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CLINICAL FACTORS AFFECTING SEIZURE OCCURRENCE FOLLOWING INTRACRANIAL MENINGIOMA SURGERY

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ABSTRACT

Background: Seizures are commonly associated with Intracranial meningiomas. The outcome of meningioma surgery is good, however, the burden of postoperative seizures and its impact on quality of life are very debilitating to the patient. This study aims to analyze the factors that are associated with post-operative seizures in intracranial meningioma. **Methodology**: Data from a prospective non-randomized sample of patients with the diagnosis of intracranial meningioma admitted for surgery in the Neurosurgery department of a referral center were collected. Demographic data and information regarding clinical, radiological, surgical, and pathological factors were recorded at admission and subsequently during management. The patients were followed up for outcome and occurrence of seizure for 1 month. **Results**: A total of 35 cases were included in the study. The majority of patients had good outcomes following surgery (85% had GOS 5 at 1 month). The incidence of postoperative seizure was 30.6%. Multivariate analysis was done and it was observed that alcohol consumption (p-value - 0.001) and requirement of postoperative ventilation (p-value - 0.004) were factors significantly associated with the occurrence of postoperative seizures. **Conclusion**: The overall outcome of meningioma surgery at this center is good. The high incidence of postoperative seizure and its association with perioperative factors like the requirement of postoperative ventilation is an important marker for the prediction of seizures. Given the impact of seizures on quality of life in benign diseases like meningioma, more studies with longer follow up need to be done to further illustrate the factors.

INTRODUCTION

Meningioma is the most common primary brain tumor, accounting for ~20-35% of all primary intracranial neoplasms. Most of these tumors are WHO Grade I with excellent outcomes following complete resection.[1–3]

Seizures are common in supratentorial meningiomas and are often presenting symptoms in these patients, whereas few suffer a seizure during the perioperative period.[4] Recurrent seizures negatively impact patients' quality of life and result in frequent hospital visits. This results in a significant burden on the socioeconomic well-being of the patient as well as the health system.[5] According to the literature, postoperative seizures are associated with several risk factors and a higher incidence occurs in patients with a previous preoperative seizure history, peritumoral brain edema, meningiomas near functional brain areas, and movement disorders before surgery.[6] The majority occur within the first week after surgery.[7]

Seizure freedom is a significant outcome measure following meningioma resection, however, this is not adequately studied.[8,9] Only a few studies exist investigating rates and predictors of pre-and postoperative seizure in meningiomas.[10–13] In the literature search for relevant studies published, only a few publications were found. Although, one of the studies did show a high incidence of seizure in supratentorial meningiomas in Bir Hospital.[14]

Meningioma is a common intracranial tumor presenting to our hospital and seizure is a common presentation. Many of these patients have new-onset seizures in the peri-/postoperative period which is significantly affecting the quality of life among these patients. This can directly help in planning specific management plan preoperatively to reduce incidence or control seizure. This can be an important study to identify the burden of problem and risk factors of seizure in meningioma, in our context.

METHODOLOGY

Study design: Prospective observational study Place of study: National Academy of Medical Sciences, Bir Hospital Data collection: Preformed proforma Study Period: March 2020 –March 2021 Ethical clearance:

Approval was taken from Institutional Review Board Written informed consent was taken from all patients.

Inclusion criteria

1) All patients above 18 years presenting with meningioma at Neurosurgery Department.

Exclusion Criteria

1) Lost to follow up
2) No consent given
3) Histopathology report other than Meningioma

Seizures were classified according to the International League Against Epilepsy classification of seizures.[47] Early Postoperative seizures were defined as those seizures occurring in the first week following surgery. Late postoperative seizures were defined as those occurring after the first week following surgery.

For this study, the extent of resection was considered gross-total for Simpson Grade 1–3 resection and subtotal for Simpson Grade 4–5 removal.[39]

Procedural Details

Patients that presented to the places of study and who met the selection criteria were selected for the study. Informed written consent was obtained from the patient or the legal guardian.

The patient's identification information and demographic data were recorded (IP Number, Name, Age, Sex, Ethnicity, Occupation, Marital Status, Religion, Address, and Phone Number). Information regarding substance use was recorded (Smoking in Pack Years, Alcohol Use None/Moderate/AUD/Binge/Extreme Binge/Heavy Drinking).[48] The date of admission was recorded.

A complete history and physical examination were done and relevant information was recorded (History of Trauma, Diabetes Mellitus, Hypertension, Liver Disease, Taking Anti-platelet Drugs, Taking Anti-coagulant, Taking corticosteroids, Headache, Vomiting, LOC, Seizure, GCS, Aphasia, Hemiparesis).

All patients underwent imaging (MRI brain with contrast). The imaging findings were recorded (Dimensions of meningioma, site, mass effect, perilesional edema). All patients underwent management of meningioma according to the protocol of the Neurosurgery Department. The patients were discharged when declared fit by the consultant neurosurgeon. The Glasgow Outcome Score was recorded at discharge. The patients followed up in the outpatient department and assessed there or were contacted by phone after 1 month.

Patients were divided into two post-operative groups, the seizure Group and the No seizure Group. The characteristics of the two groups were analyzed. In the seizure group, all those patients were included who had the first episode of seizure during the postoperative period or worsening of the seizure (change in characteristics of preexisting seizure requiring an increase of dose or addition of a second drug to the antiepileptic regimen).

Data Collection

Medical records were retrieved and admission characteristics were assessed. The required information was entered into proforma on admission after obtaining informed consent. The proforma is updated during the patient's hospital stay and at discharge. If the patient presents within one month of follow-up with a seizure, the proforma was updated with relevant information. If the patient does not return during the one-month follow-up, the patient's condition was assessed by phone call, and the proforma is updated with relevant information.

