Seizure Outcomes and Factors Correlating with Seizure Freedom Following Supratentorial Brain Tumor Surgery

Bunpot Sitthinamsuwan MD, MSc*, Sarun Jotikasthira MD*, Inthira Khampalikit MD*, Chottiwat Tansirisithikul MD*, Ekawut Chankaew MD*, Sarun Nunta-aree MD, PhD*

** Division of Neurosurgery, Department of Surgery, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand*

Background: *Seizure is one of common presentations of brain tumor. Surgical resection is helpful for controlling seizure and for eradication of compression-related symptoms.*

Objective: *This study aimed to investigate seizure outcomes and the factors that are significantly associated with long-term seizure freedom after supratentorial brain tumor surgery in patients who had seizure as a clinical manifestation.*

Material and Method: *This study was conducted in patients with tumor-related seizure who underwent supratentorial surgery at Siriraj Hospital (Bangkok, Thailand) with complete postoperative follow-up >1 year. Patients were divided into either the favorable outcome (seizure-free) group or the unfavorable outcome (not seizure-free) group. Collected data included gender, age, seizure characteristics, neurological manifestations, radiographic characteristics, histopathologic diagnosis, treatment, preoperative and postoperative antiepileptic drug (AEDs) use, and postoperative seizure outcome.*

Results: *One hundred and twenty-eight patients (53 males, 75 females) were included, with a mean age at seizure onset of 42.5±16.4 years and a mean age at surgery of 43.7±15.9 years. There were 100 patients and 28 patients in the favorable and unfavorable groups, respectively. Rate of seizure freedom following surgery was 78%. Factors contributing to seizure-free outcome in univariate analysis were older age at seizure onset, preoperative seizure duration ≤15 months, preoperative seizure frequency ≤1 episode/month, absence of cortical involvement, presence of hydrocephalus, tumor of non-glial origin, tumor of meningeal origin, absence of postoperative seizure, gross total resection, and lower number and shorter duration of postoperative use of AEDs. In multiple regression analysis, preoperative seizure frequency ≤1 episode/month, absence of postoperative seizure, and lower number of postoperative AEDs were found to be factors significantly associated with postoperative seizure freedom.*

Conclusion: *In this study, 78% of patients with brain tumor became seizure-free after surgery. Independent factors significantly correlated with seizure-free outcome included rarely occurring preoperative seizure, absence of postoperative seizure, and number of AEDs used after surgery. These results indicate that strict control of preoperative seizure, early surgical intervention, and total resection of the tumor increases the likelihood of postsurgical seizure freedom.*

Keywords: *Seizure outcome, Seizure freedom, Supratentorial brain tumor, Brain tumor surgery, Factor*

J Med Assoc Thai 2017; 100 (Suppl. 4): S59-S68
Full text. e-Journal: *http://www.jmatonline.com*

Seizure is a common clinical manifestation in patients with brain tumor. The frequency of epileptic seizure as a presenting symptom is approximately 30% to 50% in brain tumor patients[1-4]. Tumor-associated seizures significantly impair quality of life and may be refractory to antiepileptic drug (AED) therapy. Several factors impact the occurrence of seizures, including tumor type, tumor location, alteration of the peritumoral environment, and hereditary factors[3].

Surgery is the mainstay treatment in patients with brain tumor. Tumor resection is preferred when a tumor can be removed without risk of neurological morbidity. Resection relieves compressive symptoms caused by the tumor, and helps to eliminate epileptogenic focus and to recover good seizure control.

Several studies have reported seizure outcomes and factors associated with seizure outcomes after surgery. However, those studies focused primarily

Correspondence to:
Sitthinamsuwan B, Division of Neurosurgery, Department of Surgery, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok 10700, Thailand.
Phone: +66-2-4198003, Fax: +66-2-4113006
E-mail: bunpotsi@yahoo.com

on a specific type of tumor or a specific patient age group[5-13]. The aim of this study was to investigate seizure outcomes and the factors that are significantly associated with long-term seizure freedom after supratentorial brain tumor surgery in patients who had seizure as a clinical manifestation.

Material and Method

Patient population

This study was conducted in patients with tumor-related seizure who underwent supratentorial surgery at the Division of Neurosurgery, Department of Surgery, Faculty of Medicine Siriraj Hospital, Mahidol University during the 2007 to 2014 study period. All patients with supratentorial brain tumor who had seizure as a clinical manifestation, underwent surgery during this period and completed follow-up >1 year after surgery, were included. Patients who underwent previous brain surgery were excluded. The protocol for this study was approved by the Siriraj Institutional Review Board (SIRB), Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand.

Data collection

Collected data included gender, age, seizure characteristics, clinical manifestations, radiographic characteristics, histopathologic diagnosis, treatment, pre-operative and postoperative AED use, and postoperative seizure outcome. Postoperative seizure outcome was classified using International League Against Epilepsy (ILAE) classification[14]. Patients were classified into either the favorable seizure outcome or unfavorable seizure outcome group. Patients with an ILAE class 1 (seizure-free without aura) rating were classified as having a favorable outcome. Patients with an ILAE class rating of 2 to 6 (not seizure-free) were classified as having an unfavorable outcome. All patients underwent contrast-enhanced cranial magnetic resonance imaging (MRI) within one week for malignant tumors and six months for benign tumors. Interval cranial MRI was followed for surveillance of tumor recurrence. Gross total resection was defined as an absence of residual tumor on the first postoperative cranial MRI. Histopathologic diagnosis of brain tumor was definitively determined by experienced neuropathologists at our institute.

