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Original Article

Factors Influencing the Outcome of Patients with Surgically Managed Intracranial Meningioma

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Abstract

Background: *Intracranial Meningiomas are the most common primary brain tumor in adult which are predominantly non-malignant. Surgical intervention is the gold-standard treatment option for intracranial meningiomas but the surgical outcomes are influenced by various epidemiological risk factors. Understanding these factors is essential for a precise decision-making process, application of effective therapeutic intervention and prognostication.*

Aims: *This study aimed to identify the possible predictive factors influencing surgical outcome in patients with intracranial meningioma.*

Materials and Methods: *This Prospective Observational Study included 34 patients of intracranial Meningioma who had surgery in the Department of Neurosurgery, Chittagong Medical College Hospital between February 2022 to August 2023. Outcome measures were the Glasgow Outcome Scale (GOS) and Karnofsky Performance Status (KPS) score at the immediate postoperative period, "0" postoperative day, at the time of discharge, 1 month, 3 months, and 6 months post-surgery. GOS score 1-3 was considered as poor outcome.*

Results: *The mean age of the patients was 46.8±12.6 years and 70.6% were female. Most of the patients were in either ASA class I (35.3%) or Class II (55.9%), and the median KPS score was 80% before surgery. Twenty-eight (82.4%) patients survived at least six months following surgery and the 6-months mortality rate was 17.6%. Twenty-seven (79.4%) patients had a good outcome and 7 (20.6%) patients had a poor outcome. Preoperative KPS score (p=0.024), tumor location (p=0.019), and tumor volume (p=0.003) were found to have a significant association with outcome in univariate analysis. However, none of these factors retained a significant association in multivariate analysis.*

Conclusions: *In conclusion, specific influencing factors for postoperative poor outcomes revealed in univariate analysis in the present study were low preoperative KPS score, skull base meningioma, and large-size tumor.*

Keywords: *Intracranial meningioma, Outcome; Surgery. Prognostic factors; KPS Score;*

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Introduction:

Meningiomas are the most common primary brain tumor of which about 90% are benign [1]. These are slow-growing in nature, arise contiguously to the meninges, and originate from the arachnoid cap cells of the leptomeninges. They are usually globular, encapsulated tumors attached to the dura and compress the underlying brain without invading it. A meningioma may be found incidentally [2]. However, for others, as they grow along certain locations of the dura and skull base, frequently invading the skull, are quite debilitating to patients based on their location, size, and mass effect on or involvement of critical neurovascular structures. The asymptomatic meningiomas are managed conservatively with regular follow-up and brain scans, but surgical resection should be employed if a patient becomes symptomatic [3]. The exception is tuberculum sellae meningioma as because even with small tumors, they can develop visual deterioration. The surgical approach should be tailored according to specific tumor location, anatomy, and clinical findings to avoid surgery-related morbidity and mortality. The only definitive cure for meningioma is complete surgical resection. The more complete the resection, the less chance of recurrence. The anatomic location of a meningioma influences its rate of recurrence such as sphenoid wing and parasagittal in location. The rates of recurrence are understandably higher in the higher Simpson-grade resection and higher meningioma grades. Intraoperative venous consideration plays a vital role in the safe management of meningioma [4].

Preoperative tumor embolization can be considered when the tumor is large and highly vascular in nature but this should be weighed against the risk-benefit ratio. Irradiation like conventional radiation therapy, radiosurgery, and stereotactic radiation has a role in specific cases. While atypical high-grade meningiomas are associated with the worst prognosis, higher survival rates are reported for lower-grade benign meningiomas. However, in these cases, neurological deficits and long-term disability are common complications [5].

The management of these tumors poses a significant challenge to neurosurgeons due to their diverse clinical presentations, variable biological behaviors, and anatomical complexities. Surgical resection is the primary treatment modality for intracranial meningioma, aiming to achieve complete tumor removal and minimize neurological deficits. However, the surgical outcome of meningioma resection can vary significantly among patients, and numerous factors may contribute to this variability.

In this context, meningioma surgery would be beneficial as it could change the natural history, with a chance to cure when Simpson grade 1 resection is performed and reversal or improvement of neurologic signs and deficits. Neurosurgical gross-total resection still represents the gold standard for patients' treatment, with radiotherapy used as adjuvant treatment in the case of non-radically removed lesions [6].

