

Patterns in neurosurgical adverse events: intracranial neoplasm surgery

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Object. Neurosurgery is a high-risk specialty currently undertaking the pursuit of systematic approaches to measuring and improving outcomes. As part of a project to devise evidence-based safety interventions for specialty surgery, the authors sought to review current evidence in cranial tumor resection concerning the frequency of adverse events in practice, their patterns, and current methods of reducing the occurrence of these events. This review represents part of a series of papers written to consolidate information about these events and preventive measures as part of an ongoing effort to ascertain the utility of devising system-wide policies and safety tools to improve neurosurgical practice.

Methods. The authors performed a PubMed search using search terms “intracranial neoplasm,” “cerebral tumor,” “cerebral meningioma,” “glioma,” and “complications” or “adverse events.” Only papers that specifically discussed the relevant complication rates were included. Papers were chosen to maximize the range of rates of occurrence for the reported adverse events.

Results. Review of the tumor neurosurgery literature showed that documented overall complication rates ranged from 9% to 40%, with overall mortality rates of 1.5%–16%. There was a wide range of types of adverse events overall. Deep venous thromboembolism (DVT) was the most common adverse event, with a reported incidence of 3%–26%. The presence of new or worsened neurological deficit was the second most common adverse event found in this review, with reported rates ranging from 0% for the series of meningioma cases with the lowest reported rate to 20% as the highest reported rate for treatment of eloquent glioma. Benign tumor recurrence was found to be a commonly reported adverse event following surgery for intracranial neoplasms. Rates varied depending on tumor type, tumor location, patient demographics, surgical technique, the surgeon's level of experience, degree of specialization, and changes in technology, but these effects remain unmeasured. The incidence on our review ranged from 2% for convexity meningiomas to 36% for basal meningiomas. Other relatively common complications were dural closure-related complications (1%–24%), postoperative peritumoral edema (2%–10%), early postoperative seizure (1%–12%), medical complications (6%–7%), wound infection (0%–4%), surgery-related hematoma (1%–2%), and wrong-site surgery.

Strategies to minimize risk of these events were evaluated. Prophylactic techniques for DVT have been widely demonstrated and confirmed, but adherence remains unstudied. The use of image guidance, intraoperative functional mapping, and real-time intraoperative MRI guidance can allow surgeons to maximize resection while preserving neurological function. Whether the extent of resection significantly correlates with improved overall outcomes remains controversial.

Discussion. A significant proportion of adverse events in intracranial neoplasm surgery may be avoidable by use of practices to encourage use of standardized protocols for DVT, seizure, and infection prophylaxis; intraoperative navigation among other steps; improved teamwork and communication; and concentrated volume and specialization. Systematic efforts to bundle such strategies may significantly improve patient outcomes. (<http://thejns.org/doi/abs/10.3171/2012.7.FOCUS12183>)

KEY WORDS • surgical safety • adverse events • perioperative care

PROGRESS in the science of improving surgical safety has been notable in recent years. Methods for evaluating outcomes have been developed and de-

ployed,^{30,45,46,61,72,81,113} and the data have been used to research patterns of errors and complications. From these findings, solutions have been designed and tested with sometimes striking improvements, whether using simple process tools like checklists^{30,31,51,112} or technological changes.^{48,85,111} Neurosurgery is a high-risk surgical specialty that is beginning to pursue systematic, nationwide

Abbreviations used in this paper: 5-ALA = 5-aminolevulinic acid; DVT = deep venous thromboembolism; ICU = intensive care unit; SCD = sequential intermittent compression device.

approaches to measuring and improving outcomes. As part of a project funded by the US Agency for Healthcare Research and Quality to devise evidence-based checklists and protocols for specialty surgery, we sought to review current evidence in neurosurgery concerning the frequency of adverse events in practice, their patterns, and the state of knowledge about how to improve them. We hypothesized that this consolidation of existing data, even if commonly known to neurosurgeons, will not only highlight the need for devising system-wide policies and safety tools to improve neurosurgical practice but also inform future efforts to develop and implement these tools and policies. This paper reviews the patterns of neurosurgical adverse events in tumor neurosurgery.

