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Effect of seizure timing on long-term survival in patients with brain tumor

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ABSTRACT

Objective: Seizures often occur in patients with primary brain tumor (BT). The aim of this study was to determine if there is an association between the time of occurrence of seizures during the course of BT and survival of these patients.
Methods: This retrospective cohort study at Henry Ford Hospital, an urban tertiary referral center, included all patients who were diagnosed with primary BTs at Henry Ford Health System between January 2006 and December 2014. Timing of seizure occurrence, if occurred at presentation or after the tumor diagnosis during follow-up period, in different grades of BTs, and survival of these patients were analyzed.
Results: Of the 901 identified patients, 662 (53% male; mean age: 56 years) were included in final analysis, and seizures occurred in 283 patients (43%). Patients with World Health Organization (WHO) grade III BT with seizures as a presenting symptom only had better survival (adjusted hazard ratio (HR): 0.27; 95% confidence interval (CI), 0.11–0.67; $P = 0.004$). Seizures that occurred after tumor diagnosis only (adjusted HR: 2.11; 95% CI, 1.59–2.81; $P < 0.001$) in patients with WHO grade II tumors (adjusted HR: 3.41; 95% CI, 1.05–11.1; $P = 0.041$) and WHO grade IV tumors (adjusted HR: 2.14; 95% CI, 1.58–2.90; $P < 0.001$) had higher mortality. Seizures that occurred at presentation and after diagnosis also had higher mortality (adjusted HR: 1.34; 95% CI, 1.00–1.80; $P = 0.049$), in patients with meningioma (adjusted HR: 6.19; 95% CI, 1.30–29.4; $P = 0.021$) and grade III tumors (adjusted HR: 6.19; 95% CI, 2.56–15.0; $P < 0.001$).
Conclusion: Seizures occurred in almost half of the patients with BTs. The association between seizures in patients with BT and their survival depends on the time of occurrence of seizures, if occurring at presentation or after tumor diagnosis, and the type of tumor. Better survival was noted in patients with WHO grade III BTs who had seizures at presentation at the time of diagnosis, while higher mortality was noted in WHO grade II tumors who had seizure at presentation and after tumor diagnosis, and in grade IV tumors after tumor diagnosis.

1. Introduction

Epileptic seizures in patients with primary brain tumors (BTs) are considered a valuable prognostic attribute that also significantly disrupt health-related quality of life (HRQOL) [1]. Unfortunately, seizures are commonly encountered in patients with primary BTs, with prevalence ranging from 20 to 80%, depending on the type and location of the tumor [2]. Slow-growing tumors have a higher incidence of seizures than rapidly growing tumors, probably because of earlier death in the latter cases and underlying molecular mechanisms such as IDH1 mutations [3]; however, meningioma, which is typically a grade I tumor, has shown low rates [2,4–6]. Survival and HRQOL, which includes functional independence, are of paramount importance across health particularly at the intersection of neuroscience and oncology [7,8].

Limited studies exist assessing seizures as prognostic indicators in patients with BT. In patients with seizures, improved overall survival

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(OS) has been described in patients with high-grade gliomas [9] while others report better survival rates in those with low-grade glioma, although the reasons remain unclear [10]. Furthermore, seizures at presentation in high-grade BT are associated with prolonged survival [11], while those in low-grade BT in elderly population are associated with severe course [12]. There remains conflicting evidence coupled with high-observed variability in the literature of seizure prevalence stratified by BT type, grade, or location [2]. Overall, the studies published, thus far, fail to demonstrate the role of the timing of seizure occurrence at presentation or during the course of the diagnosis on the survival in patients with BT.

The aim of this study was to comprehensively analyze the association of OS with experiencing a seizure as a BT presenting symptom at diagnosis and/or developing seizures following diagnosis in a large cohort of patients with multiple BT types.

2. Methods

We report our study in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement, following Enhancing the Quality and Transparency of Health Research (EQUATOR) reporting guidelines [13].