Identification of the preoperative prognostic factors for patients with a diagnosis of intracranial meningioma undergoing surgical management is an important issue in research. Available data in the literature suggest that patient age, medical co-morbidity, preoperative Karnofsky Performance Status scores (KPS), tumor location, tumor size, tumor invasion, presenting symptoms/signs, and prior surgery are significant factors that influence the operative outcome in meningioma surgery.

Identification of the related factors influencing the surgical outcome of intracranial meningioma has been addressed in several studies, but the results are scarce. Moreover, a study from Bangladesh was lacking on this issue [7]. In this background, this study was planned and conducted to determine the factors influencing the outcome of patients with surgically managed intracranial meningioma in a neurosurgery unit of a tertiary hospital in Bangladesh.

Methods:

This Single institutional study ethics approval was granted by the local institutional ethics board. Written informed consent was obtained from all patients or guardians where applicable. This was a prospective observational study conducted in the Department of Neurosurgery, Chattogram Medical College and Hospital, Chattogram, Bangladesh from February 2022 till August 2023. Consecutive sampling technique was applied where all patients with a radiological diagnosis of intracranial meningioma admitted in the Neurosurgery department, CMCH during study period was included in the study. Those who are surgically unfit or denied to be participated in study were excluded.

A pre-designed case record form including questionnaire and checklist was used to collect data. All relevant data were noted in the pretested data sheet. Data were recorded in the form of an Excel worksheet. After completion of data collection, they were fed into SPSS version 23 for processing analysis. Continuous data were expressed as mean ± standard deviation (SD) for normally distributed data or median

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and 25%–75% interquartile range for non-normally distributed data. Categorical variables were presented as percentages (%) or proportions. The study population was divided into six-month poor and good outcomes by GOS. Between these groups, continuous and categorical variables were analyzed. Student's t–tests were used to analyze normally distributed continuous variables, while Mann–Whitney's U-test was used for non-normally distributed continuous variables. Categorical variables were compared using Fisher's exact test, as the expected count was less than 5 in more than one cell for most of the variables. The association between tumor location and outcome was assessed by the Chi-square test. Variables with $P < 0.05$ on univariate analysis for poor outcome 6 months after meningioma surgery were included in multivariate logistic regression analysis to determine the independent predictors of poor outcomes. Results were reported as OR together with a 95% CI. $P < 0.05$ was considered statistically significant.

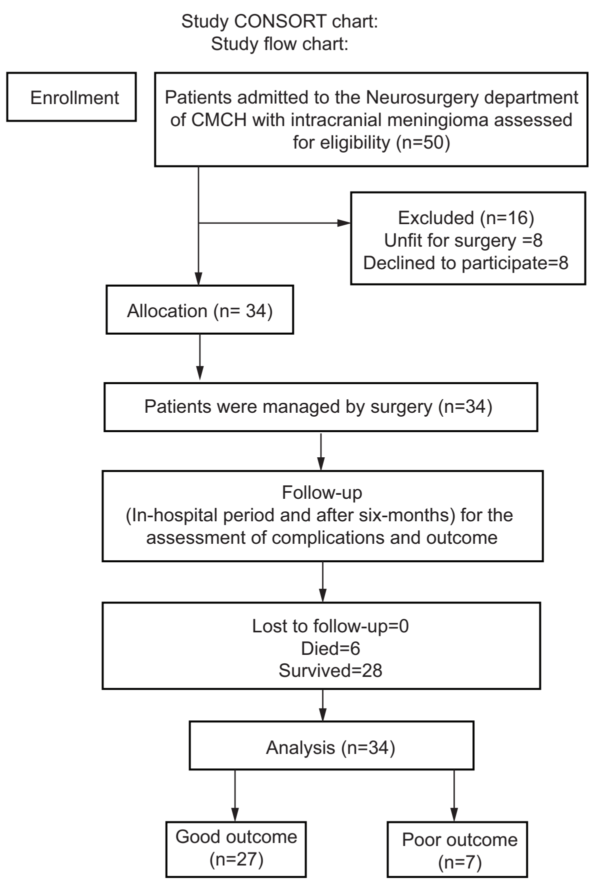

Figure 1: *Patient flow diagram (modified CONSORT diagram)*

Results:

A total of 50 patients with intracranial meningioma were admitted to the Neurosurgery department of CMCH and 34 of them were found to fulfill the eligibility criteria for the study. Outcome data were available for all of the patients and were included in the final analysis. Results and observations of the present study were described in the following tables and charts.