Scope of the Problem

According to the Healthcare Cost and Utilization Project, 40,788 procedures were performed for the treatment of benign and malignant intracranial neoplasms in 2009 (<http://hcupnet.ahrq.gov>). Studies focusing on complications specifically related to surgery for intracranial neoplasms are largely single-provider or single-institution series. Documented overall complication rates range from 9.0% to 40% with overall mortality rates of 1.5% to 16%.^{12,17,21,22,32,39,84,94,96,106} Existing data capture outcomes primarily from a limited set of academic institutions presenting selective findings on particular tumor types; they therefore hold inherently uncertain value as an indicator of patient experiences with neurosurgery on a larger scale.

Table 1 summarizes what is known from these data about the types and frequencies of commonly seen adverse events, in order of descending estimated frequency. Results are bound to vary according to the tumor type prevalent at a given institution and patient and surgeon preferences regarding the aggressiveness of the planned resection. Unlike cardiac bypass surgery,³⁶ bariatric surgery,⁵⁹ or other high-risk specialty procedures,^{61,102} there is no national database or registry of outcomes for neurosurgery. Although data from the Surveillance, Epidemiology and End Results national registry have proven useful for analysis of the epidemiology and survival rates of brain tumors,^{23,33,54,83,86} these data do not address surgery-specific outcomes. The National Inpatient Sample has borne several studies relating to neurosurgical outcomes^{8,25,26} but may not be as useful for detailed risk stratification and granular outcomes such as degree of neurological deficit given that the data were not collected specifically for the field.

Nonetheless, among the existing series reviewed, the most commonly reported adverse events are: venous thromboembolism, benign tumor recurrence, new or worsened neurological deficit, dural closure-related complications, postoperative peritumoral edema, early postoperative seizure, medical complications, wound infection, surgery-related hematoma, and wrong-site surgery. Many of these complications are interrelated, and some, particularly benign tumor recurrence, may be considered adverse events rather than preventable complications.

Methods

We performed a PubMed search of the English literature using the search terms “intracranial neoplasm,” “cerebral tumor,” “cerebral meningioma,” “glioma,” AND “complications” OR “adverse events.” Only papers that specifically discussed the relevant complication rates were included. Papers were chosen to maximize the range of rates of occurrence for the reported adverse events rather than to include all possible studies. We did not impose any threshold of minimum patients or publication year; however, we attempted to choose series that were representative of the most common complications. We focused this review on primary brain tumors only.

Venous Thromboembolism

Few studies have carefully assessed occurrences of venous thromboembolism. As malignancy itself is a hypercoagulable state,⁴² thromboembolism rates in tumor neurosurgery are significant, ranging from 3% to 26% even with DVT prophylaxis.^{2,6,14,19,21} Randomized trials have shown significant benefit from use of sequential intermittent compression devices (SCDs) in this patient population.⁹⁹ There is also benefit from low-dose anticoagulation, but guidance is unclear for balancing against increased bleeding risk following surgery for intraaxial lesions.^{14,18,73} Adherence to guidelines for SCD use is unmeasured but likely inconsistent.

New or Worsened Neurological Deficit

Neurological deficit after tumor resection is clearly related to tumor type. Patients with malignant gliomas have a higher rate of new or worsened deficit than those with benign tumors.^{12,17,21,39,94,96,106} For all tumors, more recent studies appear to show improved rates compared with earlier ones, but the source of improvement, whether technological or experiential, is unclear.

Single-institution series suggest that the use of image guidance,^{9,15} intraoperative functional mapping,^{20,27,62,78,92} and real-time intraoperative MRI guidance^{23,74,75,101} can allow surgeons to maximize resection while preserving neurological function and perhaps prolonging survival. In recent years, use of these technologies has increased.

Findings in other surgical fields indicate that greater hospital and/or surgeon volume of experience are associated with better clinical outcomes.^{10,11,49,116} Three studies using the National Inpatient Sample database suggest the same for intracranial tumor surgery.^{8,25,26} There has been a shift in recent decades to encourage subspecialization in training and practice.