Data Analysis and Statistical Analysis

Interim data analysis was performed every 3 months. Final data analysis was done upon completion of the study. The data was entered into the computer using Libre Office Calc software.

Statistical analysis was done using SPSS software. The association of clinical variables(Age, sex, Smoking, Alcohol consumption), radiologic factors, and surgical/medical management aspects with seizure was tested using chi-squared and ANNOVA tests. The combined analysis of the association between these factors and seizures in meningioma was done using univariate and multivariate linear regression models. Results are presented in tables, graphs, and diagrams. Multivariate analysis was done, to find out the factors that independently predict seizure in meningioma. A 95 % confidence interval was used, and a P value of less than 0.05 was considered statistically significant.

RESULTS

A total of 38 cases of intracranial meningioma were admitted during the study period, out of which 35 patients were included in this study. The figure illustrates the case selection process that was used.

The mean age was 52.8912.019 years(30-79 years). Intracranial meningiomas were encountered most commonly in the age group 40-50 years (Figure 1). The series included 24 female and 11 male patients (Figure. 2) showing a female predisposition.

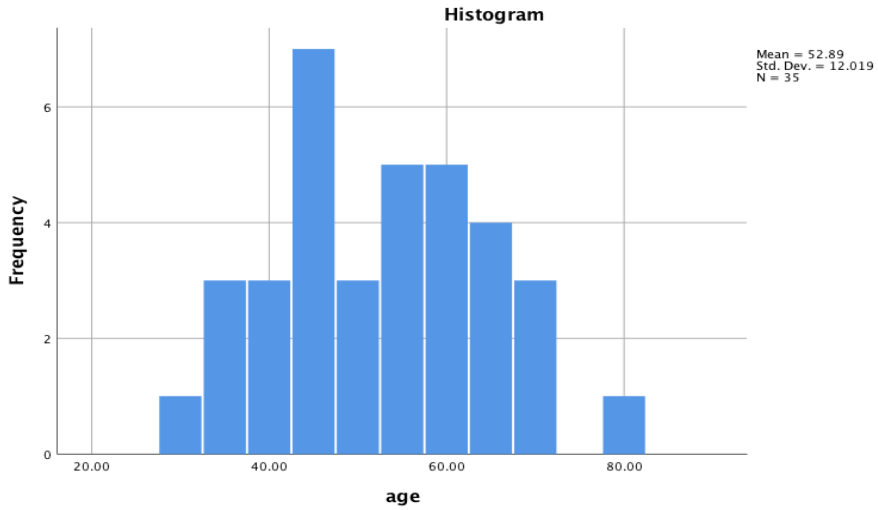

Figure 1: Age distribution of intracranial meningiomas.

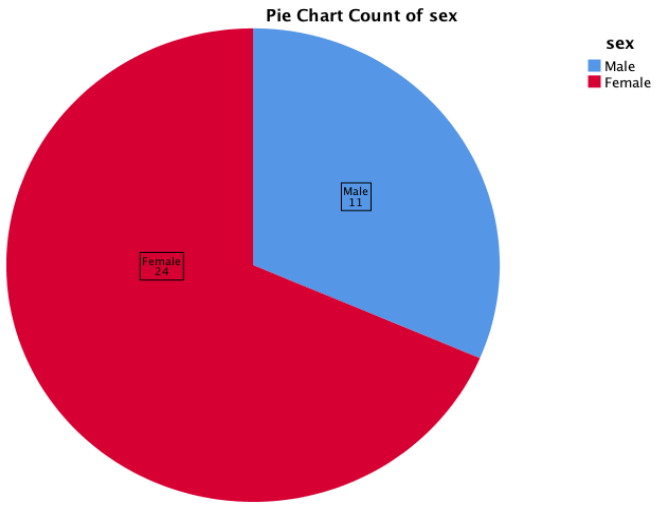

Figure 2: Sex pattern in intracranial meningiomas.

The most common clinical feature at the presentation was headache (Figure 3). It was associated with other symptoms like focal neurologic deficit and vision loss in 6% and 11% respectively. Followed by seizure, being the presenting feature in 23% of the cases.

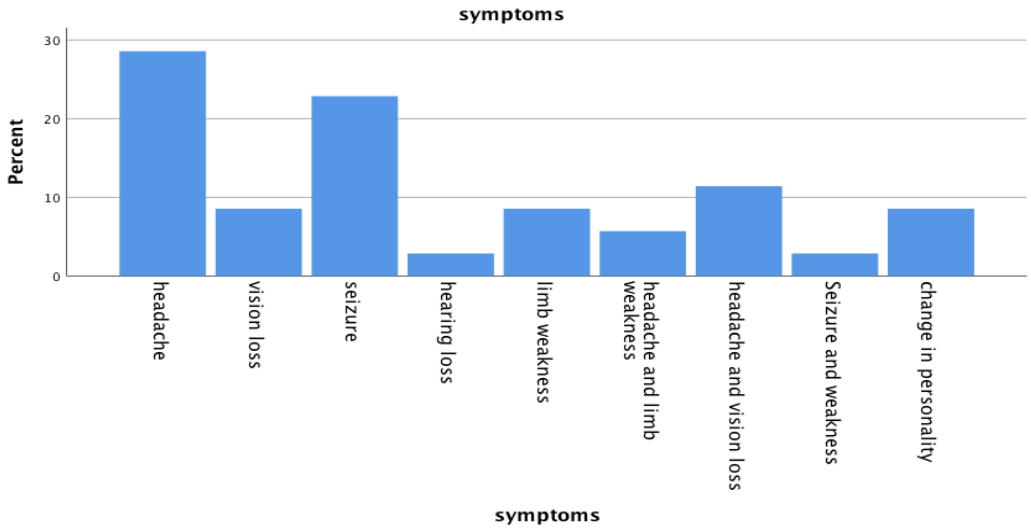

Figure 3: Presenting Symptoms.

