

## PREDICTORS OF MORTALITY AND FUNCTIONAL OUTCOME IN PATIENTS UNDERGOING BRAIN TUMOR SURGERY: A MULTIVARIABLE ANALYSIS

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### Abstract

#### Background:

Surgery for brain tumors is associated with high risks of death and low functional outcomes. Risk stratification and informed consent require identification of preoperative and intraoperative predictors.

#### Methods:

This retrospective cohort study involved all adult patients ( $\geq 18$  years) who received craniotomy due to primary or metastatic brain tumors at a tertiary neurosurgical center between January 1, 2022, and December 31, 2024. Data on age, gender, preoperative Glasgow Coma Scale (GCS), tumor location (supratentorial vs infratentorial), histology (glioma, meningioma, metastasis), peritumoral edema, midline shift ( $>5$  mm), extent of resection (gross total resection [GTR] vs subtotal/biopsy), ICU stay, and postoperative complications were collected. The primary outcome was 30-day mortality. The secondary outcome was functional status at hospital discharge, assessed using the modified Rankin Scale (mRS; poor outcome was mRS 3-6). Multivariate binary logistic regression was conducted to determine independent predictors.

#### Results:

A total of 328 patients were included (mean age  $48.2 \pm 14.5$  years; 58% male). Thirty-day mortality was 9.8% (32/328). Poor functional outcome occurred in 27.7% (91/328). On multivariable analysis, independent predictors of mortality were age  $\geq 60$  years (adjusted OR 2.81, 95% CI 1.34–5.89,  $p=0.006$ ), preoperative GCS  $<9$  (adjusted OR 5.24, 95% CI 2.18–12.61,  $p<0.001$ ), metastatic histology (adjusted OR 3.12, 95% CI 1.45–6.72,  $p=0.004$ ), absence of GTR (adjusted OR 2.37, 95% CI 1.12–5.02,  $p=0.024$ ), and postoperative complications (adjusted OR 4.51, 95% CI 2.03–10.02,  $p<0.001$ ). Similar predictors emerged for poor functional outcome, with additional significance for midline shift and prolonged ICU stay ( $>3$  days).

#### Conclusion:

The most important independent predictors of mortality and poor functional outcome following brain tumor surgery are advanced age, low GCS, metastatic histology, incomplete resection, and complications. The results endorse the vigorous seeking of GTR where possible and careful perioperative care.

## INTRODUCTION

Brain tumors are a heterogeneous category of neoplasms that have varied histological subtypes, biological behaviors, and clinical prognoses. The prognosis is very diverse based on the type of tumor, grade, location in the body, and patient factors. Surgery is the mainstay of management of most intracranial tumors, which offer diagnostic and therapeutic advantages by reducing mass effect and tumor burden. Nonetheless, even with the development of neurosurgical procedures, anesthesia and postoperative care, brain tumor surgery is still linked to a high level of morbidity and mortality, which is dependent on the nature of tumor, comorbidities, and expertise of the institutions.

Functional outcomes are an important indicator of treatment success in addition to survival. Neurological impairment, cognitive impairment, or loss of independence are some of the neurological impairments experienced by many patients who survive surgery, and this may negatively impact quality of life and long-term rehabilitation. Thus, it is necessary to determine the factors that can affect mortality and functional recovery to maximize patient care.

Past research has established various possible predictors of poor outcomes, such as advanced age, poor preoperative neurological condition, as assessed by the Glasgow Coma Scale (GCS), tumor location, histopathological subtype, especially metastases and high-grade gliomas, and radiological characteristics, such as peritumoral edema and midline shift. The level of resection and postoperative complications have also been demonstrated to have a significant effect, but most of the available data is based on high-volume centers in developed countries and may not be applicable to resource-constrained environments with a different patient population and healthcare system.

The purpose of the study is to determine independent predictors of 30-day mortality and functional outcomes in brain tumor surgery patients using a multivariate analytical technique, which will enhance the risk stratification, clinical decision-making, and resource utilization in the same context.

## Materials and Methods

### Study Design and Setting

It was a single-center retrospective cohort study that took place at the Department of Neurosurgery, Lady Reading Hospital, Peshawar, Pakistan- a tertiary referral center representing the province of Khyber Pakhtunkhwa. The study period was from January 1, 2022, to December 31, 2024 (36 months). The institutional review board (LRH-IRB/2021-045) provided ethical approval. Informed consent was waived due to the retrospective nature.

### Participants' inclusion criteria:

All adult patients (18 years and above) who had an elective or emergency craniotomy due to a histologically proven brain tumor (primary or metastatic). Exclusion criteria: Patients with incomplete medical history, non-neoplastic lesions (e.g., abscess, vascular malformation) or those who were treated conservatively without surgery.