Controversy remains regarding the impact of extent of resection on neurological and functional outcome and overall survival, in the treatment of gliomas.^{91,93} For a given glioma, it remains unclear if maximizing extent of resection or minimizing risk to functional tissue should be the optimal goal. Recent data, however, support maximizing resection. In the only randomized controlled trial addressing this issue, Stummer et al.¹⁰³ compared 5-ALA-aided resection to conventional white light microscopic resection in 322 patients with malignant glioma, finding greater radiographically confirmed resection and higher

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TABLE 1: Frequency of adverse events reported in intracranial neoplasm surgery*

AE w/ Author & Year	Sample Size (no. of pts)	Lesion Characteristics	AE Frequency (%)
venous thromboembolism			
Brandes et al., 1997	77	glioma	26
Agnelli et al., 1998	307	mixed	25
Chan et al., 1999	497	mixed	10
Chang et al., 2003	499	glioma	5 (1st), 8 (repeat)
Auguste et al., 2003	180	glioma	3
new or worsened neurological deficit			
Talacchi et al., 2010	171	eloquent glioma	20
Fadul et al., 1988	213	glioma	20
Sawaya et al., 1998	400	mixed	9
Chang et al., 2003	499	glioma	8 (1st), 18 (repeat)
Ciric et al., 1987	42	glioma	7
Black et al., 1998	57	meningioma	5
Cabantog & Bernstein, 1994	207	mixed	3
Sanai et al., 2010	141	meningioma	0
benign tumor recurrence			
Oya et al., 2011	39	sphenoorbital meningioma	18
Simpson, 1957	50	basal	13 (Grade II), 36 (Grade I)
Simpson, 1957	154	convexity/parasagittal/intraventricular	17 (Grade II), 3–5 (Grade I)
Nakamura et al., 2007	82	olfactory groove meningioma	5
Sanai et al., 2010	141	convexity meningioma	4
Morokoff et al., 2008	163	convexity meningioma	2
Obeid & Al-Mefty, 2003	15	olfactory groove meningioma	0
dural closure-related complications			
Duz et al., 2008	93	transphenoidal	24
Laws et al., 1985	158	transphenoidal	6
Sade et al., 2011	439	meningioma	3
Fatemi et al., 2008	881	transphenoidal	2
Barker et al., 2003	5497	transphenoidal	1
Sanai et al., 2010	141	meningioma	1
postop peritumoral edema			
Ciric et al., 1987	42	glioma	10
Cabantog & Bernstein, 1994	207	mixed	8
Black et al., 1998	57	meningioma	2
early postop seizure			
De Santis et al., 2002	200	mixed	12
De Santis et al., 1996	49	mixed	11
Zachenhofer et al., 2011	78	mixed	3
Sughrue et al., 2011 ¹⁰⁴	180	meningioma	1
medical complications			
Sughrue et al., 2011 ¹⁰⁵	834	meningioma	7
Sawaya et al., 1998	400	mixed	7
Black et al., 1998	57	meningioma	6
wound infection			
Sanai et al., 2010	141	meningioma	4
Hardy et al., 2010	2485	mixed	2
Sawaya et al., 1998	400	mixed	1
Chang et al., 2003	499	glioma	0.5 (1st), 1 (repeat)

(continued)

TABLE 1: Frequency of adverse events reported in intracranial neoplasm surgery* (continued)

AE w/ Author & Year	Sample Size (no. of pts)	Lesion Characteristics	AE Frequency (%)
surgery-related hematoma			
Chang et al., 2003	499	glioma	2 (1st), 4 (repeat)
Taylor et al., 1995	2305	mixed	2
Romani et al., 2009	656	meningioma	2
Sanai et al., 2010	141	meningioma	1
Palmer et al., 1994	6668	tumor & other	1
wrong-site surgery			
Cohen et al., 2010	35 cases†	NA	NA

* AE = adverse event; NA = not applicable; pts = patients.

† Case reports.

6-month progression-free survival in the 5-ALA group. Of note, the 5-ALA group experienced greater immediate postoperative neurological decline, but this difference became nonsignificant at 7 days. Multiple other series support maximization of resection for better perioperative neurological outcome, longer overall survival, or both.^{22,57,65,109} However, there are also data suggesting that extent of resection is not correlated with neurological outcome.^{96,106}

Benign Tumor Recurrence

The recurrence of tumors with benign histology is not avoidable even in the best of hands. Nonetheless, it is a commonly occurring adverse event with various causes worthy of discussion.