Statistical analysis

Demographic data were interpreted using descriptive statistics. Data are reported as number and percentage, mean $\pm$ standard deviation, or median and range. Association between postoperative seizure outcome and individual factors was analyzed using Pearson's Chi-square test, Yates continuity correction, or Fisher's exact test. Independent t-test was used to analyze differences in age at seizure onset and age at surgery between groups. Mann-Whitney U test was used to analyze duration of seizure before surgery, and number and duration of AEDs used before and after surgery between groups. Multiple forward binary logistic regression analysis was used to adjust for confounding factors associated with seizure-free outcome. Factors with a p-value <0.1 in univariate analysis were included in multivariable analysis. Strength of association was evaluated using odds ratio (OR) and 95% confidence interval (95% CI). A p-value of less than 0.05 was regarded as being statistically significant. Data were analyzed using PASW Statistics version 18.0 (SPSS, Inc., Chicago, IL, USA).

Results

One hundred and twenty-eight patients were included in this study. Of those, 53 (41.4%) and 75 (58.6%) were male and female, respectively. Mean age at seizure onset and mean age at surgery was 42.5$\pm$16.4 years (range: 0.6 to 78.3) and 43.7$\pm$15.9 years (range: 2.1 to 79.4), respectively. Median duration of seizure was 97.5 days, and the mean postoperative follow-up period was 4.2 years. One hundred patients were categorized into the favorable outcome group and 28 were allocated to the unfavorable outcome group. There was no statistically significant difference between groups for gender. Mean age at seizure onset in the unfavorable outcome group (37.1 years) was significantly lower than in the favorable outcome group (44 years) (p = 0.049); whereas, mean age at surgery and duration between seizure onset and surgery were not significantly different between groups.

In univariate analysis (Table 1), older age at seizure onset (p = 0.049), duration of seizure $\leq$15 months (p = 0.015), rarely occurring preoperative seizure ($\leq$1 episodes/month) (p<0.001), absence of cortical involvement (p = 0.034), presence of hydrocephalus (p = 0.040), tumor of non-glial origin (p = 0.033), tumor of meningeal origin (p = 0.037), and absence of postoperative seizure (p<0.001) were significantly associated with postoperative seizure-free outcome. Tumor histopathology is shown in Table 2. Regarding univariate analysis of treatment (Table 3), achievement of gross total resection was significantly associated with seizure freedom (p = 0.035). Moreover, as compared to the favorable outcome group, the unfavorable

Table 1. Demographic characteristics, clinical manifestations, radiographic characteristics, tumor pathology, and postoperative seizure outcomes by group

Variable	Favorable (n = 100)	Unfavorable (n = 28)	*p*-value
Demographic characteristics			
Female, n (%)	58 (58.0)	17 (60.7)	0.797
Age at seizure onset (year), mean ± SD	44±16.2	37.1±16.2	0.049*
Age at surgery (year), mean ± SD	45±16.1	39.2±14.5	0.088
Preoperative seizure			
Duration of seizure (day), median	87.5	136	0.058
Duration of seizure ≤15 months, n (%)	89 (89.0)	19 (67.9)	0.015*
Seizure type, n (%)			
Simple partial	22 (22.0)	10 (35.7)	0.303
Complex partial	30 (30.0)	8 (28.6)	
Generalized	48 (48.0)	10 (35.7)	
Seizure frequency, n (%)			
Rare (≤1 seizures/month)	81 (81.0)	11 (39.3)	<0.001
Frequent (>1 seizures/month)	19 (19.0)	17 (60.7)	
Neurologic manifestations			
Motor deficit, n (%)	54 (54.0)	16 (57.1)	0.659
Sensory deficit, n (%)	8 (8.0)	1 (3.6)	0.683
Language deficit, n (%)	6 (6.0)	2 (7.1)	1.000
Visual deficit, n (%)	5 (5.0)	1 (3.6)	1.000
Cranial nerve deficit, n (%)	11 (11.0)	4 (14.3)	0.740
Increased intracranial pressure, n (%)	19 (19.0)	1 (3.6)	0.073
Preoperative radiographic characteristics			
Lateralization, n (%)			
Unilateral	84 (83.0)	26 (92.9)	0.432
Bilateral	3 (3.0)	0 (0.0)	
Midline	13 (13.0)	2 (7.1)	
Extra-axial location, n (%)	40 (40.0)	5 (17.9)	0.052
Cortical involvement, n (%)	54 (54.0)	22 (78.6)	0.034*
Frontal lobe involvement, n (%)	71 (71.0)	21 (75.0)	0.858
Parietal lobe involvement, n (%)	23 (23.0)	12 (42.9)	0.065
Temporal lobe involvement, n (%)	26 (26.0)	7 (25.0)	1.000
Occipital lobe involvement, n (%)	3 (3.0)	1 (3.6)	1.000
Insular lobe involvement, n (%)	12 (12.0)	3 (10.7)	1.000
Deep structure involvement, n (%)	22 (22.0)	11 (39.3)	0.109
Perilesional edema, n (%)	83 (83.0)	21 (75.0)	0.494
Hydrocephalus, n (%)	15 (15.0)	0 (0.0)	0.040*
Tumor calcification, n (%)	14 (14.0)	1 (3.6)	0.188
Contrast enhancement, n (%)	83 (83.0)	19 (67.9)	0.135
Postoperative seizure			
Absence of seizure, n (%)	81 (81.0)	6 (21.4)	<0.001*
Seizure occurring before 72 hours, n (%)	3 (3.0)	1 (3.6)	
Seizure occurring after 72 hours, n (%)	16 (16.0)	21 (75.0)	
Postoperative radiographic characteristics			
Residual or recurrent tumor, n (%)	59 (59.0)	21 (75.0)	0.185
Encephalomalacia, n (%)	71 (71.0)	15 (53.6)	0.131
Tumor type			
Primary tumor, n (%)	95 (95.0)	25 (89.3)	0.371
Benign tumor, n (%)	62 (62.0)	17 (60.7)	1.000
Non-glial tumor, n (%)	52 (52.0)	8 (28.6)	0.033*
Meningeal tumor, n (%)	37 (37.0)	4 (14.3)	0.037*