2.1. Study design and population

This is a retrospective cohort study conducted at Henry Ford Health System in Detroit, MI, USA, a collaborative experience of the Henry Ford Comprehensive Epilepsy Program and the Hermelin Brain Tumor Center. We identified patients with a diagnosis of primary tumor of the central nervous system utilizing the Henry Ford Hospital (HFH) Tumor Registry. Adult patients (age ≥ 18 years) who were newly diagnosed with a primary BT between January 1, 2006 and December 31, 2014 were included in the study. Patients who had tumor in the spine or brainstem, who died within two months after diagnosis, or whose information regarding tumor type or a history of seizure at time of diagnosis or during follow-up was not available were excluded. This study was approved by Henry Ford Health System Institutional Review Board (IRB number 10298).

2.2. Data collection

Data regarding date of tumor diagnosis, date of death, and date of last follow-up were taken from the HFH Tumor registry. Data collected from the electronic medical record (EMR) included patient demographics, prior history of epilepsy, specific type, and grade of BT (according to the 2016 World Health Organization (WHO) Classification of Tumors of the Central Nervous System) [14], tumor location, seizures as a presenting symptom of BT, seizures occurring after tumor diagnosis and the date of such seizures, antiseizure drugs (ASDs), all treatments received for BT, and date last seen in the clinic. Additional confirmation of tumor type and grade and follow-up information were collected from the Hermelin Brain Tumor Center Registry.

2.3. Outcomes

The primary outcome was time to death during follow-up that was defined as the time between date of tumor diagnosis and date of death, or last follow-up. The secondary outcomes were seizure prevalence stratified by tumor type and location, and other factors that may be associated with seizures in patients with BTs.

2.4. Statistical analysis

Patients were divided into four seizure groups depending on the presence of seizures and the time of seizure occurrence in relation to BT diagnosis. Specifically, the four groups were no seizures, seizures as a presenting symptom only, seizures that occurred after diagnosis only, and both seizures as a presenting symptom and occurring after diagnosis. Chi-square tests were done to assess the association of seizures with demographic information, type of BT, treatments received, and BT location. Analysis of variance (ANOVA) was done to compare age at diagnosis among the seizure groups. Kaplan–Meier estimates were used to compute the median survival time (time corresponding to survival of 50%) for the different tumor types. Cox proportional hazards regression analyses with time-dependent covariates were done to assess the relationship between seizure groups and OS with hazard ratios (HR) and 95% confidence intervals (CIs) being calculated. The reference group for the HR was the no seizure group. Additional factors that were associated both with seizure occurrence and survival were included in the multivariate regression models. In addition, because of the known survival differences among the tumor grades, the Cox regression models were stratified by tumor grade for all patients and were done for each specific tumor grade. Modified Kaplan–Meier curves using time-dependent covariates for the seizure groups were done to assess OS experience within each tumor grade. No imputation was done for any missing information. All testing was set at the 0.05 alpha level. SAS version 9.4 was used for the data analyses.

3. Results

Of 901 patients identified to have a diagnosis of primary central nervous system tumor in the Henry Ford Hospital tumor registry between January 1, 2006 and December 31, 2014, 239 patients were not eligible, for having infratentorial tumor ($n = 15$), death within two months after diagnosis ($n = 31$) or insufficient clinical information ($n = 193$), leaving 662 patients with primary BT in the final analysis. Overall, 283 (43%) patients with BT experienced seizures, 110 (17%) had seizures that occurred as a presenting symptom of the tumor only, 81 (12%) developed seizures during follow-up after BT diagnosis only, and 92 (14%) experienced seizures both at presentation and during follow-up. The remaining 379 (57%) patients did not experience any seizures.

3.1. Baseline characteristics

The mean age of the eligible patients was 56 years, with 53% male, 83% Caucasian, and 12% were African American (Table 1).

Patients with seizure as a presenting symptom were younger (54 ± 15 years vs 57 ± 14 years, $P = 0.009$) and more likely to be male (63% vs 49%, $P < 0.001$) compared with those without a seizure as a presenting symptom. The overall difference in the racial distributions among the seizures groups was significant with patients with seizures during both time points more likely to be African American ($P = 0.014$, Table 1). A prior history of epilepsy was present in 3% of overall patients, with patients having seizures during both time points exhibiting the highest rate (11%) of seizure followed by patients with seizures as a presenting symptom (5%) ($P < 0.001$, Table 1).