Recurrence rates vary depending on tumor location, patient demographics, and surgical technique. McDermott's group reported on 141 convexity meningioma patients having 4% radiographical evidence for recurrence with 2% proceeding to repeat resection,⁹⁴ correlating with Simpson's results in 1957.⁹⁸ Meningiomas in more difficult locations such as those at the skull base have higher and more varied rates of recurrence, depending on the surgeon, tumor location, and Simpson grade. For example Al-Mefty, Samii, and Lee report rates of 0% (with short duration of follow-up) to 18%.^{71,77,79} Like rates of postoperative neurological deficit, recurrence rates are affected by surgical technique, surgeon's level of experience, specialization, and changes in technology such as adjunctive stereotactic radiosurgery, but these effects remain unmeasured.

Dural Closure–Related Complications

Dural closure–related complications are rare but serious. Cerebrospinal fluid leak occurs with the highest frequency following transsphenoidal operations, with rates ranging from 1% to 24%,^{8,35,40,66} and is also a significant concern after tumor resection at the skull base where dural repair can be technically challenging. This complication occurs with lower frequency in other neurosurgical procedures. A series of 439 meningioma cases was reviewed by Lee and colleagues, who reported rates of 0.4% for CSF leak; 2.3% for graft-related complications

such as chemical meningitis, cerebritis, and accumulation of extraaxial fluid; and 0.9% for infectious complications.⁹⁰ Similarly, Sanai et al.⁹⁴ found a 1.4% rate of CSF leak following convexity meningioma resection. Different strategies, including use of autologous versus nonautologous graft types, and variation with respect to suture type, postclosure sealants, and use of postoperative lumbar drainage to reduce these complications are debated but are nonetheless advocated by various authors.¹

Postoperative Peritumoral Edema

Rates of postoperative peritumoral edema appear significant, particularly in patients with intraaxial tumors, but no dedicated studies quantify such risk. Retrospective series show rates ranging from 7.7% to 9.5% for the percentage of patients experiencing symptomatic postoperative edema. Most of these patients underwent resection for glioma.^{17,22} In patients undergoing meningioma resection, postoperative edema rates are lower.¹²

Steroids are routinely given perioperatively to reduce peritumoral edema, as first described by Galicich in 1961.⁴⁴ Indeed, in Cabantog and Bernstein's 1994 series, the neurological deficits improved after addition of postoperative steroids to their protocol.¹⁷ Serious steroid medication errors have been observed, however, although the frequency has not been measured. These errors include inadvertent failure to begin steroids, failure to cease or taper the dose of the steroids, and failure to protect against their well-recognized complications.^{37,68,69} Methods for reduction of complications or errors may include use of electronic physician order entry, decision-support, and pharmacist review.⁵⁵

Intraoperatively, the surgeon must optimize patient head and body positioning to maximize venous drainage from the brain, thereby minimizing tumor edema.⁶⁰ Positioning also holds important implications for the anesthesiologist.⁸⁹

Other strategies are less well established or proven but commonly include elevation of the head of the patient's bed, maintaining expired carbon dioxide in a low-normal range postoperatively,¹¹⁰ and/or intraoperative^{3,53} and perioperative⁵⁶ CSF drainage. Adherence to these practices is variable. Unintended compromise of the

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brain's arterial or venous supply also exacerbates postoperative edema and is surgeon dependent.

Early Postoperative Seizure

Early postoperative seizures are thought to occur at a frequency between 1% and 12% for all intracranial tumors, with the greatest risk in the first 48 hours after surgery.^{29,64} Although the use of postoperative antiepileptic agents has not been definitively shown to prevent postoperative seizures, the majority of neurosurgeons routinely use them in the immediate perioperative period. Using perioperative levetiracetam for patients undergoing resection of supratentorial intraaxial tumors, Zachenhofer et al.¹¹⁷ observed a reduction in the percentage of patients with seizures from 38.5% preoperatively to 2.6% in the early postoperative period. With use of phenytoin in 49 patients with various tumors, a postoperative seizure rate of 10.6% was observed, which appeared to be an improvement over previous experience.²⁸ Conversely, Sughrue et al.¹⁰⁴ retrospectively analyzed 180 cases involving patients who underwent convexity meningioma resection and found no difference in seizure rates between those who received prophylactic anticonvulsant medication and those who did not. A randomized trial has not been published.