* *p*-value <0.05 indicates statistical significance

Table 2. Tumor histopathology and postoperative seizure outcomes by group

Tumor histopathology	Favorable (n = 100)	Unfavorable (n = 28)	Total (n = 128)
Low-grade glioma			
Diffuse astrocytoma, n (%)	12 (12.0)	3 (10.7)	15 (11.7)
Oligodendroglioma, n (%)	4 (4.0)	3 (10.7)	7 (5.5)
Oligoastrocytoma, n (%)	3 (3.0)	2 (7.1)	5 (3.9)
Gemistocytic astrocytoma, n (%)	0 (0.0)	3 (10.7)	3 (2.3)
Ependymoma, n (%)	2 (2.0)	0 (0.0)	2 (1.6)
High-grade glioma			
Glioblastoma, n (%)	17 (17.0)	4 (14.3)	21 (16.4)
Anaplastic astrocytoma, n (%)	5 (5.0)	1 (3.6)	6 (4.7)
Anaplastic oligoastrocytoma, n (%)	5 (5.0)	2 (7.1)	7 (5.5)
Gliomatosis cerebri, n (%)	0 (0.0)	2 (7.1)	2 (1.6)
Meningeal tumor			
WHO grade 1, n (%)	29 (29.0)	3 (10.7)	32 (25.0)
WHO grade 2, n (%)	6 (6.0)	1 (3.6)	7 (5.5)
WHO grade 3, n (%)	2 (2.0)	0 (0.0)	2 (1.6)
Glioneural tumor			
Dysembryoplastic neuroepithelial tumor, n (%)	1 (1.0)	1 (3.6)	2 (1.6)
Ganglioglioma, n (%)	1 (1.0)	0 (0.0)	1 (0.8)
Hematologic tumor			
Lymphoma, n (%)	2 (2.0)		2 (1.6)
Histiocytic tumor, n (%)	1 (1.0)	0 (0.0)	1 (0.8)
Metastatic tumor			
Brain metastasis, n (%)	5 (5.0)	3 (10.7)	8 (6.3)
Other tumor			
Schwannoma, n (%)	1 (1.0)	0 (0.0)	1 (0.8)
Craniopharyngioma, n (%)	3 (3.0)	0 (0.0)	3 (2.3)
Papillary tumor of the pineal region, n (%)	1 (1.0)	0 (0.0)	1 (0.8)

Table 3. Treatment modalities and antiepileptic drugs given before and after surgery by group

Variable	Favorable (n = 100)	Unfavorable (n = 28)	*p*-value
Treatment modalities			
Gross total resection, n (%)	67 (67.0)	12 (42.9)	0.035*
Radiation therapy, n (%)	45 (45.0)	15 (53.6)	0.422
Chemotherapy, n (%)	16 (16.0)	7 (25.0)	0.273
Combined radiation therapy and chemotherapy, n (%)	12 (12.0)	6 (21.4)	0.224
Preoperative AED			
Median number of AEDs	1	1	0.150
Median duration of AEDs (day)	29	61	0.150
Postoperative AED			
Median number of AEDs	1	2	<0.001*
Median duration of AED (day)	14.5	45.5	0.002*

* *p*-value <0.05 indicates statistical significance
AEDs = antiepileptic drugs

Table 4. Multivariable analysis of potential factors found to be associated with seizure-free outcome