Alcohol use was seen in 20% of the cases in this series. Most of the consumers claimed to have alcohol use disorder, with Moderate consumption being the second(Figure 4)

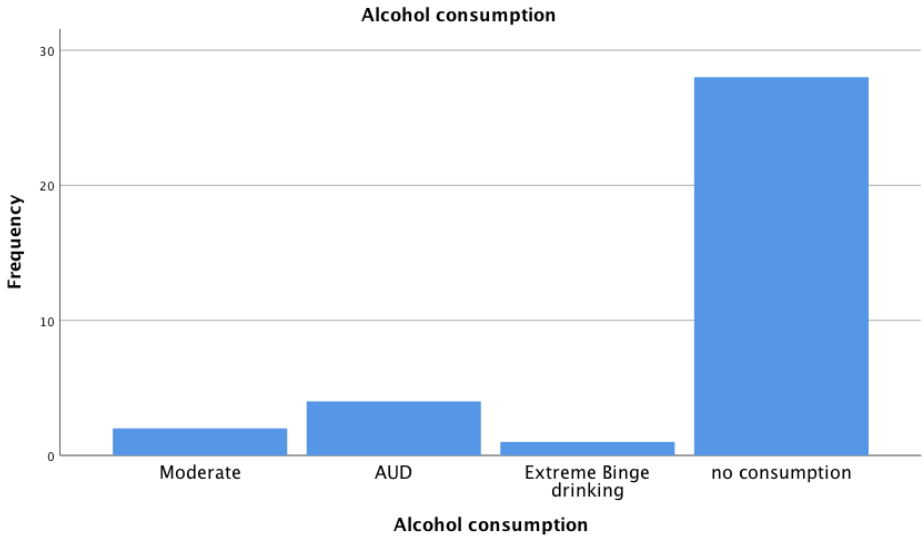

Figure 4: Drinking pattern in cases of meningiomas.

The incidence of smoking was found to be in 23% of the patients with most smokers having 10-20 smoke years of consumption of tobacco(Figure 5)

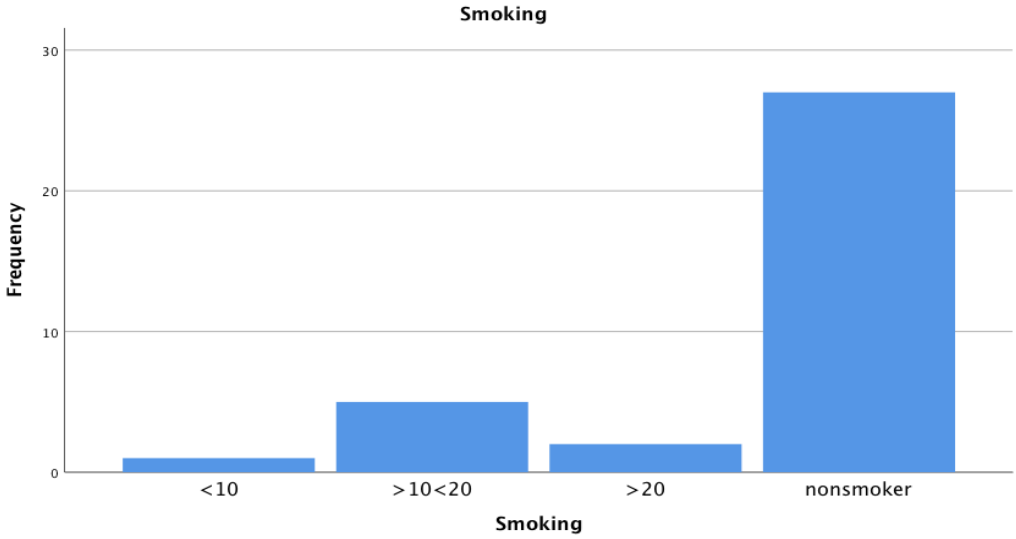

Figure 5: Consumption of Tobacco.

There was no statistically significant difference in the demographic parameters between the two groups(Table 1). The mean age was slightly lower in the seizure group but was not significant. It was found that a higher percentage of males were in the seizure group. Similarly, 25% of cases in the no-seizure group were smokers whereas 18% in the seizure group were smokers, the difference being statistically insignificant. 25% of cases in the no-seizure group were alcohol consumers whereas none in the seizure group consumed alcohol.

Table 1: Comparison of demographic parameters and risk factors with the occurrence of postoperative seizure.

	No seizure	Seizure	P value
Age (years)	54.87±12.18	48.54±10.93	0.15
Sex(Males/Female %)	25/75	45/55	0.23
Smoking(% of smokers)	25	18.18	0.65

Table 2: Comparison of clinical features with Postoperative seizures.