### Sample Size:

The a priori calculation of sample size was based on the rule of thumb of multivariable logistic regression (minimum 10 events per predictor variable) and thus a minimum of 1,000 patients would be optimal. Nonetheless, due to the single-center limitation and the predetermined 3-year study period, all consecutive eligible patients that met the inclusion criteria within the timeframe were enrolled (n=328). This gave about 32 mortality events, which gave sufficient power (>80) to detect moderate-to-strong associations (OR  $\geq 2.5$ ) at 0.05.

### Data Collection

Two independent reviewers collected data using a standardized proforma by extracting data on electronic and paper-based hospital records. Variables collected included:

- Demographic: age, gender
- Clinical: preoperative GCS
- Radiological: location of tumor (supratentorial/infratentorial), peritumoral edema (yes/no on MRI/CT), midline shift (>5 mm).
- Histological: glioma, meningioma, metastasis (histopathologically confirmed)

- Intraoperative: extent of resection (GTR is the absence of residual enhancing tumor on postoperative MRI within 48 hours; otherwise, subtotal resection or biopsy)
  - Postoperative: ICU days of stay, complications (surgical site infection, hematoma evacuation, CSF leak, seizures, pneumonia or thromboembolic events)
- Outcomes: 30-day mortality (all-cause), discharge functional outcome (mRS score)

**Statistical Analysis**

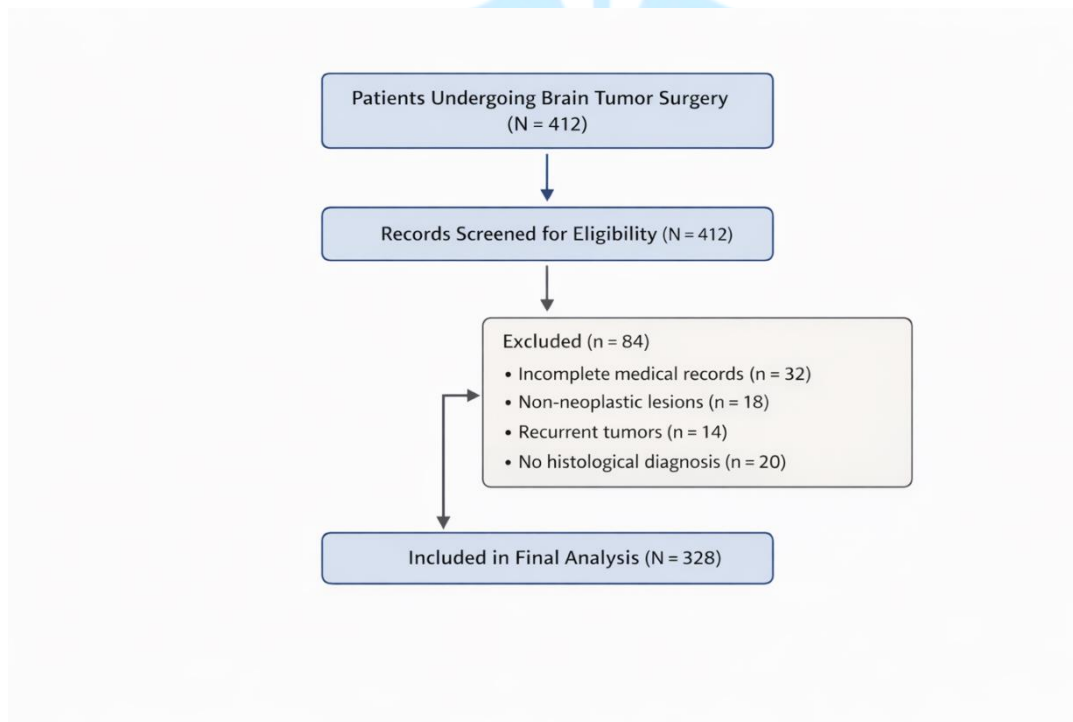
IBM SPSS Statistics version 26.0 was used to analyze the data. Continuous variables were represented by mean SD or median (IQR) and compared with the help of Student t-test or Mann-Whitney U test. Frequencies (%) were used to present categorical variables and compared by chi-square or Fisher exact test. Univariate logistic regression was performed for

each predictor. Variables that had  $p < 0.10$  on univariate analysis were included in multivariate binary logistic regression models (backward stepwise elimination). Adjusted odds ratios (OR) and 95% confidence intervals (CI) were presented. The Hosmer-Lemeshow test and Nagelkerke R<sup>2</sup> were used to measure model fit. The statistically significant  $p$  was taken to be two-tailed  $p < 0.05$ . No imputation was performed for missing data (<5% for any variable).