	Crude OR (95% CI)	*p*-value	Adjusted OR (95% CI)	*p*-value
Preoperative seizure frequency				
Frequent seizure (>1 seizures/month)	1.00		1.00	
Rare seizure (≤1 seizures/month)	6.59 (2.66 to 16.34)	<0.001*	4.62 (1.46 to 14.65)	0.009*
Postoperative seizure				
Seizure occurring after 72 hours	1.00		1.00	
Absence of seizurePostoperative AED	17.72 (6.18 to 50.83)	<0.001*	15.73 (4.91 to 50.40)	<0.001*
Number of AEDs	0.98 (0.97 to 0.99)	0.001*	0.44 (0.19 to 0.98)	0.046*

* *p*-value<0.05 indicates statistical significance

AEDs = antiepileptic drugs

In addition to the variables listed in Table 4, the following variables were included in multiple forward binary logistic regression analysis: age at seizure onset, age at surgery, seizure duration, duration of seizure ≤15 months, increased intracranial pressure, extra-axial location, cortical involvement, parietal lobe involvement, hydrocephalus, non-glial tumor, meningeal tumor, gross total resection, and postoperative duration of AEDs

outcome group used a significantly larger number of AEDs ($p<0.001$), and had a longer duration of AED use ($p = 0.002$) after the operation.

The strength of association between potential factors and seizure-free outcome as evaluated by multivariable analysis is shown in Table 4. Of several analyzed variables, three factors were found to be significantly associated with seizure-free outcome. Rarely occurring preoperative seizure was 4.62 times more likely to be correlated with favorable outcome than frequently occurring preoperative seizure ($p = 0.009$). Absence of postoperative seizure was 15.73 times more likely to be associated with favorable outcome than presence of seizure within 72 hours after surgery ($p<0.001$). Larger number of postoperative AEDs was associated with decreased rate of seizure freedom (OR 0.44; $p = 0.046$).

Discussion

Many patients with brain tumor have seizure as a primary clinical presentation. Uncontrolled and frequent seizures impair patient quality of life. The pathogenesis of brain tumor-related seizure is multifactorial, to include: tumor cells releasing neurotransmitters, and neuropeptides that compromise balance between excitation and inhibition[15]; extensive inflammatory reaction in the peritumoral area[16]; changes in gap junction proteins[17]; disruption of the blood-brain barrier[18]; abrupt tissue damage leading to necrosis, hemosiderin deposition, and edema[19]; dysfunction of the peritumoral glia and neurons[20,21]; and, inhibition of GABAergic function in peritumoral tissue[22].

Radical tumor resection without risk of additional neurological damage is the surgical objective. Tumor resection relieves compressive symptoms caused by the tumor, delays tumor growth, improves survival, and achieves postoperative seizure control[23-25]. In patients with medically intractable epilepsy, concurrent resection of both the tumor and epileptogenic brain tissue renders significantly better seizure control than tumor resection alone[26].

In our study, the rate of seizure freedom after brain tumor surgery was 78.1%, which is comparable to the 65 to 90% seizure freedom rates reported in previous studies[23,27-31]. Regarding age of patients, two large systematic reviews reported that age was not associated with seizure freedom after surgical resection of supratentorial low-grade gliomas and glioneural tumors[8,9]. Our study found that patients with older age at surgery tended to have a higher rate of seizure-free outcome, but the difference was not statistically significant. However, the favorable outcome group had a significantly older age at seizure onset than the unfavorable outcome group in this study ($p = 0.049$).

Regarding duration of seizure, our result was similar to that of the two a forementioned systematic reviews that reported significantly higher rates of seizure-freedom in patients with ≤1 year duration of epilepsy[8,9]. Our study showed that seizure duration ≤15 months was significantly associated with favorable outcome in univariate analysis, but not in multiple regression analysis. Some previous studies reported preoperative seizure control as a predictor of seizure outcome after brain tumor resection[8,10]. Our study also found that well-controlled seizure before surgery,

represented by ≤1 preoperative seizures per month, was significantly associated with postoperative seizure freedom in both univariate and multivariable analysis. These results imply that early resection of epileptic brain tumors and appropriate preoperative seizure control bring about better seizure outcomes.

Seizure outcome is also influenced by seizure semiology. A lower rate of seizure freedom after surgery was correlated with presence of simple partial seizure (OR: 0.46, 95% CI: 0.26 to 0.80; $p = 0.002$)[8] and secondarily generalized seizure (OR: 0.40, 95% CI: 0.24 to 0.66; $p<0.001$)[9]. However, there was no significant difference in seizure outcome among simple partial, complex partial, and generalized seizures in this study.