Presenting with -	No seizure	Seizure	P value
Headache(%)	8.4	45.5	0.98
Seizure(%)	20.8	45.4	0.13
Hemiparesis(%)	12.5	18	0.65
Cranial nerve deficits(%)	41.66	36.36	0.76

On analysis of clinical features(Table 2), patients with meningiomas were more likely to present with headaches, and more percentage of patients in the seizure group presented with headaches (45.5%). Similarly, more percentage of patients in the seizure group were those with seizure as presenting features (45.4%). Though these factors were not statistically significant in the head-to-head comparison. There was no significant association in other parameters as well. The percentage of cases in the no seizure group for hypertension, diabetes, and COPD were 16.66%, 12.5%, and 8.3% respectively whereas 9 % of patients in the seizure group were diabetic. There were no patients with hypertension and COPD in the seizure group.

The imaging characteristic that was seen to be associated more with seizure was perilesional edema however statistical significance was not observed(Table 3). More cases of meningioma at the base of the skull were found in the no-seizure group. The average volume of meningioma in both groups is similar.

Table 3: Comparison of Imaging characteristics with seizure occurrences.

	No seizure	seizure	P value
Location			0.34
Non Skull Base	9	6	
Base of skull	15	5	
Perilesional edema(%)	45.83	54.54	0.63
Volume (ml)	113.45±87.81	104.25±69.65	0.78

The association of various surgical factors with the occurrence of seizures shows a statistically significant relation between postoperative ventilation requirement and the occurrence of the seizure (p-value - 0.008). The requirement for blood transfusion and surgical duration was similar in both groups. There was no statistical difference in the grade of tumor between the groups. There was no statistically significant association between resection status and post-operative seizures(p-value-0.41).

Table 4: Comparison of surgical factors with seizure occurrence.

	No seizure	Seizure	P value
Requirement of blood transfusion (%)	54.16	63.36	0.59
Surgical duration <4 hours >4 hours	 8 16	 4 7	 0.86
Requirement of Postoperative ventilation(%)	12.4	54.54	0.008
Resection status Gross total Subtotal	 17 6	 6 5	 0.41
Histopathology Grade I Higher Grades (II and III)	 22 2	 10 1	 0.69

The most common postoperative complication was operative site hematoma, all of which did not require operative intervention. Followed by hydrocephalus in a tentorial meningioma and dyselectrolytemia in 2 patients. Among these, only cases with dyselectrolytemia were observed to be in the seizure occurrence group, however, the association was not statistically significant. Multivariate analysis of variance was done to find out the factors that were more likely to increase the risk of postoperative seizure. The analysis is presented in table 5. In patients with seizures, the factors significantly associated were alcohol consumption and the requirement for postoperative ventilation.

Table 5: Multivariate analysis of factors associated with postoperative seizures in meningioma.

Dependent variable: Post-operative seizure

	Unstandardized B	Coefficients Std. Error	Stan. Coefficient Beta	t	P value
Age	-0.01	0.01	-0.16	-0.58	0.57
Sex	0.03	0.22	0.03	0.12	0.91
Hypertension	-0.34	0.39	-0.23	-0.86	0.41
Diabetes	-0.06	0.43	-0.42	-0.14	0.89
COPD	-0.15	0.49	-0.07	-0.3	0.77
Smoking	0.11	0.35	0.1	0.3	0.77
Alcohol	**0.28**	**0.09**	**0.99**	**3.08**	**0.01**
Hemiparesis	0.29	0.43	0.22	0.69	0.5
Cranial nerve deficit	-0.06	0.24	-0.06	-0.24	0.81
Preop Seizure	-0.81	0.4	-0.79	-2.01	0.07
Volume(ml)	0.01	0.02	0.14	0.58	0.57
Perilesional edema	0.04	0.23	0.04	0.15	0.88
Non-Skull Base Location	0.22	0.06	0.03	0.67	0.64
Skull Base Location	0.39	0.28	0.42	1.39	0.19
Surgical duration	-0.49	0.37	0.05	-0.13	0.89
Resection status	-0.14	0.07	-0.49	-2.02	0.068

CONTD

	Unstandardized B	Coefficients Std. Error	Stan. Coefficient Beta	t	P value
Blood transfusion	0.14	0.27	0.15	0.51	0.62
Mechanical Ventilation	**-0.49**	**0.21**	**-0.47**	**-2.32**	**0.04**
Cavity hematoma	0.47	0.44	0.28	1.04	0.31
Hydrocephalus	-0.52	0.64	-0.19	-0.82	0.43
Dyselectrolytemia	0.5	0.45	-0.25	1.12	0.29
GOS at discharge	-0.77	0.4	-0.74	-1.9	0.84
Histology	0.11	0.45	0.07	0.25	0.81

Note: Statistically significant variables are highlighted in bold characters.

DISCUSSION

Intracranial meningioma is one of the commonest intracranial tumors. The mean age of patients in our study was 52.89±12.019 years(30-79 years). This is similar to the mean age reported in larger cohort studies.[32,33,51] Brokinkel et al. Studied the outcome of surgery by grouping patients into elderly(age>65years) and younger(age<65years) with 162 and 338 cases in each group respectively where they observed the median age in the elderly group at 71 years and median 51 years in the young group. This shows that meningioma is a disease of the aging population and a long duration is taken for it to become symptomatic.[49]

In our study intracranial meningioma was more common in females(68.6%). Previous studies have also found more incidence of meningioma in females.[52,53] An association between hormones and meningioma risk is suggested by findings of increased incidence of postpubertal disease in women versus men (2:1) with the ratio as high as 3.15:1 during peak reproductive age.[53,54] Wiemels et al. Publish an epidemiological study which extrapolated various factors that might lead to an increased incidence in females. The association of meningiomas with estrogen and progesterone receptors as well as links to breast cancer and hormone replacement therapy are under study.[52,37,53] These studies show the expression of hormonal receptors in meningioma, however, their functional significance is still controversial.