Table-I

Demographic characteristics of the patients (n=34)

Characteristics	Frequency (%)
Age	
21-40 years	11 (32.3)
41-60 years	19 (55.9)
>60 years	4 (11.8)
Sex	
Female	24 (70.6)
Male	10 (29.4)

The mean age of the patients was 46.8±12.6 years and ages ranged between 21-71 years. Table 1 shows that the age group of 41-60 years occupied the major proportion (55.9%) of patients. There was a female predominance (70.6%) with a female-to-male ratio of 2.4:1

Table-II

Baseline clinical characteristics of the patients (n=34)

Characteristics	Frequency (%)/ Median (IQR)
Comorbidity	
Hypertension	12 (35.3)
Diabetes mellitus	8 (23.6)
Ischemic heart disease	1 (2.9)
Presenting symptoms	
Headache	31 (91.2%)
Vomiting	17 (50.0)
Hemiparesis	17 (50.0)
Seizure	13 (38.2)
Diminution of vision	13 (38.2)
Behavioral disturbances	7 (20.6)
Cranial nerve palsy	5 (14.7)
Ataxia	4 (11.8)
ASA class I	12 (35.3)
ASA class II	19 (55.9)
ASA class III	3 (8.8)
Preoperative KPS score	80.0 (67.5-80.0)

IQR: Interquartile range; ASA: American Society of Anesthesiologists

Hypertension was the most frequent comorbidity (35.5%), followed by diabetes mellitus (23.6%). The most frequently reported symptom at presentation was headache (91.2%), hemiparesis (50%), and vomiting

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(50%), followed by seizure (38.2%), and diminution of vision (38.2%). Most of the patients were in either ASA Class I (35.3%) or Class II (55.9%), or the median preoperative KPS score was 80% (Table 2).

Table-III

Preoperative radiological findings of the patients (n=34)

Characteristics	Frequency (%) / Median (IQR)
Tumor laterality	
Right	21 (61.8)
Left	13 (38.2)
Location of tumor	
Convexity	16 (47.1)
Midline	9 (26.5)
Posterior fossa	3 (8.8)
Sphenoid wing	5 (14.6)
Intraventricular	1 (2.9)
Tumor margin	
Ill-defined	8 (23.5)
Well-defined	26 (76.5)
Peritumoral edema	30 (88.2)
Tumor volume, cm^3	40.5 (28.1-66.2)

The right-sided tumor was more common (61.08%). Convexity meningioma (47.1%) was the most common in location, and tumor margin was well-defined in the majority of the cases (76.5%).

Table-IV

Operative and postoperative findings (n=34)

Characteristics	Frequency (%) / Median (IQR)
Brain invasion	2 (5.9)
Duration of surgery, minutes	220 (180-277)
WHO Histological grading	
Grade I	32 (94.1)
Grade II	1 (2.9)
Grade III	1 (2.9)
Simpson grade of resection	
Grade I	19 (55.9)
Grade II	11 (32.4)
Grade III	1 (2.9)
Grade IV	3 (8.8)
Postoperative complications	
Transient Hemiparesis	9 (26.5)
Wound infection	6 (17.6)
Permanent hemiparesis	4 (11.8)
Operation-related hemorrhage	3 (8.8)
CSF leak	2 (5.9)
Hydrocephalous	2 (5.9)
Transient Speech disturbance	1 (2.9)
Cranial nerve palsy	1 (2.9)

Brain invasion was present in only 2 (5.9%) of the patients. Out of 34 patients, 19 (55.9%) developed complications in the postoperative period, and transient hemiparesis was the most frequent complication (26.5%), followed by wound infection (17.6%).