The relationship between tumor location and seizure-free outcome is variable. Radhakrishnan et al reported significant unfavorable outcome in temporal location of long-term epilepsy-associated brain tumor ($p = 0.008$)[32]. Other studies (including the present study) found no association between temporal lobe location and seizure outcome[5,8,9], and we found no significant association between specific location of tumor and seizure outcome. In our study, patients with extra-axial tumor tended to have seizure-free outcome, because most of the extra-axial tumors were meningioma, with seizure freedom being achieved in 37 of 41 meningioma patients (90.2%). In contrast, most of the intra-axial tumors in our study were glioma and glioneural tumor, with seizure freedom being achieved in only 48 of 68 patients (70.6%). However, this difference in tumor locations did not achieve statistical significance. There was a significant decrease in seizure freedom rate in our patients with tumor involving the cerebral cortex ($p = 0.034$). Patients with cortically-based tumors or infiltrative tumors involving the cerebral cortex, particularly glioneural tumor and glioma, generally have seizure as a primary clinical manifestation before tumor discovery. Location in or proximity to the cortical gray matter were factors predicting occurrence of epilepsy in patients with glioma[33]. Disorganization of dysplastic neurons, extensive inflammation in the perilesional area, partial cortical deafferentation in slow-growing tumors, blood-brain barrier disruption, and increased glutamate concentration in the peritumoral environment contribute to epileptogenesis[3,16,34,35]. Our findings revealed that presence of hydrocephalus in preoperative neuroimaging was a factor significantly correlated with favorable seizure outcome in univariate analysis, but not in multivariable analysis. Most of the tumors with hydrocephalus in our study were located in the deep midline region, which is associated with a lower risk of seizure when compared with tumors situated in the more superficial portion of the cerebral hemisphere[8]. Deep midline tumors often involve the ventricular system, which can result in obstructive hydrocephalus. Complete removal of these tumors can relieve symptoms caused by hydrocephalus, and might improve seizure.

From a therapeutic point of view, accomplishment of gross total resection was found to be a positive predictor of seizure outcome in univariate analysis ($p = 0.035$). This result was similar to the results reported in several other studies[8,9,23,31]. Radical resection of brain tumor usually yields postoperative seizure-free outcome by elimination of epileptogenic tumor and adjacent brain tissue that predisposes the patient to occurrence of repeated seizures. Nevertheless, this variable was not a potential predicting factor for favorable outcome of seizure in multiple logistic regression analysis in our study. From our review of the literature, radiotherapy and chemotherapy also influence seizure outcome. A number of case series showed positive effect of radiation therapy on tumor-related seizure[36-38]. A reduction in seizure of greater than 75% was achieved in 80% of patients[37,39], and seizure control was achieved in 54.2% of patients undergoing stereotactic radiosurgery with gamma knife for brain tumor[40,41]. Ionizing radiation may damage epileptogenic neurons or induce alterations in the peritumoral environment, leading to decreased seizure activity[34]. Chemotherapy was also found to be beneficial for seizure reduction, with seizure freedom observed in some patients[42-44]. Kahlenberg et al reported valuable effect of radiation ($p = 0.02$) and chemotherapy ($p = 0.03$) for seizure control. Patients with presurgical seizures who received radiation or chemotherapy had significantly better seizure outcomes than those who did not[6]; however, these correlations were not observed in our study.

In our study, the number of AEDs used for postoperative seizure control was a significant factor correlated with postoperative seizure outcome. The higher the number of AEDs used after the operation, the lower the likelihood of long-term seizure freedom after surgery. The absence of postoperative seizure was also a strong predictor of long-term seizure freedom. Seizure emerging before 72 hours after the operation did not significantly increase the risk of long-term postoperative seizure, whereas seizure occurring after 72 hours following surgery was significantly associated with persistent postoperative seizure in multiple logistic regression analysis.

Conclusion

In this study, 78% of patients with brain tumor became seizure-free after surgery. Independent factors significantly correlated with seizure-free outcome included rarely occurring preoperative seizure, absence of postoperative seizure, and number of AEDs used after surgery. Other variables that were found to be significant in univariate analysis that might affect postoperative seizure outcome included age at seizure onset, duration of seizure, extra-axial location, absence of cortical involvement, presence of hydrocephalus, tumor of non-glial origin, tumor of meningeal origin, and achievement of gross total tumor resection. These results indicate that strict control of preoperative seizure, early surgical intervention, and total resection of the tumor increases the likelihood of postsurgical seizure freedom.

What is already known on this topic?

Seizure is a common presenting symptom in patients with brain tumor. In addition to relief mass effect, resection of epileptogenic brain tumor is helpful to control seizure.

What this study adds?

The majority of patients with brain tumor achieve seizure-free after brain tumor surgery. Rare pre-operative seizure is an important predictive factor of postoperative seizure freedom. Therefore, appropriate seizure control before surgery is a key point in management of epileptic brain tumor. Furthermore, early surgical resection for prevention of chronic epilepsy and gross total resection have positive effect on postoperative seizure outcome.

Acknowledgements

The authors gratefully acknowledge Dr. Sasima Tongsai, Clinical Epidemiology Unit, Office for Research and Development, Faculty of Medicine Siriraj Hospital, Mahidol University for assistance with statistical analysis.

Potential conflicts of interest

None.