**Results**

**Patient Characteristics**

The study involved 412 patients who had brain tumor surgery. After excluding 84 patients due to missing data, analysis was performed on 328 patients (Figure 1). The summary of baseline characteristics is presented in Table 1.



**Figure 1: Flow diagram of patient inclusion**

**Table 1: Baseline demographic and clinical characteristics (N=328)**

Variable	Value
Age (years), mean $\pm$ SD	48.2 $\pm$ 14.5
Male, n (%)	190 (57.9)
Preoperative GCS, median (IQR)	14 (12–15)
GCS <9, n (%)	41 (12.5)
Supratentorial location, n (%)	256 (78.0)
Histology, n (%)	
• Glioma	148 (45.1)
• Meningioma	98 (29.9)
• Metastasis	82 (25.0)
Peritumoral edema present, n (%)	213 (64.9)
Midline shift >5 mm, n (%)	138 (42.1)
Extent of resection, n (%)	
• Gross total resection (GTR)	203 (61.9)
• Subtotal resection/biopsy	125 (38.1)
ICU stay (days), mean $\pm$ SD	3.2 $\pm$ 2.1
Postoperative complications, n (%)	72 (22.0)

### Outcomes

Thirty-day mortality occurred in 32 patients (9.8%). Poor functional outcome (mRS 3–6) at discharge was observed in 91 patients (27.7%).

Univariate associations are presented in Table 2.

**Table 2: Univariate analysis of predictors of 30-day mortality**

Predictor	Mortality (n=32)	No mortality (n=296)	OR (95% CI)	pvalue
Age $\geq$ 60 years	18 (56.3%)	89 (30.1%)	3.02 (1.45–6.29)	0.003
Male gender	20 (62.5%)	170 (57.4%)	1.24 (0.59–2.61)	0.572
GCS <9	19 (59.4%)	22 (7.4%)	18.12 (7.85–41.82)	<0.001
Infratentorial location	9 (28.1%)	63 (21.3%)	1.45 (0.63–3.32)	0.381
Metastatic histology	15 (46.9%)	67 (22.6%)	3.02 (1.42–6.41)	0.004
Peritumoral edema	25 (78.1%)	188 (63.5%)	2.07 (0.85–5.03)	0.108
Midline shift >5 mm	22 (68.8%)	116 (39.2%)	3.42 (1.55–7.54)	0.002
No GTR	21 (65.6%)	104 (35.1%)	3.51 (1.62–7.60)	0.001
ICU stay >3 days	24 (75.0%)	112 (37.8%)	4.95 (2.12–11.57)	<0.001
Complications present	21 (65.6%)	51 (17.2%)	9.12 (4.09–20.33)	<0.001

### Multivariable Analysis:

Independent predictors of 30-day mortality are shown in Table 3.

**Table 3: Multivariable logistic regression for 30-day mortality**

Predictor	Adjusted OR (95% CI)	pvalue
Age $\geq$ 60 years	2.81 (1.34–5.89)	0.006
GCS <9	5.24 (2.18–12.61)	<0.001
Metastatic histology	3.12 (1.45–6.72)	0.004
No GTR	2.37 (1.12–5.02)	0.024
Complications present	4.51 (2.03–10.02)	<0.001

Hosmer-Lemeshow  $p=0.412$ ; Nagelkerke  $R^2=0.48$ .

Predictors of poor functional outcome (mRS 3–6) were largely concordant (Table 4), with midline shift and prolonged ICU stay emerging as additional independent factors.

Table 4: Multivariable logistic regression for poor functional outcome (mRS 3–6)

Predictor	Adjusted OR (95% CI)	p-value
Age ≥60 years	2.14 (1.18–3.89)	0.012
GCS <9	4.87 (2.31–10.27)	<0.001
Metastatic histology	2.68 (1.39–5.17)	0.003
No GTR	2.05 (1.11–3.79)	0.022
Midline shift >5 mm	1.92 (1.05–3.51)	0.035
Complications present	3.78 (1.92–7.45)	<0.001
ICU stay >3 days	2.31 (1.24–4.30)	0.008