Table-V

Outcome of the patients during discharge and three months after surgery

Variable	Frequency	Percentage
At discharge		
Discharge	29	85.3
Death in hospital	5	14.7
KPS score at discharge (n=29)		
≥80	19	65.5
<80	10	34.5
KPS score at 3-months (n=28)		
e"80	21	75.0
<80	7	25.0
GOS score at discharge (n=29)		
3	3	10.3
4	19	65.5
5	7	24.1
GOS score at 3-months (n=28)		
3	1	3.6
4	8	28.6
5	19	67.9

The median length of hospital stay was 10 (IQR: 7-15) days. Among the surviving patients, the majority of them had good outcomes and were able to carry on normal daily activities at discharge and three months follow-up.

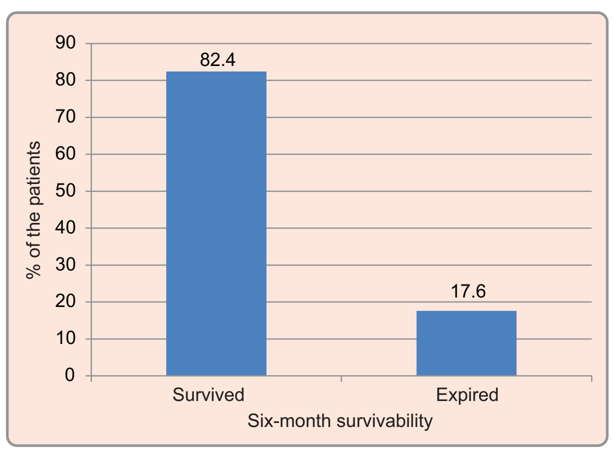

Figure 2: *Distribution of the patients based on their six-month survivability after surgery*

Out of 34 patients operated on, 28 (82.4%) survived at least six months following surgery. The expired 6 cases, giving the six-month mortality rate of 17.6% (Figure 2).

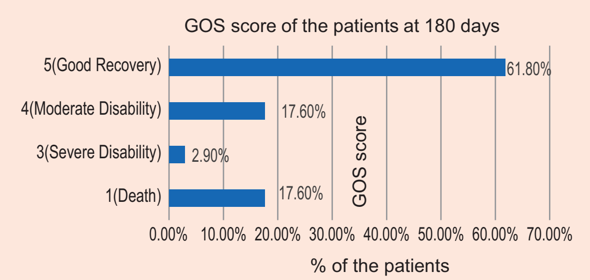

Figure 3: *Distribution of the patients based on their six-month GOS score*

At the final follow-up (six months), out of 34 patients, 21 (61.8%) patients had a GOS score of 5 (indicating good recovery), and another 6 (17.6%) patients had recovery with moderate disability. Other than the 6 (17.6%) patients who expired before the final follow-up, one (2.9%) patient was found to have a GOS score of 3 (severe disability) at the final follow-up (Figure 3).

In the final follow-up among the surviving patients, the majority (89.3%, 25/28) had KPS scorese”80, indicating of good outcome, and were able to carry on normal daily activities.

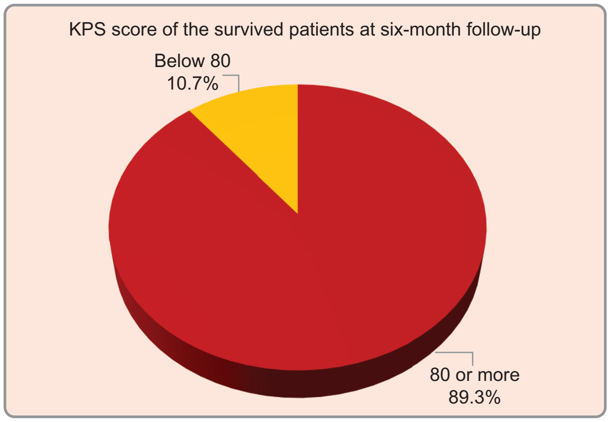

Figure 4: *Distribution of the survived patients based on their six-month KPS score (n=28)*