The most common presenting feature in our study was a headache. It was the sole feature in 45% of cases. The second most common feature was a seizure(28.6%). Headache was most commonly associated with seizures and cranial nerve deficits. The cranial nerve deficits were present according to the location of the tumor, mostly the optic nerve involvement in the anterior cranial fossa tumor. The incidence of preoperative seizure in meningioma ranges from 12-35% in various studies. The studies show that it is more frequently present in supratentorial tumors, particularly those that have significant peritumoral edema.[55,39,13]

In our study, 25% of alcohol consumers were in the no-seizure whereas none were found in the seizure group. The relationship between alcohol and seizures is multifaceted and complicated. Alcohol increases seizure threshold in users through a complex mechanism that acts through effects on calcium and chloride flux through the ion-gated Glutamate, NMDA, and GABA receptors. During withdrawal, the threshold is decreased and

seizures are seen.[57] Through these pathways alcohol acts in the brain like a depressant drug, consequently increasing the seizure threshold. As a rebound phenomenon, seizures frequently appear after abrupt cessation of prolonged intoxication. Acute alcohol intoxication, on the other hand, may precipitate seizures because of the excitatory effects of alcohol but this is unusual. Hence, Alcohol should be regarded as both anti- and pro-convulsant.[58] In individuals who are heavy drinkers, the abrupt cessation of prolonged intoxication results in withdrawal seizures; drug withdrawal seizures may also occur in individuals who abuse a mixture of alcohol and sedative drugs. In addition, seizures in alcohol-dependent patients may be due to some diseases commonly associated with alcoholism, such as cerebral trauma, infections, and stroke, and it has been suggested that the long-term neurotoxic effects of alcohol could also lead to epilepsy.[59] Only one randomized trial to assess the effects of alcohol in patients with epilepsy has been performed. Hoppener et al. recruited 52 patients with partial and generalized epilepsy into a double-blinded trial in The Netherlands. One to three drinks of orangeade with vodka were given over 2 hour period twice weekly for 16 consecutive weeks to the active group, while the control group was given orangeade only. Throughout the study, medication remained unchanged, and Anti Epileptic Drug concentrations were monitored. Seizures and EEG activity were recorded by experienced observers. Seizure frequency, the level of EEG activity, and carbamazepine, ethosuximide, phenytoin, and valproate concentrations did not change significantly in the patients receiving alcohol compared with the control group. Hence, concluding that moderate social drinking is safe in epileptics.[60]

The most common location of meningioma in our study was Convexity Meningioma (23%), followed by Sphenoid Wing Meningioma(19.4%) and Olfactory Groove Meningioma(16.7%). Parasagittal Meningioma was seen in 13.9% of cases. Among the cases who had a seizure at presentation, 60% had a non-skull base location of the tumor. It has been shown in previous studies that non-skull base locations like convexity and parasagittal areas predispose the patient to seizures.[27] This was true in our study as well. The incidence of preoperative epilepsy in supratentorial has been reported to be from 29 to 67%.[29,61,30] Some authors (Ramamurthi et al., 1980; Chozick et al., 1996)[29,4] have reported that meningioma in the parietal lobe has a significantly higher incidence of postoperative epilepsy than others, but it did not appear to be significantly different in the present study. However, the preoperative seizure was not observed to be associated with the occurrence of the postoperative seizure(p-value 0.07).

The preoperative imaging characteristics that were analyzed were tumor volume, location, and peritumoral edema. The mean volume of mass was lower in the seizure group but the relationship was not statistically significant. Perilesional edema was more frequent in the seizure group, but without statistical significance. Lieu et al. found a significant association of perilesional edema with seizure in their study. In their meta-analysis, Englot et al. also concluded that brain edema is an important factor determining seizure occurrence pre as well as postoperatively.[27,13] Simis et al.[6] concluded in their study that peritumoral edema was associated with the size of the tumor, with the occurrence of seizures, and also affected recurrences. The cause of peritumoral edema is still not clear, however, the role of the Vascular Endothelial Growth Factor, Blood-brain barrier disruption, and recently Glymphatic dysfunction have been studied.[62,63,64] The increased amount of Glutamate and Aspartate found in the edema fluid may explain the excitatory role in causing seizures.[65]

On analysis of surgical factors, the requirement of post-operative ventilation was found to be significantly associated with the occurrence of postoperative seizure. The requirement of post-operative ventilation is a factor dependent on multiple variates and needs to be studied further for the delineation of confounding factors. The chief factors that lead to prolonged ventilation like the large size of the tumor, difficult location, and prolonged surgical duration were individually not found to be significantly associated with the occurrence of a seizure, however.

Multivariate analysis showed a statistically significant association between alcohol consumption having a protective role and post-operative ventilation requirement being a risk for postoperative seizure. The previous studies that studied the role of various factors in the occurrence of postoperative seizure have found factors like tumor location (non-skull base), and peritumoral edema significantly associated with postoperative seizure.[17,27,41,42,67] Komotar et al. studied the use of prophylactic antiepileptics in the preventionpost-operativetive seizures where they concluded that there is no role of prophylactic antiepileptics in the prevention of early seizure occurring within 1 week of surgery.[10] Similarly, Sughrue et al. Found the overall incidence of postoperative seizure to be very low in their study, and eventually, no additional benefit was observed from the use of prophylactic drugs.[68]

CONCLUSION

The occurrence of postoperative seizure after meningioma surgery is 30.6%. The overall outcome of meningioma surgery is good with a GOS of 5 in 85% of cases at 1 month. The factors associated with the occurrence of postoperative seizure were alcohol consumption and the requirement for postoperative ventilation. Perilesional edema and the location of the tumor seem to play some role in the occurrence of a seizure, however, more study needs to be done to prove its significance, as statistical significance was not observed in this study. Looking at the burden of antiepileptic therapy and the impact of seizures on the

quality of life of a patient with a benign disease like meningioma, more studies need to be conducted to further explore the causes of post-operative seizure and their prevention.