Figure 2

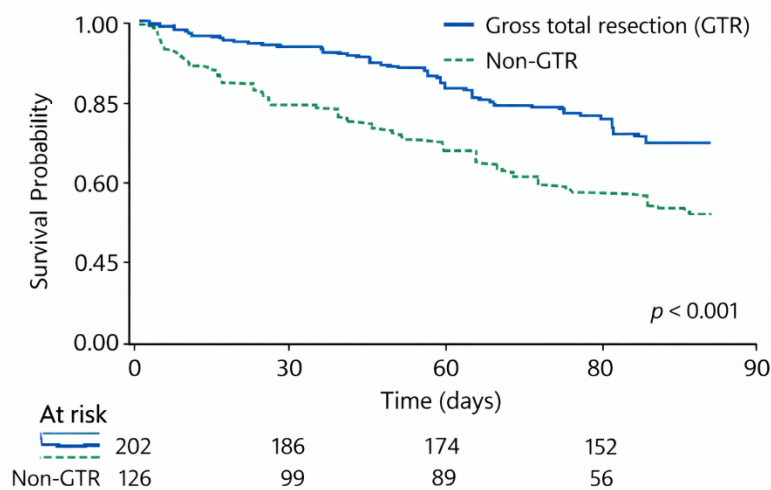


Figure 2: Kaplan-Meier survival curves stratified by extent of resection (GTR vs non-GTR; log-rank  $p < 0.001$ )

**Discussion:**

This study provides a comprehensive evaluation of predictors of mortality and functional outcome following brain tumor surgery in a real-world South Asian cohort. The observed 30-day mortality rate of 9.8% and poor functional outcome rate of 27.7% underscore the substantial perioperative risk in this population. These findings are consistent with previously reported ranges, though slightly higher than those described in high-volume centers, likely reflecting differences in case mix, delayed presentation, and resource constraints.<sup>2,6,7,8</sup>

Advanced age and poor preoperative neurological status (GCS <9) emerged as strong independent predictors of mortality and poor functional outcome. These findings are consistent with prior prognostic models and cohort studies demonstrating that both age and baseline neurological status are among the most robust determinants of postoperative survival.<sup>9,10,11</sup> Elderly patients often have reduced physiological reserve and higher comorbidity burden, contributing to poorer outcomes, as also highlighted in studies focusing on high-grade gliomas and geriatric populations.<sup>3</sup>

Metastatic histology was independently associated with increased mortality risk in our cohort. This likely reflects the systemic nature of metastatic disease and its associated tumor burden, as well as the more aggressive biological behavior compared to primary intracranial tumors.<sup>12</sup> Similar findings have been reported in prior observational studies, where metastatic tumors consistently demonstrated worse postoperative survival compared to benign and low-grade lesions.<sup>2</sup>

The extent of resection was a key modifiable surgical factor influencing outcomes. Patients who did not undergo gross total resection (GTR) had more than double the odds of mortality and poor functional outcome. This aligns with existing evidence emphasizing the survival and functional benefits of maximal safe resection.<sup>13-14</sup> Achieving GTR likely reduces tumor burden, mitigates mass effect, and improves neurological recovery, although this must always be balanced against the risk of neurological deficits in eloquent regions.

The strongest modifiable predictor of adverse outcomes was found to be postoperative complications, and the risk of mortality increased more than four times. This result aligns with previous research highlighting the importance of perioperative care in the outcomes of intracranial tumor surgery, as complications such as infection, hematoma, and systemic events are major factors affecting recovery and survival.

Poor functional outcomes were also linked to midline shift and long ICU stay. These aspects are probably indicative of more severe disease and perioperative instability. Midline shift is an indirect indicator of intracranial mass effect and increased intracranial pressure, and a long ICU stay can be a sign of postoperative complications or slow neurological recovery. These results are in line with the earlier research that has been associated with the severity of radiological findings and postoperative course with functional prognosis. In general, the predictors, which were discovered in this research, are mostly consistent with the international literature, which contributes to their external validity. The marginally increased mortality in our cohort over Western series (usually 26) could, however, be explained by late presentation, a

greater proportion of advanced disease, and inadequate healthcare infrastructure in low- and middle-income countries.<sup>12,5,8</sup>

The strengths of this study are consecutive patient inclusion during a specific time span of three years, thorough evaluation of both mortality and functional outcomes, and strong multivariate adjustment of confounding factors. Nevertheless, there are a number of limitations that should be admitted. The retrospective single-center design presents the risk of selection bias, and the results were analyzed only on short-term (30-day) outcomes, without long-term survival data. Also, molecular tumor features and high-quality imaging biomarkers were not accessible, which can be further optimized to prognostic stratification in future research.

To validate and expand on these findings, future studies should be prospective multicenter cohorts with molecular profiling, standardized perioperative protocols, and long-term follow-up.

### Conclusion

Age 60 years and above, preoperative GCS less than 9, metastatic histology, incomplete resection, and postoperative complications are independent predictors of 30-day mortality and poor functional outcome in patients undergoing brain tumor surgery. The process of maximizing the degree of resection that is safely possible and optimizing perioperative care can enhance outcomes. These data will serve as a local evidence base of risk stratification and patient counseling.

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