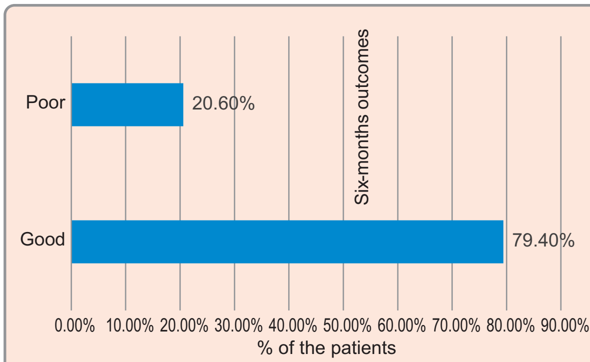

Figure 5. *Distribution of the patients based on their six-month outcomes*

Table-VI

Association between baseline clinical characteristics and outcome of the patients (n=34)

Characteristics	Six-month outcome		P value
	Good (n=27) Frequency (%) / Median (IQR)	Poor (n=7) Frequency (%) /Median (IQR)	
Smoking	5 (18.5)	3 (42.9)	0.315*
Comorbidity			
Present	13 (48.1)	4 (57.1)	1.0*
Absent	14 (51.9)	3 (42.9)	
Presenting symptoms			
Vomiting	13 (48.1)	4 (57.1)	1.0*
Hemiparesis	12 (44.4)	5 (71.4)	0.396**
Seizure	12 (44.4)	1 (14.3)	0.210*
Diminution of vision	8 (29.6)	5 (71.4)	0.079*
ASA class			
Class I	8 (32.0)	1 (16.7)	0.642*
Class II & III	17 (68.0)	5 (83.3)	
Preoperative KPS score	80 (80-80)	70 (40-80)	0.024†

Data were expressed as frequency (%) or median (IQR). *Fisher’s exact test; †Mann-Whitney U test

Table-VII

Association between of baseline radiological findings and outcome of the patients (n=34)

Characteristics	Six-month outcome		P value
	Good (n=27)	Poor (n=7)	
Tumor laterality			
Right	17 (63.0)	4 (57.1)	1.0*
Left	10 (37.0)	3 (42.9)	
Location of tumor			
Midline	9 (33.3)	0 (0)	0.019**
Posterior fossa	3 (11.1)	0 (0)	
Convexity	13 (48.1)	3 (42.9)	
Sphenoid wing Intraventricular	2 (7.4)0 (0)	3 (42.9)1 (14.2)	
Tumor margin			
Ill-defined	6 (22.2)	2 (28.6)	1.0*
Well-defined	21 (77.8)	5 (71.4)	
Peritumoral edema	24 (88.9)	6 (85.7)	1.0*
Tumor volume, cm^3 Median (IQR).	60.0 (38.5-60.0)	71.5 (48.1-98.3)	0.003†

Data were expressed as frequency (%) or median (IQR). *Fisher's exact test; **Chi-square test; †Mann-Whitney U test.

Table-VIII

Logistic regression analysis with six-month poor outcome as the dependent variable

Variables	OR	95% CI for OR		P value
		Lower	Upper	
Preoperative KPS score				
≥80 vs. <80	2.201	0.183	26.441	0.534
Tumor volume, cc^3	1.038	1.000	1.077	0.051
Tumor location	2.945	0.870	9.968	0.083

OR: Odds ratio; CI: Confidence interval

Overall, considering the six-month outcome, out of 34 patients, 27 (79.4%) patients had a good outcome, and the rest of the 7 (20.6%) patients had poor outcomes (Figure 5).

Table 6 shows that preoperative comorbidity status, presenting symptoms, and preoperative ASA class have no significance with the 6-month outcome. Preoperative KPS score on the other hand influences the outcome, as the patients with good outcomes have comparatively better KPS scores than the patients with poor outcomes.

Among the different radiological features, tumor location and tumor volume has significant association with six-month outcome in the present study ($p < 0.05$).

With the 6-months poor outcome serving as the dependent variable, a multivariate binary logistic regression analysis was carried out utilizing the variables that showed a significant association with the outcome in the univariate study (Table 8). None of the variables were found to have an independent association with the 6-month outcome.

Discussion:

The study encompasses the results of the analysis of 34 patients who were surgically managed for intracranial meningiomas in the Neurosurgery Department of CMCH, Chattogram, Bangladesh from February 2022 –August 2023. The postoperative outcome for evaluating prognostic factors was analyzed using the KPS and GOS scores to measure the degree of disability. The change in KPS and GOS provides the possibility of assessing negative predictors that lead to a deterioration in the patient's functional status following surgery.