REFERENCES

1. Zhang B, Zhao G, Yang HF, Wang D, Yu JL, Huang HY. Assessment of risk factors for early seizures following surgery for meningiomas using logistic regression analysis. J Int Med Res, 2011; 39(5): 1728–35.
2. Dolecek TA, Propp JM, Stroup NE, Kruchko C. CBTRUS statistical report: primary brain and central nervous system tumors diagnosed in the United States in 2005-2009. Neuro-Oncol, 2012 Nov; 14 Suppl 5: v1-49.
3. Sughrue ME, Cage T, Shangari G, Parsa AT, McDermott MW. Clinical characteristics and surgical outcomes of patients presenting with meningiomas arising predominantly from the floor of the middle fossa. Neurosurgery, 2010 Jul; 67(1): 80–6; discussion 86.
4. Chozick BS, Reinert SE, Greenblatt SH. Incidence of seizures after surgery for supratentorial meningiomas: a modern analysis. J Neurosurg, 1996 Mar; 84(3): 382–6.
5. Chen WC, Chen EY, Gebre RZ, Johnson MR, Li N, Vitkovskiy P, et al. Epilepsy and driving: potential impact of transient impaired consciousness. Epilepsy Behav EB, 2014 Jan; 30: 50–7.
6. Simis A, Pires de Aguiar PH, Leite CC, Santana PA, Rosemberg S, Teixeira MJ. Peritumoral brain edema in benign meningiomas: correlation with clinical, radiologic, and surgical factors and possible role on recurrence. Surg Neurol, 2008 Nov; 70(5): 471–7; discussion 477.
7. Mauro AM, Bomprezzi C, Morresi S, Provinciali L, Formica F, Iacoangeli M, et al. Prevention of early postoperative seizures in patients with primary brain tumors: preliminary experience with oxcarbazepine. J Neurooncol, 2007 Feb; 81(3): 279–85.
8. Schoenegger K, Oberndorfer S, Wuschitz B, Struhal W, Hainfellner J, Prayer D, et al. Peritumoral edema on MRI at initial diagnosis: an independent prognostic factor for glioblastoma? Eur J Neurol, 2009 Jul; 16(7): 874–8.
9. İldan F, Erman T, Göçer Aİ, Tuna M, Bağdatoğlu H, Çetinalp E, et al. Predicting the Probability of Meningioma Recurrence in the Preoperative and Early Postoperative Period: A Multivariate Analysis in the Midterm Follow-Up. Skull Base, 2007 May; 17(3): 157–71.
10. Komotar RJ, Raper DMS, Starke RM, Iorgulescu JB, Gutin PH. Prophylactic antiepileptic drug therapy in patients undergoing supratentorial meningioma resection: a systematic analysis of efficacy. J Neurosurg, 2011 Sep; 115(3): 483–90.
11. Sanai N, Sughrue ME, Shangari G, Chung K, Berger MS, McDermott MW. Risk profile associated with convexity meningioma resection in the modern neurosurgical era. J Neurosurg, 2010 May; 112(5): 913–9.
12. Chaichana KL, Pendleton C, Zaidi H, Olivi A, Weingart JD, Gallia GL, et al. Seizure control for patients undergoing meningioma surgery. World Neurosurg, 2013 Apr; 79(3–4): 515–24.
13. Englot DJ, Magill ST, Han SJ, Chang EF, Berger MS, McDermott MW. Seizures in supratentorial meningioma: a systematic review and meta-analysis. J Neurosurg, 2016 Jun; 124(6): 1552–61.
14. G.R. Sharma, Bista P, Kumar P. Intracranial Meningioma Surgery: Our Experience in Bir Hospital. Nepal J Neurosci, 2013; 10(1): 17–23.
15. Al-Rodhan N, Laws E. The history of intracranial meningiomas. Meningiomas N Y Raven Press, 1991; 1(1): 1–7.
16. Mackay RP. EPENDYMOBLASTOMA IN THE FOURTH VENTRICLE, WITH NEW BONE FORMATION. Arch Neurol Psychiatry, 1935 Oct 1; 34(4): 844–53.
17. Meningiomas. Their classification, regional behaviour, life history, and surgical end results: By Harvey Cushing, m.d., with the collaboration of Louise Eisenhardt, m.d. Springfield, Illinois, 1938. Charles C. Thomas. Price $15.00. Am J Surg, 1938 Nov 1; 42(2): 448.
18. Kurland LT, Schoenberg BS, Annegers JF, Okazaki H, Molgaard CA. The incidence of primary intracranial neoplasms in Rochester, Minnesota, 1935-1977. Ann N Y Acad Sci, 1982; 381: 6–16.
19. Sutherland GR, Florell R, Louw D, Choi NW, Sima AA. Epidemiology of primary intracranial neoplasms in Manitoba, Canada. Can J Neurol Sci J Can Sci Neurol, 1987 Nov; 14(4): 586–92.
20. Buerki RA, Horbinski CM, Kruser T, Horowitz PM, James CD, Lukas RV. An overview of meningiomas. Future Oncol Lond Engl, 2018 Sep; 14(21): 2161–77.
21. Wiemels J, Wrensch M, Claus EB. Epidemiology and etiology of meningioma. J Neurooncol, 2010 Sep; 99(3): 307–14.
22. Vernooij MW, Ikram MA, Tanghe HL, Vincent AJPE, Hofman A, Krestin GP, et al. Incidental Findings on Brain MRI in the General Population. N Engl J Med, 2007 Nov 1; 357(18): 1821–8.
23. Annegers JF, Schoenberg BS, Okazaki H, Kurland LT. Epidemiologic Study of Primary Intracranial Neoplasms. JAMA Neurol, 1981 Apr 1; 38(4): 217–9.
24. Nakasu S, Hirano A, Shimura T, Llena JF. Incidental meningiomas in autopsy study. Surg Neurol, 1987 Apr; 27(4): 319–22.
25. Go RS, Taylor BV, Kimmel DW. The natural history of asymptomatic meningiomas in Olmsted County, Minnesota. Neurology, 1998 Dec; 51(6): 1718–20.
26. Niiro M, Yatsushiro K, Nakamura K, Kawahara Y, Kuratsu J. Natural history of elderly patients with asymptomatic meningiomas. J Neurol Neurosurg Psychiatry, 2000 Jan; 68(1): 25–8.