References

1. Glantz MJ, Cole BF, Forsyth PA, Recht LD, Wen PY, Chamberlain MC, et al. Practice parameter: anticonvulsant prophylaxis in patients with newly diagnosed brain tumors. Report of the Quality Standards Subcommittee of the American Academy of Neurology. Neurology 2000; 54: 1886-93.
2. Herman ST. Epilepsy after brain insult: targeting epileptogenesis. Neurology 2002; 59 (9 Suppl 5): S21-6.
3. van Breemen MS, Wilms EB, Vecht CJ. Epilepsy in patients with brain tumours: epidemiology, mechanisms, and management. Lancet Neurol 2007; 6: 421-30.
4. Maschio M. Brain tumor-related epilepsy. Curr Neuropharmacol 2012; 10: 124-33.
5. Im SH, Chung CK, Cho BK, Lee SK. Supratentorialganglioglioma and epilepsy: postoperative seizure outcome. J Neurooncol 2002; 57: 59-66.
6. Kahlenberg CA, Fadul CE, Roberts DW, Thadani VM, Bujarski KA, Scott RC, et al. Seizure prognosis of patients with low-grade tumors. Seizure 2012; 21: 540-5.
7. Chaichana KL, Parker SL, Olivi A, Quinones-Hinojosa A. Long-term seizure outcomes in adult patients undergoing primary resection of malignant brain astrocytomas. Clinical article. J Neurosurg 2009; 111: 282-92.
8. Englot DJ, Berger MS, Barbaro NM, Chang EF. Predictors of seizure freedom after resection of supratentorial low-grade gliomas. A review. J Neurosurg 2011; 115: 240-4.
9. Englot DJ, Berger MS, Barbaro NM, Chang EF. Factors associated with seizure freedom in the surgical resection of glioneuronal tumors. Epilepsia 2012; 53: 51-7.
10. Chaichana KL, Pendleton C, Zaidi H, Olivi A, Weingart JD, Gallia GL, et al. Seizure control for patients undergoing meningioma surgery. World Neurosurg 2013; 79: 515-24.
11. Kim SK, Wang KC, Cho BK. Intractable seizures associated with brain tumor in childhood: lesionectomy and seizure outcome. Childs Nerv Syst 1995; 11: 634-8.
12. Khan RB, Hunt DL, Boop FA, Sanford RA, Merchant TE, Gajjar A, et al. Seizures in children with primary brain tumors: incidence and long-term outcome. Epilepsy Res 2005; 64: 85-91.
13. Jo KI, Shin HJ, Hong SC. Seizure outcomes of lesionectomy in pediatric lesional epilepsy with brain tumor-single institute experience. Brain Dev 2013; 35: 810-5.
14. Wieser HG, Blume WT, Fish D, Goldensohn E, Hufnagel A, King D, et al. ILAE Commission Report. Proposal for a new classification of

outcome with respect to epileptic seizures following epilepsy surgery. Epilepsia 2001; 42: 282-6.
15. Rajneesh KF, Binder DK. Tumor-associated epilepsy. Neurosurg Focus 2009; 27: E4.
16. Aronica E, Gorter JA, Redeker S, Ramkema M, Spliet WG, van Rijen PC, et al. Distribution, characterization and clinical significance of microglia in glioneuronaltum ours from patients with chronic intractable epilepsy. Neuropathol Appl Neurobiol 2005; 31: 280-91.
17. Ruda R, Bello L, Duffau H, Soffietti R. Seizures in low-grade gliomas: natural history, pathogenesis, and outcome after treatments. Neuro Oncol 2012; 14 (Suppl 4): iv55-64.
18. Ivens S, Kaufer D, Flores LP, Bechmann I, Zumsteg D, Tomkins O, et al. TGF-beta receptor-mediated albumin uptake into astrocytes is involved in neocortical epileptogenesis. Brain 2007; 130: 535-47.
19. Riva M. Brain tumoral epilepsy: a review. Neurol Sci 2005; 26 (Suppl 1): S40-2.
20. Goel S, Wharton SB, Brett LP, Whittle IR. Morphological changes and stress responses in neurons in cerebral cortex infiltrated by diffuse astrocytoma. Neuropathology 2003; 23: 262-70.
21. Shamji MF, Fric-Shamji EC, Benoit BG. Brain tumors and epilepsy: pathophysiology of peritumoral changes. Neurosurg Rev 2009; 32: 275-84.
22. Conti L, Palma E, Roseti C, Lauro C, Cipriani R, de Groot M, et al. Anomalous levels of Cl- transporters cause a decrease of GABAergic inhibition in human peritumoral epileptic cortex. Epilepsia 2011; 52: 1635-44.
23. Chang EF, Potts MB, Keles GE, Lamborn KR, Chang SM, Barbaro NM, et al. Seizure characteristics and control following resection in 332 patients with low-grade gliomas. J Neurosurg 2008; 108: 227-35.
24. Smith KA, Ashby LS, Gonzalez LF, Brachman DG, Thomas T, Coons SW, et al. Prospective trial of gross-total resection with Gliadel wafers followed by early postoperative Gamma Knife radiosurgery and conformal fractionated radiotherapy as the initial treatment for patients with radiographically suspected, newly diagnosed glioblastoma multiforme. J Neurosurg 2008; 109 (Suppl): 106-17.
25. Bauer R, Ortler M, Seiz-Rosenhagen M, Maier R, Anton JV, Unterberger I. Treatment of epileptic seizures in brain tumors: a critical review. Neurosurg Rev 2014; 37: 381-8.
26. de Groot M, Reijneveld JC, Aronica E, Heimans JJ. Epilepsy in patients with a brain tumour: focal epilepsy requires focused treatment. Brain 2012; 135: 1002-16.
27. Britton JW, Cascino GD, Sharbrough FW, Kelly PJ. Low-grade glial neoplasms and intractable partial epilepsy: efficacy of surgical treatment. Epilepsia 1994; 35: 1130-5.
28. Zentner J, Hufnagel A, Wolf HK, Ostertun B, Behrens E, Campos MG, et al. Surgical treatment of neoplasms associated with medically intractable epilepsy. Neurosurgery 1997; 41: 378-86.
29. Luyken C, Blumcke I, Fimmers R, Urbach H, Elger CE, Wiestler OD, et al. The spectrum of long-term epilepsy-associated tumors: long-term seizure and tumor outcome and neurosurgical aspects. Epilepsia 2003; 44: 822-30.
30. Choi JY, Chang JW, Park YG, Kim TS, Lee BI, Chung SS. A retrospective study of the clinical outcomes and significant variables in the surgical treatment of temporal lobe tumor associated with intractable seizures. Stereotact Funct Neurosurg 2004; 82: 35-42.
31. Melo JGSP, Centeno RS, Malheiros SMF, Ferraz FAP, Stavale JN, Carrete HH, et al. Clinical features and surgical outcome of patients with indolent brain tumors and epilepsy. J Epilepsy Clin Neurophysiol 2007; 13: 65-9.
32. Radhakrishnan A, Abraham M, Vilanilam G, Menon R, Menon D, Kumar H, et al. Surgery for "Long-term epilepsy associated tumors (LEATs)": Seizure outcome and its predictors. Clin Neurol Neurosurg 2016; 141: 98-105.
33. Schaller B, Ruegg SJ. Brain tumor and seizures: pathophysiology and its implications for treatment revisited. Epilepsia 2003; 44: 1223-32.
34. Ricci R, Bacci A, Tugnoli V, Battaglia S, Maffei M, Agati R, et al. Metabolic findings on 3T 1H-MR spectroscopy in peritumoral brain edema. Am J Neuroradiol 2007; 28: 1287-91.
35. You G, Sha Z, Jiang T. The pathogenesis of tumor-related epilepsy and its implications for clinical treatment. Seizure 2012; 21: 153-9.
36. Rossi GF, Scerrati M, Roselli R. Epileptogenic cerebral low-grade tumors: effect of interstitial stereotactic irradiation on seizures. Appl Neurophysiol 1985; 48: 127-32.
37. Rogers LR, Morris HH, Lupica K. Effect of cranial irradiation on seizure frequency in adults with low-grade astrocytoma and medically intractable epilepsy. Neurology 1993; 43: 1599-601.

