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Perioperative Outcomes following Surgery of Brain Tumors: Assessment and Analysis of Risk Factors

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ABSTRACT

Introduction

Cranial neurosurgery carries significant morbidity and mortality. Hence it is imperative to combine the latest available technological equipment with surgeon's experience to prevent or reduce perioperative complications. It is also equally important to have a preoperative general assessment of the patient with functional status in particular to predict postoperative outcomes.

Methods

This is a prospective study consisting of 122 patients selected over a period of 5 years (March 2017-March 2022). The patient database was retrieved from the medical record department, Nobel Institute of Neurosciences, Nobel Medical College Teaching Hospital, Biratnagar, Nepal and the approval of Institutional review committee was obtained. Age, gender, tumor related factors (site, extent and size), preoperative Glasgow Coma Scale (GCS) score, Karnofsky Performance Status (KPS) score and Modified Rankin scale (mRS) grade and their correlation with patient's perioperative outcome were assessed.

Results

Significant correlation was found between preoperative KPS score, mRS grade and patient's perioperative outcome (low KPS score <70 and high mRS grade was associated with adverse outcomes). There was no positive correlation between age, gender and tumor related factors with outcomes.

Conclusion

Low KPS score <70 and a high Modified Rankin scale score were associated with adverse perioperative outcomes in patient's undergoing elective craniotomy for brain tumor surgery.

Keywords

Brain tumor; preoperative KPS (Karnofsky performance status score); preoperative mRS (Modified Rankin scale score)

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INTRODUCTION

For evaluation of outcome of any surgery, assessment of factors affecting the perioperative recovery is important. Especially in neurosurgery, which has one of the highest morbidity rates amongst surgical subspecialties, periodic assessment of the predictors would enable a center to upgrade its services by assessment of baseline data and evaluate the benefits of replacing old surgical techniques by newer technology. With surgery still remaining the treatment of choice for brain tumors, neurosurgeons have a challenge to remove the tumor in totality whilst retaining the normal neuronal physiology.

Today, principal of Safe Maximal Resection (SMR) appears to be the emerging paradigm of neurosurgery. Technological adjuncts such as navigation, intraoperative ultrasonography (USG), magnetic resonance imaging (MRI), neuro-physiological monitoring helps operating surgeons to do safe maximal resection and achieve tumor progression free state. As a result, patients have reduced length of hospital stay with lower peri-operative costs and early recovery. In countries with resource-limited services, systematic documentation of perioperative events also enables comparison across various centers. Post-operative complications are unavoidable and there are many ways to classify them in the literature.[1]

Our institute, Nobel Institute of Neurosciences is a tertiary referral center in Eastern Nepal. With our dedicated neurosurgical services, roughly 400-500 patients undergo some form of surgical intervention each year with about fifty brain tumor surgeries per year. This report is an attempt to document the perioperative outcomes in patients undergoing brain tumor surgery and review the current literature.

METHODS

This is a prospective study analyzed by maintaining the database of patients receiving neurosurgical service in our center. We maintained a database of all patients undergoing brain surgery. We have included only the patients who underwent surgery for brain tumors. Institution review committee approved our study. We analyzed the data from March 2017 to March 2022 (5 years) while conducting this study.

During the surgery, standard micro neurosurgical principles were followed. Intraoperative adjuncts like navigation machines, intraoperative MRI, neurophysiological monitoring was used where necessary. Antibiotic prophylaxis using Cephalosporins was given before surgery. Patients received corticosteroids (dexamethasone) which was tapered postoperatively. DVT prophylaxis in the form thrombo-elastic stockings were utilized, along with pharmacological prophylaxis (heparin or low-molecular weight heparin) reserved for patients with prolonged immobilization.

The outcomes were assessed using complications that occurred during and / or after surgery (regional and systemic complications), Karnofsky Performance Scale (KPS) at the time of admission and modified Rankin Score (mRS) at the time of three months follow-up. Favorable outcome was defined as either improvement or no change prior surgical intervention whereas, unfavorable outcome was defined as any worsening seen post-surgery. The level of consciousness of patients before and after the intervention was monitored using Glasgow Coma Scale (GCS). Postoperative complications were classified as per the new classification of complications in Neurosurgery by Ibanez et al.[1] Regional complications included presence of significant surgical site infections (as per definitions of Centers of Disease Control, USA), worsening or onset of seizures, presence of pseudo meningocele and hydrocephalus. The systemic complications included all other complications like chest infection, deep vein thrombosis and urinary tract infection. Mortality was also noted. We also assessed other potential risk factors that may influence the perioperative recovery of a patient. These included preoperative predictors like clinic-epidemiological characteristics (age, gender and preoperative GCS status, surgery related variables (location of tumor), extent of resection and tumor related factors (histology, location).