3.2. Grading and location of tumor

The four defined seizure phenotypic groups analyzed by WHO grading showed that the majority BTs were WHO grade IV (56%), all of which were glioblastomas; followed by WHO grade I (21%), all of which were meningioma; WHO grade II (13%), which included astrocytoma, oligodendroglioma, and oligoastrocytoma; and WHO grade III (10%) including anaplastic astrocytoma, anaplastic oligodendroglioma, and anaplastic meningioma (Table 2). The WHO grading was associated with the patterns of seizures ($P < 0.001$, Table 2) with the highest rate of seizure in patients with a WHO grade II tumor (34% had seizure as a presenting symptom only, and 25% had seizures both as a presenting symptom and during follow-up) and the lowest rate of seizure in patients with WHO I, meningioma (24% had a seizure at presentation and/or during follow-up).

Table 1
Baseline characteristics.

Characteristics	Total patients (N = 662)	Patients without seizures (n = 379)	Patients with seizure as a presenting symptom only (n = 110)	Patients with seizure as a presenting symptom and seizure after tumor diagnosis (n = 92)	Patients with seizure after tumor diagnosis only (n = 81)	P value
Age, years	56.1 ± 14.2	57.0 ± 13.8	54.9 ± 15.1	52.9 ± 14.3	57.2 ± 14.2	0.052
Male	354 (53)	183 (48)	70 (64)	58 (63)	43 (53)	**0.007**
Race						**0.014**
Caucasian	552 (83)	319 (84)	98 (89)	70 (76)	65 (80)	
African American	77 (12)	37 (10)	7 (6)	21 (23)	12 (15)	
Other	13 (2)	9 (2)	3 (3)	0 (0)	1 (1)	
Unknown	20 (3)	14 (4)	2 (2)	1 (1)	3 (4)	
Prior history of epilepsy	21 (3)	5 (1)	5 (5)	10 (11)	1 (1)	<**0.001**

Data are n (% within each column) or mean ± SD.
p-value < 0.05 was considered statistically significant.

Table 2
Seizure occurrence in patients with different World Health Organization Tumor grade.

Seizure occurrence	Meningioma (n = 139)	WHO Grade II tumor[a] (n = 85)	WHO Grade III tumor[b] (n = 67)	WHO Grade IV tumor[c] (n = 371)	P value
No seizures	105 (76)	26 (31)	40 (60)	208 (56)	<**0.001**
Seizure as a presenting symptom only	13 (9)	29 (34)	16 (24)	52 (14)	
Seizure as a presenting symptom and seizure occurred after tumor diagnosis	13 (9)	21 (25)	8 (12)	50 (13)	
Seizure occurred after tumor diagnosis only	8 (6)	9 (11)	3 (4)	61 (16)	

Data are n (% of total available data within each column).
p-value < 0.05 was considered statistically significant.
[a] Seventeen patients had astrocytoma, 67 patients had oligodendroglioma, and 1 patient had oligoastrocytoma.
[b] Forty-two patients had anaplastic astrocytoma, 21 patients had anaplastic oligodendroglioma, and 4 patients had anaplastic meningioma.
[c] All patients had glioblastoma.

The distribution of tumor location was 46% frontal, 34% temporal, 26% parietal, 9% occipital, 4% deep midline, 2% cerebellum, 2% insular, and 16% other location (Table 3). Patients with seizures were more likely to have a tumor in the cortical region (93% vs 85%, P = 0.001) compared with those without seizures. Patients without a seizure were more likely to have tumors in the cerebellum (3% vs 0%, P = 0.018) compared with patients with a seizure at either time point, while patients who had seizure occurring after tumor diagnosis only were more likely to have tumor in the parietal lobe (41% vs 24%, P = 0.001) compared with the other seizure groups.

3.3. Treatment for brain tumor

Antiseizure drugs were prescribed immediately after tumor diagnosis in 500 (76%) of the patients regardless of presence of seizure. Of the 460 patients without seizure as a presenting symptom, 302 (66%) of

Table 3
Location of brain tumor and treatments received.

