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Analysis of the factors related to mortality in patients with primary brain and central nervous system tumors

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Original Article

Abstract

BACKGROUND: The present study aimed to assess the factors associated with the mortality of patints with brain tumor surgery at Be'sat Hospital in Sanandaj, Kurdistan, Iran.

METHODS: In this prospectively cross-sectional study, 108 patients diagnosed with brain tumor and followed by a surgery during April to December of 2014 were recruited. Eighteen cases were excluded from the study due to lack of information about their treatment outcomes. Patients' information including age, gender, tumor type, tumor location, type of treatment, and extent of resection was collected by a checklist. Clinical outcome of the patients in six months after surgery was determined through phone calling to patients. All analyses conducted in SPSS software using logistic regression.

RESULTS: Forty-seven (52.2%) of the studied subjects were women. The age of cases ranged from 3 to 83 years with total mean of 43.4 ± 21.9 years. In six months after treatment, 41 (45.6%) of the treated patients died. After excluding 9 children from final analysis and modeling the data by logistic regression, statistically significant associations were observed between death from central nervous system (CNS) tumor and male gender [odds ratio (OR): 5.25, 95% confidence interval (CI): 1.38–21.99], higher age (OR: 1.07, 95% CI: 1.02–1.13), partial vs. total resection (OR: 20.24, 95% CI: 1.21–337.51), and high malignant potential tumors (OR: 14.77, 95% CI: 4.85–45.02).

CONCLUSION: The results showed that both demographic (advanced age and male gender) and clinical factors (high malignant potential tumors and partial removal of tumor) related to the worse outcome in patients with primary CNS tumors during six months after surgery.

KEYWORDS: Brain Neoplasms, Central Nervous System Neoplasms, Mortality, Risk Factors

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Introduction

Nearly a hundred histologically distinct types of primary central nervous system (CNS) tumors have been recognized, each of them having its own spectrum of clinical presentations, treatments, and outcomes. Primary brain tumors are divided into benign and malignant tumors that originate directly from the brain and its appendages.[1,2] The incidence of brain tumors has increased in all age groups over the past two decades. According to the central brain tumor registry of the united states (CBTRUS), the incidence

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rate of all primary malignant and non-malignant brain and CNS tumors was 21.97 cases per 100000 for a total count of 356858 incident tumors diagnosed during 2015 in the United States of America (USA).[3,4] The estimated number of new cases with brain and other nervous system tumors has been reported 23770 (7.3 per 100000) with 16050 deaths (fatality rate: 67.5%) in 2016.[5]

Although primary malignant CNS tumors are now registered in the national cancer registry (NCR) of Iran, there is no availability of nationwide CNS tumor epidemiologic data due to failure in surveillance system and incompleteness of collected data. Based on two previous review studies, the annual incidence of primary brain tumors in Iran is estimated to be 2.70 to 5.69 per 100000.[6,7]

Brain tumor can occur in both genders at any age, but its incidence and histology is different between age and sex groups. There is a modest rise before age 10 and a steady increase after age 15, with a maximum incidence between 75 and 84 years age group. Based on USA statistics, the incidence and mortality of brain and other nervous system tumors is higher in men. Furthermore, the incidence of all brain tumors, except meningioma, is higher in men.[5] Surgery is important to remove a large tumor, but large tumor resection has more risk than small tumors. Although complementary treatments such as radiotherapy and chemotherapy are beneficial because of their high precision, they have some limitations.[7,8]

Albeit emergence of new diagnostic and therapeutic techniques led to improvement in treatment of brain tumors, high mortality after surgery or combination therapy is still a challenging issue for neurosurgeons that can be influenced by different factors. According to the exiting evidence, demographic variables, such as age and gender, and clinical factors such as tumor characteristics (type, size, grade, stage, and location), extent of surgical resection, skills of surgeon, and also pre- and post-operative cares should be seriously considered.[9-11]

As mentioned earlier, the follow-up of patients with brain tumor after surgery to determine the outcome and assessing the potential related factors is essential. The aim of this study was to assess the potential risk factors related to the mortality in patients with brain and CNS tumors in six months after surgery.

Materials and Methods

In this prospectively cross-sectional study, all patients diagnosed with brain tumor during 2014 that underwent treatment (surgery) of tumor at Be'sat Hospital in Sanandaj, Iran, were investigated. The total number of patients included in the study was 108 individuals, primarily. Eighteen patients were excluded from the study due to lack of information about their treatment outcomes.

Data were collected using a checklist from patient medical records that was archived in the hospital. Patient information including age, gender, tumor type, tumor location, type of treatment, and extent of resection was extracted from patient's medical records. Clinical outcome, and death or survival (relative/complete cure) of each patient was obtained in six months after surgery follow-up by phone calls to either the patient or her/his family. It should be noted that during fallow-up and calling to the patients, the aim of the research was explained and oral informed consent for data collection was taken from all individuals who entered in the study.

All analyses were conducted in SPSS software (version 20, IBM Corporation, Armonk, NY, USA). In analyzing the data, we first used independent sample t-test and chi square to assess the relation between studied variables, death, and studied outcome; then the values of odds ratio (OR), corresponding 95% confidence interval (CI) for OR, and significance values were calculated for each

factor using logistic regression method.

It was noted that after the description of patients' characteristics and in order to determine the association between studied factors and mortality in six months after brain tumor surgery, 9 children aged < 15 years were excluded from the analysis due to the differences between children and adult brain tumors.