38. Warnke PC, Berlis A, Weyerbrock A, Ostertag CB. Significant reduction of seizure incidence and increase of benzodiazepine receptor density after interstitial radiosurgery in low-grade gliomas. Acta Neurochir Suppl 1997; 68: 90-2.
39. Chalifoux R, Elisevich K. Effect of ionizing radiation on partial seizures attributable to malignant cerebral tumors. Stereotact Funct Neurosurg 1996; 67: 169-82.
40. Schrottner O, Eder HG, Unger F, Feichtinger K, Pendl G. Radiosurgery in lesional epilepsy: brain tumors. Stereotact Funct Neurosurg 1998; 70 (Suppl 1): 50-6.
41. Quigg M, Barbaro NM. Stereotactic radiosurgery for treatment of epilepsy. Arch Neurol 2008; 65: 177-83.
42. Brada M, Viviers L, Abson C, Hines F, Britton J, Ashley S, et al. Phase II study of primary temozolomide chemotherapy in patients with WHO grade II gliomas. Ann Oncol 2003; 14: 1715-21.
43. Pace A, Vidiri A, Galie E, Carosi M, Telera S, Cianciulli AM, et al. Temozolomide chemotherapy for progressive low-grade glioma: clinical benefits and radiological response. Ann Oncol 2003; 14: 1722-6.
44. Sherman JH, Moldovan K, Yeoh HK, Starke RM, Pouratian N, Shaffrey ME, et al. Impact of temozolomide chemotherapy on seizure frequency in patients with low-grade gliomas. J Neurosurg 2011; 114: 1617-21.

ผลการรักษาอาการชักและปัจจัยที่สัมพันธ์กับการปราศจากอาการชักภายหลังการผ่าตัดเนื้องอกสมองในตำแหน่งสมองส่วนบน

บรรพต สิทธินามสุวรรณ, ศรัณย์ โชติกเสถียร, อินธิรา ขัมภลิขิต, โชติวัฒน์ ตันศิริสิทธิกุล, เอกวุฒิ จันแก้ว, ศรัณย์ นันทอารี

ภูมิหลัง: อาการชักเป็นอาการนำที่พบบ่อยของเนื้องอกสมอง การผ่าตัดเนื้องอกช่วยในการควบคุมอาการชักและรักษาอาการที่เกิดจากการกดเบียดของเนื้องอก