	Total patients (N = 662)	Patients without seizures (n = 379)	Patients with seizure as a presenting symptom only (n = 110)	Patients with seizure as a presenting symptom and seizure after tumor diagnosis (n = 92)	Patients with seizure after tumor diagnosis only (n = 81)	P value
Location of tumor						
Cortical region	583 (89)	320 (85)	106 (96)	86 (93)	71 (89)	**0.004**
Frontal lobe	299 (46)	160 (43)	53 (48)	50 (54)	36 (46)	0.248
Parietal lobe	169 (26)	87 (23)	27 (25)	23 (25)	32 (41)	**0.017**
Temporal lobe	221 (34)	120 (32)	43 (39)	31 (34)	27 (34)	0.620
Insular lobe	14 (2)	7 (2)	2 (2)	4 (4)	1 (1)	0.457
Occipital lobe	62 (9)	39 (10)	10 (9)	6 (7)	7 (9)	0.699
Cerebellum	13 (2)	13 (3)	0 (0)	0 (0)	0 (0)	**0.018**
Deep midline	24 (4)	19 (5)	1 (1)	2 (2)	2 (3)	0.144
Other location	99 (15)	58 (16)	11 (10)	19 (21)	11 (14)	0.205
Treatments						
Surgery	634 (96)	355 (94)	110 (100)	90 (98)	79 (98)	**0.019**
Type of surgery						0.457
Total resection	223 (35)	123 (35)	35 (32)	35 (39)	30 (38)	
Subtotal resection	256 (40)	146 (41)	48 (44)	30 (33)	32 (41)	
Biopsy	138 (22)	72 (20)	26 (24)	24 (27)	16 (20)	
Not specified	17 (3)	14 (4)	1 (1)	1 (1)	1 (1)	
Chemotherapy with radiation	516 (83)	278 (81)	97 (91)	73 (83)	68 (86)	0.091
Chemotherapy	21 (3)	16 (5)	1 (1)	4 (5)	0 (0)	0.080
Radiation	45 (8)	27 (8)	6 (6)	5 (6)	7 (10)	0.722
MRI-guided laser ablation	6 (1)	5 (1)	0 (0)	0 (0)	1 (1)	0.437
Palliative care with hospice admission	148 (25)	62 (18)	24 (22)	26 (31)	36 (49)	<**0.001**

Data are n (% of total available data within each column).
p-value < 0.05 was considered statistically significant.

them were prescribed an ASD. The most common ASDs prescribed were levetiracetam (47%), followed by phenytoin (34%), benzodiazepines (5%), valproic acid (2%), lacosamide (2%), lamotrigine (2%), and topiramate (2%), and other ASDs were used in the remaining 5% of cases.

Surgical procedures were performed in 96% of all patients, of which 35% total resection, 40% subtotal resection, and 22% biopsy only, and 3% without a specified type of surgery (Table 3). Patients without a seizure were less likely to receive any type of surgery (94% vs ≥98%, P = 0.019). Treatment modalities were not different among the seizure groups except for admission to hospice that was more likely in patients who developed seizure only after BT diagnosis (49% vs. 21%, P < 0.001).

3.4. Survival and seizures

During 12 years of follow-up, 428 (65%) of the patients died. The median OS was 27.7 months (95% CI = 23.3 to 32.1 months) and varied by tumor grade. The median OS was not reached for meningiomas and grade II tumors, was 35.8 months (95% CI = 24.0 to 62.9) for grade III tumor, and 17 months (95% CI = 15.7 to 17.9) for grade IV tumors. In the survival analyses, seizures that occurred after tumor diagnosis only were associated with higher mortality (adjusted HR: 2.11; 95% CI, 1.59–2.81; P < 0.001), in patients with WHO grade II (adjusted HR: 3.41; 95% CI, 1.05–11.1; P = 0.041) and grade IV (adjusted HR: 2.14; 95% CI, 1.58–2.90; P < 0.001) tumors. Seizures occurring at presentation and after BT diagnosis were also associated with higher mortality (adjusted HR: 1.34; 95% CI, 1.00–1.80; P = 0.049) in patients with WHO I (adjusted HR: 6.19; 95% CI, 1.30–29.4; P = 0.021) and grade III (adjusted HR: 6.19; 95% CI, 2.56–15.0; P < 0.001) tumors. On the opposite, seizures that occurred as a presenting symptom only were associated with better survival (adjusted HR: 0.27; 95%CI, 0.11–0.67; P = 0.004) for patients with WHO grade III BTs (Table 4 and Fig. 1).