The epidemiological analysis revealed that the incidence of meningiomas in terms of occurrence was more common in the age group of 41-60 years with 55.9% of patients presenting in this age group. The overall ratio of female to male was 2.4:1. Age and female-to-male ratio in the present study were comparable to meningioma patients' characteristics in the literature [6,7,8,9].

Initial patient symptomatology depending on their location directly related to adjacent neural structure compression or to raise intracranial pressure. Common presentations include headache resulting from elevated intracranial pressure, seizures, and focal neurologic deficits from compression of eloquent brain areas and cranial nerves [10]. In this study, headache (91.2%) was the most presented symptom, followed by a neurological deficit (50%), vomiting (50%), seizures (38.2%), and diminution of vision (38.2%). This result is consistent with the study by Lemee et al. and Utama et al. (2022)[9,11], in which very few patients reported no symptoms while the majority of the patients had neurologic deficits and seizures.

Additionally, 17 (50%) patients in this study had a systemic disease. Hypertension was the most frequent comorbidity (35.5%), followed by diabetes mellitus (23.6%). According to research by Muskens et al. (2019), the incidence of systemic diseases like hypertension and diabetes is positively correlated with the development of meningiomas. Individuals with a history of hypertension and diabetes show an even stronger correlation [12].

The site of lesion as exemplified in this study was found to be convexity 47.1% which was consistent with previous literature from Bangladesh [7,8].Most of our meningiomas were located over cerebral convexities followed by parasagittal meningiomas. In contrast, studies based on large samples demonstrated that meningiomas at the base of their skulls was the commonest location, followed by convexity meningiomas, and parasagittal meningiomas [10,11].

Meningiomas are graded according to the WHO tumor classification system. The most recent WHO recommendation (2016) divides meningiomas into 15 subtypes into three categories based on histological criteria. This scoring system has important implications for the treatment strategy because it correlates with the risk of recurrence and overall survival [13]. About eighty percent of meningioma cases are WHO Grade I was discovered to be the most prevalent histopathological finding in this study 32 of 34 patients, or 94.1%), followed by WHO Grade 2 (2.9%) and WHO Grade 3 (2.9%), which was consistent with the findings of Utama et al. [9]. In the study of Khalil et al. [7], based on histological criteria majority of the tumors were WHO Grade 1 (85.71%), followed by WHO Grade 2 (9.52%), WHO Grade 3 (4.76%).

The surgical approach aimed at achieving complete tumor removal if possible, taking into consideration patient and tumor characteristics. Based on the surgical report and postoperative imaging, the extent of resection was assessed by the surgeon using the Simpson grade scale. Gross total resection was defined as a Simpson grade I, II, or III resection, according to the European Association of Neuro-Oncology [14]. GTR was achieved in 91.2% (31/34) of the cases in the present series.

Early postoperative hematoma and infections in neurosurgery often have a negative impact on patient's survival and neurologic status. This is particularly relevant in meningioma surgery, where surgical treatment is often curative, and the patient's prognosis is not limited by the disease. Out of 34 patients, 19 (55.9%) developed complications in the postoperative period, and transient hemiparesis was the most frequent complication (26.5%), followed by wound infection (17.6%) in the present series.

In the present study, out of 34 patients operated on, 28 (82.4%) survived at least six months following surgery. The rest of the 6 cases expired, giving the six-month mortality rate of 17.6%. Among these 6 cases, 5 cases expired within 30 days from surgery (the 30-day mortality rate was 14.7%). The incidence of death within 30 days was 2.3% in this study. Meningioma surgery has been linked to several reports of 30-day mortality. In contrast to Bartek et al. [15], who found 0.6 % mortality within 30 days, Lemee et al. [11] found 5.4% mortality within 30 days, and the incidence of death within 30 days was 2.3% in the study of Utama et al. [9]. This suggests that the present study's 30-day mortality rate was higher than the reports in the literature. Here, in this study, we also observed that out of 6 expired cases, 4 cases were expired in the intensive care unit setup within 7 Postoperative days. The most common cause of death was immediate postoperative hemodynamic instability

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and ICU-related complications. Also, the small sample size of the present study might be responsible for this higher mortality rate.