27. Lieu AS, Howng SL. Intracranial meningiomas and epilepsy: incidence, prognosis and influencing factors. Epilepsy Res, 2000 Jan; 38(1): 45–52.
28. Chozick BS, Reinert SE, Greenblatt SH. Incidence of seizures after surgery for supratentorial meningiomas: a modern analysis. J Neurosurg, 1996 Mar; 84(3): 382–6.
29. Ramamurthi B, Ravi B, Ramachandran V. Convulsions with meningiomas: incidence and significance. Surg Neurol, 1980 Dec; 14(6): 415–6.
30. Chow SY, Hsi MS, Tang LM, Fong VH. Epilepsy and intracranial meningiomas. Zhonghua Yi Xue Za Zhi Chin Med J Free China Ed, 1995 Feb; 55(2): 151–5.
31. Anderson D, Khalil M. Meningioma and the ophthalmologist. A review of 80 cases. Ophthalmology, 1981 Oct; 88(10): 1004–9.
32. Bosnjak R, Derham C, Popović M, Ravnik J. Spontaneous intracranial meningioma bleeding: clinicopathological features and outcome. J Neurosurg, 2005 Sep; 103(3): 473–84.
33. Hashiba T, Hashimoto N, Izumoto S, Suzuki T, Kagawa N, Maruno M, et al. Serial volumetric assessment of the natural history and growth pattern of incidentally discovered meningiomas. J Neurosurg, 2009 Apr; 110(4): 675–84.
34. Rogers L, Barani I, Chamberlain M, Kaley TJ, McDermott M, Raizer J, et al. Meningiomas: knowledge base, treatment outcomes, and uncertainties. A RANO review. J Neurosurg, 2015 Jan; 122(1): 4–23.
35. Watts J, Box G, Galvin A, Brotchie P, Trost N, Sutherland T. Magnetic resonance imaging of meningiomas: a pictorial review. Insights Imaging, 2014 Feb; 5(1): 113–22.
36. Louis DN, Perry A, Reifenberger G, von Deimling A, Figarella-Branger D, Cavenee WK, et al. The 2016 World Health Organization Classification of Tumors of the Central Nervous System: a summary. Acta Neuropathol (Berl), 2016 Jun; 131(6): 803–20.
37. Zada G, Başkaya MK, Shah MV. Introduction: surgical management of skull base meningiomas. Neurosurg Focus. 2017 Oct; 43(VideoSuppl2): Intro.
38. Mirimanoff RO, Dosoretz DE, Linggood RM, Ojemann RG, Martuza RL. Meningioma: analysis of recurrence and progression following neurosurgical resection. J Neurosurg, 1985 Jan; 62(1): 18–24.
39. Simpson D. The recurrence of intracranial meningiomas after surgical treatment. J Neurol Neurosurg Psychiatry, 1957 Feb; 20(1): 22–39.
40. Sun SQ, Hawasli AH, Huang J, Chicoine MR, Kim AH. An evidence-based treatment algorithm for the management of WHO Grade II and III meningiomas. Neurosurg Focus, 2015 Mar; 38(3): E3.
41. Oya S, Kawai K, Nakatomi H, Saito N. Significance of Simpson grading system in modern meningioma surgery: integration of the grade with MIB-1 labeling index as a key to predict the recurrence of WHO Grade I meningiomas. J Neurosurg, 2012 Jul; 117(1): 121–8.
42. Walcott BP, Nahed BV, Brastianos PK, Loeffler JS. Radiation Treatment for WHO Grade II and III Meningiomas. Front Oncol, 2013 Sep 2; 3: 227.
43. Bria C, Wegner RE, Clump DA, Vargo JA, Mintz AH, Heron DE, et al. Fractionated stereotactic radiosurgery for the treatment of meningiomas. J Cancer Res Ther, 2011 Mar; 7(1): 52–7.
44. Lambertz N, Hindy NE, Adler C, Rump K, Adamzik M, Keyvani K, et al. Expression of aquaporin 5 and the AQP5 polymorphism A(-1364)C in association with peritumoral brain edema in meningioma patients. J Neurooncol, 2013 Apr; 112(2): 297–305.
45. Reszec J, Hermanowicz A, Rutkowski R, Turek G, Mariak Z, Chyczewski L. Expression of MMP-9 and VEGF in Meningiomas and Their Correlation with Peritumoral Brain Edema. BioMed Res Int, 2015; 2015: 1–8.
46. Sughrue ME, Kane AJ, Shangari G, Rutkowski MJ, McDermott MW, Berger MS, et al. The relevance of Simpson Grade I and II resection in modern neurosurgical treatment of World Health Organization Grade I meningiomas. J Neurosurg, 2010 Nov; 113(5): 1029–35.
47. Scheffer IE, Berkovic S, Capovilla G, Connolly MB, French J, Guilhoto L, et al. ILAE classification of the epilepsies: Position paper of the ILAE Commission for Classification and Terminology. Epilepsia, 2017; 58(4): 512–21.
48. Drinking Patterns and Their Definitions [Internet]. [cited 2019 Oct 7]. Available from: https: //www.ncbi.nlm.nih.gov/pmc/articles/PMC6104961/
49. Brokinkel B, Holling M, Spille DC, Heß K, Sauerland C, Bleimüller C, et al. Surgery for meningioma in the elderly and long-term survival: comparison with an age- and sex-matched general population and with younger patients. J Neurosurg, 2017 Apr; 126(4): 1201–11.
50. Hasseleid BF, Meling TR, Rønning P, Scheie D, Helseth E. Surgery for convexity meningioma: Simpson Grade I resection as the goal: clinical article. J Neurosurg, 2012 Dec; 117(6): 999–1006.
51. Yamasaki F, Yoshioka H, Hama S, Sugiyama K, Arita K, Kurisu K. Recurrence of meningiomas. Cancer, 2000 Sep 1; 89(5): 1102–10.
52. Wiemels J, Wrensch M, Claus EB. Epidemiology and etiology of meningioma. J Neurooncol, 2010 Sep; 99(3): 307–14.
53. Claus EB, Black PM, Bondy ML, Calvocoressi L, Schildkraut JM, Wiemels JL, et al. Exogenous hormone use and meningioma risk: What do we tell our patients? Cancer, 2007 Aug 1; 110(3): 471–6.
54. Lee E, Grutsch J, Persky V, Glick R, Mendes J, Davis F. Association of meningioma with reproductive factors. Int J Cancer, 2006 Sep 1; 119(5): 1152–7.
55. Waagemans ML, van Nieuwenhuizen D, Dijkstra M, Wumkes M, Dirven CMF, Leenstra S, et al. Long-term Impact of Cognitive Deficits and Epilepsy on Quality of Life in Patients With Low-Grade