Additional variables included in the regression analyses were age, gender, race, and parietal location. Cortical location was also associated with both seizures and survival but was not included in the model because it was highly correlated with parietal location, which had a stronger association with survival.

4. Discussion

This is the first study to analyze the association of seizures at presentation and following the diagnosis in a diverse group of patients with BT in relation to survival of these patients. In this large cohort of patients with BT, we found that seizures occurred in 43% of patients. Of these patients, 17% had seizures at presentation only, 12% developed seizures only during follow-up after tumor diagnosis, and 14% presented with seizures and also had them during follow-up. Patients with seizure as a presenting symptom were more likely to be male and younger. Patients who had seizures at presentation and during follow-up were more likely to be African American, more likely to have tumor in the cortical area, and to receive surgery. Patients who had seizures only during follow-up were more likely to have tumor in the parietal lobe, a prior history of epilepsy, and admission to hospice after initial diagnosis. Patients with WHO grade II tumor had the highest rate of seizures either as a presenting symptom or after tumor diagnosis in our study, which was consistent with previous studies [9,13].

The majority of demographic and clinical findings in our patient population corroborated with published research implying that a conventional cohort was studied. The incidence of seizures in patients with BT in our study (30% as a presenting symptom and 26% after tumor diagnosis) was comparable with previous studies. Prior reported incidence of seizures before or at the time of tumor diagnosis ranges from 14 to 51% [2,13–15] and the incidence of seizures after tumor diagnosis was reported in 10–45% [2,14]. The higher frequency of seizures as the first clinical presentation in patients with low-grade gliomas has previously been reported [12], which is consistent with our findings. Younger age and male predominance of patients presenting with seizures was seen in our study and is consistent with prior studies showing seizure as a presenting symptom most commonly seen in WHO grade II tumor, which occur more frequently in younger patients [16], and glioma, which occur more frequently in males [16]. In addition to age and gender differences, we also found that African American patients were more likely to develop seizures only after tumor diagnosis; we did not have a clear reason from our data to explain this finding.

Tumor location and grading influence the occurrence of seizures. Meningiomas, known to be the most common BT and are typically

Table 4
Association between seizure occurrence and mortality[a].

Patients with brain tumor	Timing of seizure	Unadjusted		Adjusted[b]	
		HR[c] (95CI)	P value	HR[c] (95CI)	P value
All patients[d]	Seizure occurred as a presenting symptom only	0.90 (0.68–1.19)	0.452	0.90 (0.68–1.20)	0.488
	Seizure occurred as a presenting symptom and seizure occurred after tumor diagnosis	1.33 (1.00–1.77)	0.053	**1.34 (1.00–1.80)**	**0.049**
	Seizure occurred after tumor diagnosis only	**2.28 (1.73–3.00)**	**<0.001**	**2.11 (1.59–2.81)**	**<0.001**
Patients with meningioma	Seizure occurred as a presenting symptom only	1.53 (0.43–5.40)	0.512	1.34 (0.33–5.41)	0.685
	Seizure occurred as a presenting symptom and seizure occurred after tumor diagnosis	3.40 (0.96–12.0)	0.057	**6.19 (1.30–29.4)**	**0.021**
	Seizure occurred after tumor diagnosis only	1.37 (0.18–10.5)	0.764	0.88 (0.11–7.20)	0.904
Patients with WHO Grade II tumor	Seizure occurred as a presenting symptom only	0.37 (0.13–1.07)	0.066	0.44 (0.14–1.34)	0.146
	Seizure occurred as a presenting symptom and seizure occurred after tumor diagnosis	2.27 (0.06–1.25)	0.094	0.40 (0.08–2.03)	0.268
	Seizure occurred after tumor diagnosis only	1.96 (0.65–5.90)	0.234	**3.41 (1.05–11.1)**	**0.041**
Patients with WHO Grade III tumor	Seizure occurred as a presenting symptom only	0.58 (0.26–1.28)	0.175	**0.27 (0.11–0.67)**	**0.004**
	Seizure occurred as a presenting symptom and seizure occurred after tumor diagnosis	**4.77 (2.07–11.0)**	**<0.001**	**6.19 (2.56–15.0)**	**<0.001**
	Seizure occurred after tumor diagnosis only	1.25 (0.17–9.33)	0.829	0.64 (0.07–5.62)	0.686
Patients with WHO Grade IV tumor	Seizure occurred as a presenting symptom only	1.04 (0.75–1.42)	0.843	1.11 (0.81–1.53)	0.525
	Seizure occurred as a presenting symptom and seizure occurred after tumor diagnosis	1.25 (0.90–1.72)	0.180	1.26 (0.91–1.75)	0.165
	Seizure occurred after tumor diagnosis only	**2.31 (1.73–3.09)**	**<0.001**	**2.14 (1.58–2.90)**	**<0.001**

