
13. Kleihues P, Louis DN, Scheithauer BW, Rorke LB, Reifenberger G, Burger PC, et al. The WHO classification of tumors of the nervous system. J Neuropathol Exp Neurol. 2002; 61:215–25. discussion 226–19. [PubMed: 11895036]
14. Dutta D, Vanere P, Gupta T, Munshi A, Jalali R. Factors influencing activities of daily living using FIM-FAM scoring system before starting adjuvant treatment in patients with brain tumors: results from a prospective study. J Neurooncol. 2009; 94:103–10. [PubMed: 19255726]
15. Noble S, Pasi J. Epidemiology and pathophysiology of cancer-associated thrombosis. Br J Cancer. 2010; 102 (Suppl 1):S2–9. [PubMed: 20386546]
16. Bick RL. Cancer-associated thrombosis. The New England journal of medicine. 2003; 349:109–11. [PubMed: 12853582]
17. Lip GY, Chin BS, Blann AD. Cancer and the prothrombotic state. Lancet Oncol. 2002; 3:27–34. [PubMed: 11908507]
18. Abrahams JM, Torchia MB, McGarvey M, Putt M, Baranov D, Sinson GP. Perioperative assessment of coagulability in neurosurgical patients using thromboelastography. Surg Neurol. 2002; 58:5–11. discussion 11–2. [PubMed: 12361636]
19. Auguste KI, Quinones-Hinojosa A, Gadkary C, Zada G, Lamborn KR, Berger MS. Incidence of venous thromboembolism in patients undergoing craniotomy and motor mapping for glioma without intraoperative mechanical prophylaxis to the contralateral leg. J Neurosurg. 2003; 99:680–4. [PubMed: 14567603]
20. Vitale FV, Rotondo S, Sessa E, Parisi A, Giaimo V, D'Angelo A, et al. Low molecular weight heparin administration in cancer patients with hypercoagulability related complications and carrying brain metastases: a case series study. J Oncol Pharm Pract. 2011; 18:10–6. [PubMed: 21228085]
21. Perry JR, Julian JA, Laperriere NJ, Geerts W, Agnelli G, Rogers LR, et al. PRODIGE: a randomized placebo-controlled trial of dalteparin low-molecular-weight heparin thromboprophylaxis in patients with newly diagnosed malignant glioma. J Thromb Haemost. 2010; 8:1959–65. [PubMed: 20598077]

22. Auguste KI, Quinones-Hinojosa A, Berger MS. Efficacy of mechanical prophylaxis for venous thromboembolism in patients with brain tumors. Neurosurg Focus. 2004; 17:E3. [PubMed: 15633989]

23. Levin JM, Schiff D, Loeffler JS, Geerts W, Agnelli G, Rogers LR, et al. Complications of therapy for venous thromboembolic disease in patients with brain tumors. Neurology. 1993; 43:1111–4. [PubMed: 8170553]

24. Semrad TJ, O'Donnell R, Wun T, Chew H, Harvey D, Zhou H, et al. Epidemiology of venous thromboembolism in 9489 patients with malignant glioma. J Neurosurg. 2007; 106:601–8. [PubMed: 17432710]

25. Brandes AA, Scelzi E, Salmistraro G, Ermani M, Carollo C, Berti F, et al. Incidence of risk of thromboembolism during treatment high-grade gliomas: a prospective study. Eur J Cancer. 1997; 33:1592–6. [PubMed: 9389920]

26. Anderson FA Jr, Spencer FA. Risk factors for venous thromboembolism. Circulation. 2003; 107:I9–16. [PubMed: 12814980]

27. Goldhaber SZ. Risk factors for venous thromboembolism. J Am Coll Cardiol. 2010; 56:1–7. [PubMed: 20620709]

28. Sciacca FL, Ciusani E, Silvani A, Corsini E, Frigerio S, Pogliani S, et al. Genetic and plasma markers of venous thromboembolism in patients with high grade glioma. Clin Cancer Res. 2004; 10:1312–7. [PubMed: 14977830]

Table 1

Pre- and peri-operative characteristics of patients undergoing surgery for an intracranial tumor (study population *n*=4293)

Characteristics	Total number (%)
Pre-operative characteristics	
Age*	51.6±14.7
Comorbidities	
Coronary artery disease	134 (3%)
Congestive heart failure	34 (0.8%)
Atrial fibrillation	64 (1%)
Diabetes	251 (6%)
Hypertension	678 (16%)
Sleep apnea	35 (0.8%)
Obesity	37 (0.9%)
KPS**	80 (80–90)
Presenting symptoms	
Headaches	1251 (29%)
Seizures	782 (18%)
Nausea/vomiting	225 (5%)
Vertigo	368 (9%)
Ataxia	626 (15%)
Motor deficit	874 (20%)
Sensory deficit	554 (13%)
Language deficit	512 (12%)
Vision deficit	832 (19%)
Cognitive deficit	778 (18%)
Tumor type	
Tumor size*	3.5±1.8
Glioma	1576 (37%)
Grade I Glioma	64 (1%)
Grade II Glioma	281 (7%)
Grade III Glioma	283 (7%)
Grade IV Glioma	948 (22%)
Metastatic tumor	536 (12%)
Craniopharyngioma	53 (1%)
Pituitary adenoma	507 (12%)
Meningioma	826 (19%)
Schwannoma	237 (6%)
Ependymoma	60 (1%)
Tumor location	
Extra-axial tumor	1623 (38%)
Frontal lobe	1276 (30%)

Characteristics	Total number (%)
Temporal lobe	566 (13%)
Parietal lobe	596 (14%)
Occipital lobe	132 (3%)
Intraventricular	129 (3%)
Thalamic	59 (1%)
Pineal region	18 (0.4%)
Skull base	298 (7%)
Sellar/suprasellar	597 (14%)
Cerebellar	195 (5%)
Brainstem	28 (0.7%)
Infratentorial	536 (12%)
Patient Positioning	
Supine	3520 (82%)
Prone	558 (13%)
Park bench	215 (5%)
Extent of resection	
Gross total resection	3777 (88%)
Biopsy	284 (7%)
DVT/PE	126 (3%)
DVT	84 (2%)
PE	32 (0.7%)
Both DVT/PE	10 (0.2%)

Notes:

* Mean±standard deviation,

** median (interquartile range).

Table 2

Associations of pre- and peri-operative variables with the development of deep venous thrombosis and/or PE for adult patients undergoing craniotomy for tumor

Stepwise multivariate associations with DVT/PE		
Variables	**Odds ratio (95% CI)**	***P* value**
Poorer KPS	1.040 (1.026–1.052)	<0.0001
KPS≤70	1.721 (1.161–2.549)	0.007
High grade glioma	1.702 (1.176–2.465)	0.005
Older age	1.033 (1.020–1.046)	<0.0001
Age>65	1.854 (1.252–2.745)	0.002
Hypertension	1.785 (1.180–2.699)	0.006
Motor deficit	1.854 (1.244–2.763)	0.002