วัตถุประสงค์: เพื่อศึกษาผลการรักษาอาการชักและปัจจัยที่สัมพันธ์อย่างมีนัยสำคัญทางสถิติกับการปราศจากอาการชักในระยะยาวภายหลังการผ่าตัดเนื้องอกสมองในตำแหน่งสมองส่วนบนของผู้ป่วยเนื้องอกสมองที่มีอาการชักเป็นหนึ่งในอาการทางคลินิก

วัสดุและวิธีการ: การศึกษานี้ดำเนินการในผู้ป่วยที่มีอาการชักสัมพันธ์กับการตรวจพบเนื้องอกสมองโดยผู้ป่วยได้รับการผ่าตัดเนื้องอกสมอง ณ โรงพยาบาลศิริราช ได้รับการติดตามผลการรักษาหลังผ่าตัด เป็นเวลามากกว่า 1 ปี แบ่งผู้ป่วยออกเป็น 2 กลุ่ม ได้แก่ กลุ่มที่ได้ผลการรักษาอาการชักเป็นที่น่าพอใจ (กลุ่มผู้ป่วยที่ปราศจากอาการชักหลังผ่าตัด) และกลุ่มที่ได้ผลการรักษาอาการชักไม่เป็นที่น่าพอใจ (กลุ่มผู้ป่วยที่ยังคงมีอาการชักหลังผ่าตัด) ข้อมูลที่รวบรวม ได้แก่ เพศ อายุ ลักษณะของอาการชัก อาการทางระบบประสาท ลักษณะทางรังสีของเนื้องอก การวินิจฉัยทางพยาธิวิทยา การรักษา ข้อมูลเกี่ยวกับยากันชักก่อนและหลังผ่าตัด รวมทั้งผลการรักษาอาการชัก

ผลการศึกษา: ผู้ป่วยทั้งหมด 128 ราย (ชาย 53 รายและหญิง 75 ราย) อายุเฉลี่ยขณะเริ่มมีอาการชักเท่ากับ 42.5±16.4 ปี และอายุเฉลี่ยขณะได้รับการผ่าตัดเท่ากับ 43.7±15.9 ปี ผู้ป่วย 100 รายอยู่ในกลุ่มที่ได้ผลการรักษาอาการชักเป็นที่น่าพอใจและ 28 รายอยู่ในกลุ่มที่ได้ผลการรักษาอาการชักไม่เป็นที่น่าพอใจ อัตราการปราศจากอาการชักหลังผ่าตัดเท่ากับร้อยละ 78 ในการวิเคราะห์ทางสถิติแบบตัวแปรเดียว พบว่าปัจจัยที่สัมพันธ์กับการปราศจากอาการชักหลังผ่าตัดอย่างมีนัยสำคัญทางสถิติ ได้แก่ อายุขณะที่เริ่มมีอาการชักที่มากกว่าระยะเวลาตั้งแต่ที่เริ่มมีอาการชักจนกระทั่งผ่าตัดน้อยกว่า 15 เดือน ความถี่ของอาการชักก่อนผ่าตัดน้อยกว่า 1 ครั้งต่อเดือน เนื้องอกที่ไม่ได้อยู่ในตำแหน่งผิวสมอง การตรวจพบภาวะน้ำคั่งโพรงสมอง เนื้องอกสมองที่ไม่ใช่ชนิดเกลีย เนื้องอกที่กำเนิดจากเยื่อหุ้มสมอง การปราศจากอาการชักหลังผ่าตัด การตัดเนื้องอกออกทั้งหมด จำนวนชนิดของยากันชักหลังผ่าตัดที่น้อยกว่า และระยะเวลาใช้ยากันชักหลังผ่าตัดที่สั้นกว่า ในการวิเคราะห์ทางสถิติแบบหลายตัวแปรโดยการวิเคราะห์แบบถดถอยพหุ พบว่าปัจจัยที่สัมพันธ์กับการปราศจากอาการชักหลังผ่าตัดอย่างมีนัยสำคัญทางสถิติ ได้แก่ ความถี่ของอาการชัก ก่อนผ่าตัดน้อยกว่า 1 ครั้งต่อเดือน การปราศจากอาการชักหลังผ่าตัดและจำนวนชนิดของยากันชักหลังผ่าตัดที่น้อยกว่า

สรุป: ในการศึกษานี้ร้อยละ 78 ของผู้ป่วยเนื้องอกสมองปราศจากอาการชักหลังผ่าตัด ปัจจัยอิสระที่สัมพันธ์กับการปราศจากอาการชักหลังผ่าตัดอย่างมีนัยสำคัญทางสถิติ ได้แก่ จำนวนครั้งของอาการชักที่น้อยก่อนได้รับการผ่าตัด การปราศจากอาการชักหลังผ่าตัดและจำนวนชนิดของยากันชักหลังผ่าตัด ผลการศึกษาดังกล่าวบ่งชี้ว่าการควบคุมอาการชักก่อนผ่าตัดอย่างเหมาะสม การผ่าตัดตั้งแต่ระยะแรกที่ตรวจพบเนื้องอกและการตัดเนื้องอกออกทั้งหมด ช่วยเพิ่มโอกาสที่จะหายหรือปราศจากอาการชักหลังผ่าตัด