Meningiomas. Neurosurgery, 2011 Jul 1; 69(1): 72–9.
56. Ravindranath K, Vasudevan MC, Pande A, Symss N. Management of pediatric intracranial meningiomas: an analysis of 31 cases and review of literature. Childs Nerv Syst, 2013 Apr; 29(4): 573–82.
57. Hillbom M, Pieninkeroinen I, Leone M. Seizures in alcohol-dependent patients: epidemiology, pathophysiology and management. CNS Drugs, 2003; 17(14): 1013–30.
58. Yamane H, Katoh N. Alcoholic epilepsy. A definition and a description of other convulsions related to alcoholism. Eur Neurol, 1981; 20(1): 17–24.
59. Hauser WA, Ng SK, Brust JC. Alcohol, seizures, and epilepsy. Epilepsia, 1988; 29 Suppl 2: S66-78.
60. Höppener RJ, Kuyer A, van der Lugt PJ. Epilepsy and alcohol: the influence of social alcohol intake on seizures and treatment in epilepsy. Epilepsia, 1983 Aug; 24(4): 459–71.
61. Chozick BS, Reinert SE, Greenblatt SH. Incidence of seizures after surgery for supratentorial meningiomas: a modern analysis. J Neurosurg, 1996 Mar; 84(3): 382–6.
62. Simis A, Pires de Aguiar PH, Leite CC, Santana PA, Rosemberg S, Teixeira MJ. Peritumoral brain edema in benign meningiomas: correlation with clinical, radiologic, and surgical factors and possible role on recurrence. Surg Neurol, 2008 Nov; 70(5): 471–7.
63. Toh CH, Siow TY, Castillo M. Peritumoral Brain Edema in Meningiomas May Be Related to Glymphatic Dysfunction. Front Neurosci, 2021 Apr 22; 15: 674898.
64. Kawaguchi T, Kameyama S, Tanaka R. Peritumoral Edema and Seizure in Patients with Cerebral Convexity and Parasagittal Meningiomas. Neurol Med Chir (Tokyo), 1996; 36(8): 568–74.
65. Kimura T, Ohkubo M, Igarashi H, Kwee IL, Nakada T. Increase in glutamate as a sensitive indicator of extracellular matrix integrity in peritumoral edema: a 3.0-tesla proton magnetic resonance spectroscopy study. J Neurosurg, 2007 Apr; 106(4): 609–13.
66. Sughrue ME, Rutkowski MJ, Chang EF, Shangari G, Kane AJ, McDermott MW, et al. Postoperative seizures following the resection of convexity meningiomas: are prophylactic anticonvulsants indicated? Clinical article. J Neurosurg, 2011 Mar; 114(3): 705–9.
67. Tsuji M, Shinomiya S, Inoue R, Sato K. Prospective Study of Postoperative Seizure in Intracranial Meningioma. Psychiatry Clin Neurosci, 1993 Jun; 47(2): 331–4.
68. Sughrue ME, Rutkowski MJ, Chang EF, Shangari G, Kane AJ, McDermott MW, et al. Postoperative seizures following the resection of convexity meningiomas: are prophylactic anticonvulsants indicated?: Clinical article. J Neurosurg, 2011 Mar; 114(3): 705–9.