The surgical outcome parameters were assessed by the GOS which was 79.4% of GOS 4-5 and 20.6% of GOS 1-3 in the present study, which was similar to the study of Niban et al. [16] where 80% and 20% of the patients, respectively, had GOS score of 4-5 and 1-3. The scoring of the patients was done with GOS d"3 taken as a poor outcome and GOS more than 3 taken as representative of a good outcome. The outcome was also assessed based on the post-operative KPS score. Among the surviving patients at discharge, 3-months and 6-months majority of them had good outcome and were able to carry on normal daily activities without any need of special care (KPS score 80 or more in 89.3%).

Available data in the literature suggest that age, sex, medical co-morbidity, preoperative KPS, tumor location, tumor size, mode of vascularization and adherence of the tumor, presenting symptoms/signs, prior surgery or radiotherapy are indeed significant factors that influence the operative outcome in meningioma surgery [16-19].In the present study, the mean age of the patients with poor outcomes (49.7±15.1 years) was higher than the patients with good outcomes (46.0±12.1 years), but the difference was not significant statistically. Despite a higher prevalence of meningioma among women, sex did not influence the surgical outcomes of the patients with intracranial meningioma in the present study, which agreed with the study of Kerbner et al. [18], and Han et al. [20]. However, Brodbelt et al. [3] observed that women had better outcomes than men at all ages and Wang et al. [21] observed that overall survival following microsurgical resection was significantly reduced in female patients than male patients with intracranial meningioma.

In the study of Grossman et al. [22] the Charlson comorbidity score is a strong, consistent predictor of outcomes in elderly patients with intracranial meningioma after surgery. Sade and his colleague [6] found that, with one risk level decrease in medical co-morbidity, the risk of unfavorable outcomes decreased by 87% following meningioma surgery. However, the present study failed to establish any such association between comorbidity status and surgical outcome. According to Sade and colleagues [6] severity and presence of symptoms were a significant influential factor for surgical outcomes, but the present study disagreed with these findings.

Poor preoperative clinical conditions (ASA score and KPS score) were significantly associated with subsequent poor outcomes following meningioma surgery in previous studies [18-22]. In the present study, the association between preoperative KPS score and 6-month surgical outcome reached statistical significance in univariate analysis. ASA class has no significant with the 6-months outcome. Preoperative KPS score on the other hand influences the outcome, as the patients with good outcomes has comparatively better KPS scores than the patients with poor outcomes.

In the present study among the different radiological features, tumor location and tumor volume have a significant association with six-month outcome in the present study ($p<0.05$). Tumor volume was significantly higher and the proportion of patients' tumor location at the sphenoidal wing was significantly higher in patients with poor outcomes than their counterparts. Study results are contradictory regarding the tumor location with a focus on attachment as a possible prognostic factor.

Among different factors only three factors, namely, preoperative KPS score, tumor location, and tumor volume were found to have a significant influence on outcome in the present study. However, probably due to the small sample size, none of these factors retained significant association in the multivariate analysis. Nevertheless, the present study has identified predictive factors and at-risk populations for early postoperative poor outcomes. This work would be of special interest in the prevention of early postoperative deterioration or in the planning of closer postoperative monitoring of at-risk populations to allow early diagnosis and early treatment if such postoperative complications occur.

Conclusion:

The present study determines different influencing factors based on preoperative variables in patients with surgically managed intracranial meningiomas. Specific influencing factors for postoperative poor outcomes revealed in univariate analysis were low preoperative KPS score, skull base meningioma specially sphenoid wing meningioma, and large-size tumor. This specific information may help in the decision-making process for surgical treatment of intracranial meningiomas and

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balance operative treatment versus additional treatment options, such as irradiation.

Limitation of the study:

In our study, patients were selected from a single tertiary level center, and outcome assessment is restricted to GOS. Other important parameters, including cognitive disability, etc., have not been assessed. The follow up period was six months only. Further study covering these limitation may add value to the management of intracranial meningioma management strategy.

Conflict of Interest: None to disclose.

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