While conducting the statistical analysis, bivariate analysis was performed first to determine the association of risk factors with the outcome. Binary logistic regression analysis using enter method was used for multivariate analysis. Only the risk factors that were significant in bivariate analysis were included in multivariate analysis. Results were tabulated as confidence intervals and p-value. Statistical analysis was performed using SPSS software version 22.

RESULTS

A total of 122 cases were operated upon in the study period. The demographic profile, clinical characteristics of patients, form of surgical technique used, tumor specific features are outlined in detail in Table 1. The mean age group of patients in our study was 38.58 ± 16.44 years. Regarding the type of tumors meningiomas were most frequently encountered. Other histological subtypes are outlined in Table 2.

Perioperative characteristics of the patients

Among the patients operated 13.9% regional complications were encountered. Cranial nerve palsy was the major (4.1%) contributor of the

Table 1. Demographic profile of study population

Demographic characteristics		Number	Percentage
Age (years)	Range: 38.58 ± 16.44		
Gender	Male	56	45.9%
	Female	66	54.1%
Predominant clinical feature	Headache	34	27.9%
Pre-op GCS	13-15	99	81.1%
	9-12	21	17.2%
	3-8	2	1.6%
Karnofsky Performance Status (KPS) score	>70	98	80.3%
	<70	24	19.7%
Site of tumor	Scalp	1	0.8%
	Extradural	1	0.8%
	Infratentorial	23	18.9%
	Supratentorial	97	79.5%
Extent of resection	Gross total resection	90	73.8%
	Biopsy	4	3.3%
	Decompression	7	5.7%
	Complete excision	21	17.2%
Size of tumor (less than 3 or more than 3)	> 3 cm	77	63.1%
	< 3 cm	45	36.9%

regional complication. Systemic complications occurred in 10.7 % of population and chest infection was the major (4.1%) systemic complication present.

Overall morbidity and mortality

The overall mortality was 2.5 % out of the total surgery. Table 3 shows major causes of post-operative mortality and morbidity. Amongst the causes of mortality, medical cause was the most frequent cause of mortality amongst the operated cases.

Average duration of hospital stay was 10.72 ± 6.06 days. We had one case of recurrent petroclival meningioma with lower cranial nerve palsy who underwent re-do surgery with hospital stay of 65 days. Three patients died during the post operative period. Details of the causes of death and the events leading to death are outlined in Table 4.

The anticipated risk factors were analyzed for the clinical outcome. Logistic regression was used. All the possible factors were initially tested using bivariate analysis. Strength of association was analyzed using Spearman's/ Pearson's correlation coefficient. Only the factors that were found significant were analyzed for predicting the overall outcome.

On bivariate analysis of risk factors with outcome of patient, preoperative Karnofsky Performance Status (KPS) score, requirement of tracheostomy

Table 2. Histological spectrum of brain tumors

Tumor types/ Histology feature	Number	Total
Glial and Meningeal tumors	49	89
Glial tumors	40	
Meningioma		
Other tumors	13	33
Pituitary macroadenoma	6	
Craniopharyngioma	4	
Medulloblastoma	3	
Hemangioblastoma	2	
Germ cell tumor	1	
Extraventricular neurocytoma	1	
Ependymoma	1	
Osteoma	1	
Colloid cyst	1	
Lipoma		

Table 3. Postoperative complications

Complications	Number	Percentage
Systemic	5	4.1%
Chest infection	3	2.5%
Death	2	1.6%
Urinary tract infection	1	0.8%
DVT		
Regional	5	4.1%
Cranial nerve palsy	4	3.3%
Hydrocephalus	4	3.3%
Pseudomeningocele	2	1.6%
Seizure	2	1.6%
Meningitis	2	1.6%
Surgical site infection		

Table 4. Details of the mortality

Clinical details	Tumor and nature	Events
Seizures and papilledema	Malignant germ cell tumor WHO -IV	Hydrocephalus and Ventriculitis
Visual field defects	Pituitary macroadenoma	Meningitis
Visual field defects	Pituitary macroadenoma	COVID-19 positive, Lower respiratory tract infection

Table 5. Bivariate analysis of the risk factors

Risk factors	p-value	Adjusted OR	95% Confidence interval (CI)	
			Lower	Upper
Pre-operative KPS	0.000	32.333	3.670	284.872
Tracheostomy	0.006	19.000	1.055	342.154
mRS score (for neurologic disability)	0.000	57.55	14.556	227.144

Table 6. Multivariate analysis of risk factors for overall morbidity

Risk factors	p-value	Adjusted OR	Outcome	95% Confidence interval (CI)	
				Lower	Upper
Pre-operative KPS	0.00	0.161	Unfavorable	-0.131	0.416
			Favorable	0.776	0.911
Modified Rankin scale for Neurologic disability on follow up	0.000	0.730	Unfavorable	4.957	5.900
			Favorable	0.866	1.099
Requirement of Tracheostomy	0.038	0.027	Unfavorable	1.742	1.972
			Favorable	1.954	2.011

during hospital stay and mRS score for neurologic disability on follow-up were significant for complications. Patients with presence of any peri-operative complications were more likely to affect peri-operative outcomes of patients. Patients with low preoperative (KPS) scores and high mRS scores prior discharge were predictive of higher unfavorable outcome. On multivariate analysis, KPS scale, tracheostomy and mRS score of the factors were significant. Results of multivariate analysis is shown in the Table 5.