The one clear error associated with prophylactic anticonvulsant use is prescribing these agents for prolonged periods, due to risk of myelosuppression and drug interactions.⁴⁷ One single-center study reveals, however, that despite national practice guidelines recommending restriction of prophylactic antiepileptic drugs to a 1-week course, 68% of patients were erroneously prescribed antiepileptic drugs for extended periods—in some cases, indefinitely.⁶⁷

Use of increasingly popular minimally invasive techniques, including the endoscopic endonasal approach, will likely reduce the incidence of early postoperative seizures in patients whose tumors can be treated with these techniques,⁶³ though randomized studies may not be feasible.

Medical Complications

The most common medical complications observed in large series are pneumonia, followed by renal dysfunction and arrhythmia, and the incidence rates do not appear to vary according to tumor histology.^{4,12,17,21,32,96,105,106} Neurological deficit is strongly associated with the development of medical complications.¹⁰⁵

Common strategies recommended in the surgical literature include use of intraoperative checklists,⁵¹ perioperative screening protocols and medical optimization,⁴¹ ICU quality improvement interventions,⁹⁷ and hospitalist consultation,⁸⁸ but these strategies remain unexplored specifically in the neurosurgical literature.

Wound Infection

Patients with tumors are particularly susceptible to surgical-site infection, because many are immunosuppressed from steroid use and/or chemotherapy and because many have extensive soft-tissue changes from radiation therapy.^{5,52,76} Overall surgical-site infection rates

in tumor resection are not documented in the literature but appear to be significant. Rates of infection range from 0.5% to 4% in removal of intra- and extraaxial lesions.^{21,50,94,96} Although the role of prophylactic antibiotics in cranial neurosurgery was debated after its initial use by Cairns in 1947,⁸² more recent data strongly support timely prophylactic antibiotic use in this patient population.^{7,13,16,34,43,95,108} Additionally, broader surgical guidelines support methods such as maintaining intraoperative normothermia, appropriate methods of hair removal, confirmation of proper asepsis, and antisepsis of skin and instruments.¹¹⁵ The Surgical Care Improvement Project has been implemented and has reported on specific procedural groupings with good effect,¹⁰² but the results have not yet been incorporated into neurosurgical data. In neurosurgery, use of an endoscopic approach for certain lesions may be beneficial⁶³ but has not been evaluated prospectively.

Surgery-Related Hematoma

Postoperative hemorrhage is a significant and potentially devastating concern. Overall rates range from 1.1% to 4.4%.^{21,80,87,94,107} Eighty-eight percent of these hemorrhages occurred within the first 6 hours after surgery.¹⁰⁷

Options commonly employed to minimize the risk of postoperative hematoma include meticulous intraoperative hemostasis, use of absorbable topical hemostatic agents,³⁸ technical maneuvers including peripheral and central tack-up stitches,⁵³ minimization of postoperative hypertension and fluid shifts,¹⁰⁰ and judicious use of perioperative antithrombotic prophylaxis. No convincing randomized studies have been done on this topic, however. One of the most important preventive measures for this event is correction of coagulopathy and early discontinuation of antiplatelet and anticoagulation therapy preoperatively. There are also strategies to recognize bleeding early enough to avert mortality or new deficit, including vigilant neurological monitoring and routine postoperative imaging for high-risk patients.⁵⁸

Wrong-Site Surgery

Cohen et al.²⁴ described wrong-site surgery as perhaps “the most regrettable and egregious error a surgeon can commit.” These cases are persistent and often highly publicized. Their analysis of 35 cases of wrong site operations suggested that operating at the incorrect site in neurosurgery most frequently results from communication breakdown, failure to follow standard checks, and technical factors such as mislabeled imaging.²⁴

Conclusions

Surgery for intracranial neoplasms carries a high risk of adverse events. A significant proportion may be avoidable using practices to encourage standardized protocols, improved teamwork and communication, increased use of beneficial technologies, and concentrated experiences and specializations. Compared with other surgical fields, however, these strategies have been sparingly used in cranial tumor surgery. Concerted efforts aimed at large-scale monitoring of neurosurgical complications and consistent

quality improvement within these highlighted realms may significantly improve patient outcomes. These ideas are discussed in more detail in the summary paper of this series.¹¹⁴

Disclosure

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