p-value < 0.05 was considered statistically significant.
[a] Results from Cox proportional hazard regression with time-dependent covariate for seizures occurred after diagnosis.
[b] Adjusted for age at diagnosis, gender, race, and parietal locations.
[c] Reference group is patients without seizures.
[d] Stratified by tumor grade.

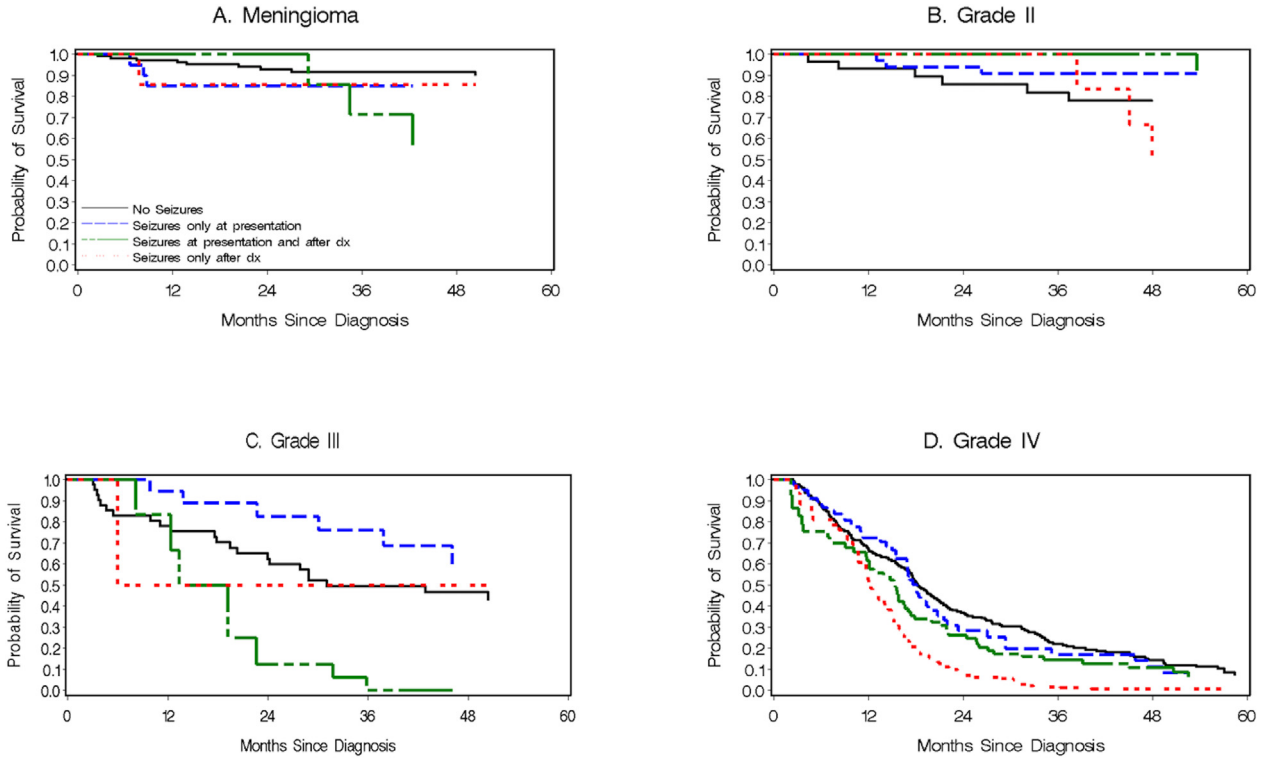

Fig. 1. Survival curves in different types of brain tumors in patients with (A) meningioma, (B) WHO grade II brain tumors, (C) WHO grade III brain tumors, and (D) WHO grade IV brain tumors, shown in the four groups: with no seizures (black solid line), with seizures only at presentation (blue dashed line), with seizures at presentation and after diagnosis (green dashed line), and with seizures only after diagnosis (red dashed line). (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