DISCUSSION

Peri-operative outcomes reflect both the effectiveness and injury occurring to the patient after a surgery. Whilst there are many studies in the literature that describe long term outcomes and the affects occurring after brain tumor surgery, only spurious papers exist that study and analyze peri-operative risk factors associated with brain tumor surgery. Our effort is to add to the existing knowledge the factors that affect the immediate recovery of patients in a university-based hospital in eastern Nepal. Patients with intracranial tumors exhibit a wide range of symptoms. Tumor-related symptoms may be confused with treatment-related symptoms. Headache, vomiting, blurring of vision, neurological deficits and cognitive deficits are some common symptoms that may be seen both in tumor and non-tumor conditions. Hence forth a surgeon needs to be vigilant in distinguishing the cause of the presenting symptoms should one occur. In this era of safe maximal resection, maintenance of near-normal neurophysiology is the utmost priority and now as morbidity reduction is the dictum, neurosurgeons are more concerned about reducing the factors causing increased peri-operative morbidity and mortality.

Patients age and gender:

Although there is heterogeneity in presentation (age wise) in affected patients, there is overall decline in functional status 3-6 months following surgery. This decline increases slightly with age. Advanced age≥70 years was associated with increased perioperative mortality (5.7%) as compared to younger individuals <70 years (2.9%). However no significant difference in perioperative mortality was

found in children <16 years and adults between 16 – 69 years.[2] In a study done by Moiyadi et al and Shetty et al, age <18 years was predictive of increased risk of perioperative mortality.[2] In elective craniotomies, the overall morbidity in all age groups were found to be ranging from 10.6-38%[4-7] and the overall mortality was 1.0-2.9%.[4-6] With respect to the elective cranial surgeries performed in elderly patients, the morbidity rate ranged between 19-53.2%[8-10] and the morbidity was 1.2-5.6%.[8,10,11] However, some groups found that older age has no effect on overall outcome, length of stay and mortality.[9,12-15] In our study however age did not appear to be a predictor of perioperative outcome of mortality. Some studies have shown that female patients had lower mortality and adverse discharge condition as compared to males.[16,17] However others proved that gender difference was not responsible for difference in outcome[2] and the same was reflected in our study.

Preoperative GCS score and outcome:

Patients presenting with altered mental status preoperatively were associated with increased risk of postoperative mortality and thus has a negative predictive value on survival outcome following craniotomy for brain tumor resection.[17,18] In a study by Cinotti et al, preoperative GCS score ≤14 was a powerful predictor of adverse postoperative neurological complications and hence outcome.[19] In their study it was shown that low GCS score patients were more susceptible to longer ICU stays. However, our study did not show any association of low preoperative GCS score with adverse postoperative neurological outcome.

Preoperative KPS score and outcome:

Preoperative KPS score was considered as a predictor of outcome following glioma surgery.[20-24] It was also found that elderly patients with Glioblastoma, low admission KPS score had decreased survival.[25] Some studies have shown that preoperative KPS score of <70 was associated with higher perioperative mortality.[26,27] Some studies have shown that low preoperative KPS score in the elderly predicts the risk of short term mortality and increased length of hospital stay.[15,26,27] However, there are some studies (that analyzed all age groups) that do not come to the same conclusion.[3,5] The correlation between low KPS score and long term care complications, neurologic, systemic or infectious complications were analyzed in which some studies found a positive correlation[3,5,28] while others ruled out any association.[7,10,26,29-31] In addition, low preoperative KPS score was associated with longer hospital stay and decreased resilience to complications.[15] In our study, we found that lower preoperative KPS score was a significant risk factor for unfavorable outcome in patients undergoing craniotomy for brain tumor surgery.

Preoperative Modified Rankin Scale score and outcome:

Studies have shown that higher mRS score at the time of admission were associated with unfavorable outcome, prolonged hospital stay and mortality[3,15,32,33] while others have found that preoperative mRS score has no correlation with surgery related complications.[15] However, our study has shown that a higher mRS score was associated with unfavorable outcome.

CONCLUSION

We conclude that, to prevent surgery related complications in patients undergoing craniotomy for brain tumor surgery, it is of utmost importance to have a functional assessment. Our study has shown that low preoperative KPS score and high mRS grade were significantly associated with unfavorable outcomes during perioperative period and thus need a specific attention.

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CONFLICT OF INTEREST

The author(s) declare that they do not have any conflicts of interest with respect to the research, authorship, and/or publication of this article.

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