benign, account for 1/3 of the tumors [17] with seizures in 1/3 of these cases [18]. In our study, meningiomas contributed for 1/5 of the tumors, and seizures were noted in 1/4 of these cases. An association between tumor involving cortex and a high incidence of seizures was consistent with many previous studies [13,19–22]. Patients with temporal lobe involvement have shown to be at the highest risk to develop seizures because of high epileptogenicity of the mesial temporal lobe structure [22,23]; however, our findings did not support this finding. Almost half (40–60%) of the patients with BT located in each lobe (either frontal, insular, temporal, parietal, or occipital lobes) were noted to have seizures at some time in their life. Nevertheless, seizures occurring after tumor diagnosis only were associated with parietal lobe involvement.

Patients with WHO grade III BT presenting with seizures and no other seizure events thereafter lived longer even after adjusting for age at diagnosis, gender, race, and parietal location. It is possible that seizures at presentation in those with WHO grade III BT aid in earlier detection and treatment of the BT. Seizure were associated with longer survival in patients with high-grade glioma and glioblastoma in previous studies [9,15]. Another theory is that seizure at presentation in WHO grade III BTs may also reflect a phenotypic or molecular association with grade II gliomas, which commonly present with seizures. Data on seizure as a presenting symptom as a prognostic factor for patients with meningioma are limited, and there is no association between seizure as a presenting symptom only and survival in patients with meningioma in our cohort. Many previous studies supported that the presence of seizure as a presenting symptom is also a favorable prognostic factor for patients with low-grade glioma [10,24,25]; however, this has not been reproduced in all studies [9]. Patients with WHO grade II gliomas who continued to have seizures after diagnosis had worse outcomes in a prior study [10]. In our study, we demonstrated an association between seizures that occurred only after tumor diagnosis and mortality in patients with WHO grades II and IV BT, but not in those with meningioma or WHO grade III tumor. However, we did show an association between seizures at both time points (presentation and during follow-up) and mortality in patients with meningioma and WHO grade III tumors. Additional studies investigating the rate and/or presence of tumor progression in patients who present with and continue to have seizures during their disease, in meningioma and WHO grade III tumors may shed light on this finding. Previous studies support the hypothesis that ongoing seizures after surgical treatment of tumor have an association with tumor progression in patients with low-grade gliomas and malignant astrocytomas [4,26]. No prior study has been conducted to demonstrate an association between the occurrence of seizures after tumor diagnosis and survival of patients with high-grade BT.

The major strength of this study is long-term follow-up (up to 12 years) of a large cohort (N = 662) of patients with a diverse representation of primary BT histologies including glioma and meningioma. We also were able to illustrate the prognostic significance of seizures that occurred after tumor diagnosis. This study has limitations. This is a single center retrospective study, with 21% of the initial cohort excluded for insufficient data, which may limit the generalizability of study results. Second, we lack information on functional status at the time of tumor diagnosis, which has been shown to influence survival especially in high-grade tumors. Finally, information of the effectiveness of seizure control was not available; it is possible that uncontrolled seizures might affect patient outcomes.

5. Conclusion

Seizures occur in almost half of patients with BT. The association between seizures in patients with BT and their survival depends on the time of occurrence of seizures, if occurring at presentation or after tumor diagnosis, and the type of BT. This is the first study to correlate seizures as a presenting symptom only of BT to better survival in WHO grade III BTs while higher mortality to WHO grade II tumors

presenting with seizures that continue after tumor diagnosis and to WHO grade IV tumors with seizures after diagnosis. As the relationship between seizures and tumor phenotype (grade, behavior, and survival) is further elucidated, clinicians may be able to improve HRQOL and OS through improved seizure control and/or prevention. We propose that the time of seizure occurrence during the course of BT diagnosis might be another valuable tool in predicting the disease progression of those impacted by BTs and possibly help in earlier detection and management for longer survival of these patients.

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Declaration of competing interest

None of the authors have any conflict of interest to disclose. We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

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