Results

A total of 108 patients diagnosed with brain tumor and followed by a surgery during 2014 were recruited. Eighteen cases were excluded from the study due to lack of information about their treatment outcomes. The mean age ± standard deviation (SD) for other remaining subjects (90 patients) was 43.4 ± 21.9 years. They spanned from 3 to 83 years old, and 52.2% of them were female. More patients (98%) were Iranian Kurds ethnically. The most common type of diagnosed tumors was meningioma (37.8%). Furthermore, 74.4% of tumor site was supratentorial. For 71% of patients, surgery without any supplementary treatment was the only treatment option, whereas 29% had an additional treatment after surgery. Additional or complementary treatments were chemotherapy, radiotherapy, or both chemotherapy and radiotherapy. For 87.8%, the total surgical procedure was performed. In terms of treatment outcome, 22.2% of cases had complete response, 32.2% had partial response, and 45.6% died. Table 1 displays more details of patient characteristics in the study.

Table 1. Demographic and clinical characteristics of studied patients

Variables	All patients (n = 90)	Cases aged ≥ 15 years (n = 81)
Age (Mean ± SD)	43.40 ± 21.96	47.50 ± 19.16
Gender [n (%)]		
Female	47 (52.2)	44 (54.3)
Male	43 (47.8)	37 (45.7)
Surgical resection [n (%)]		
Partial	11 (12.2)	9 (11.1)
Total	79 (87.8)	72 (88.9)
Treatment type [n (%)]		
Surgery	64 (71.1)	62 (76.5)
Surgery + chemotherapy	6 (6.7)	4 (4.9)
Surgery + radiotherapy	7 (7.8)	7 (8.6)
Surgery + radiotherapy + chemotherapy	13 (14.4)	8 (9.9)
Tumor location [n (%)]		
Infra tentorial	23 (25.6)	15 (18.5)
Supra tentorial	67 (74.4)	66 (81.5)
Tumor type [n (%)]		
Meningioma	34 (37.8)	33 (40.7)
Glioblastoma	21 (23.3)	21 (25.9)
Astrocytoma	12 (13.3)	10 (12.3)
Ependymoma	8 (8.9)	6 (7.4)
Medulloblastoma	4 (4.4)	-
Schwannoma	4 (4.4)	4 (4.9)
Pituitary adenoma	3 (3.3)	3 (3.7)
Colloid cyst	2 (2.2)	2 (2.5)
Craniopharyngioma	1 (1.1)	1 (1.2)
Choroid plexus papilloma	1 (1.1)	1 (1.2)
Outcome [n (%)]		
Death	41 (46.0)	36 (44.4)
Cured	49 (54.0)	45 (55.6)

Table 2. Association between clinical outcome and demographic and clinical variables (n = 81)

Variables	Cured (relatively or completely cured), [n (%)]	Died, [n (%)]	P	OR (95% CI)
Gender			< 0.001	6.25 (2.37–16.47)
Female	33 (75.0)	11 (25.5)		
Male	12 (32.4)	25 (67.6)		
Surgical resection			0.004	12.57 (1.49–106.02)
Total	44 (61.1)	28 (38.9)		
Partial	1 (11.1)	8 (88.9)		
Treatment type			0.020	-
Surgery	38 (61.3)	24 (38.7)		
Surgery + chemotherapy	0 (0.0)	4 (100.0)		
Surgery + radiotherapy	5 (71.4)	2 (28.6)		
Surgery + radiotherapy + chemotherapy	2 (25.0)	6 (75.0)		
Tumor location			0.100	0.39 (0.11-1.34)
Infra tentorial	11 (73.3)	4 (26.7)		
Supra tentorial	34 (51.5)	32 (48.5)		
Tumor type			0.001	4.92 (1.91–12.68)
Potentially low malignant tumors (Meningioma, Schwannoma, and others)	32 (72.7)	12 (27.3)		
Potentially high malignant tumors (Glioblastoma, Astrocytoma, Ependymoma)	13 (35.1)	24 (64.9)		
Age (Mean ± SD)	47.1 ± 16.8	48.0 ± 22.0	0.800*	

OR: Odds ratio; CI: Confidence interval; * Independent t test result

Since 9 patients from all 90 studied patients were children aged less than 13 years, we excluded them in univariate and multivariate analysis, and information from 81 remaining patients was analyzed. Table 2 summarizes the univariate analysis to assess the relationship between clinical outcomes of studied patients with demographic and clinical factors in 81 patients.

As shown in table 2, death from brain tumor six months after surgery was significantly associated with gender (P < 0.001), surgical resection (P = 0.004), treatment type (P = 0.020) and tumor type (P = 0.001).

In order to control potential confounders, the logistic regression model was performed. The OR, corresponding 95% CI, and significance values for each factor were calculated (Table 3).

As shown in table 3, although three variables including male gender (P < 0.001), partial resection of surgery (P = 0.020), and potentially high malignant tumors (P < 0.001) were significantly associated with death in six months after brain surgery in univariate analysis, two demographic factors including higher age (P = 0.010), male gender (P = 0.010), and also two clinical factors, potentially high malignant tumors (P < 0.001) and partial resection of tumor (P = 0.030), were significant factors in the final model.

Discussion

In the present study, we followed all patients with brain tumors that underwent surgery and other complementary treatments for six months after surgery. Our results showed that 45.6% of studied patients were dead. Higher age, male gender, potentially high malignant tumors, and partial resection were four significant factors associated with mortality of patients with CNS tumors after treatment.

The results indicated that the chance of death from brain tumors after treatment increased with increasing age. The association between higher age and death in patients treated for CNS tumors is highlighted in several studies.

Table 3. Logistic regression results for variables associated with mortality in patients with brain tumor

Variable	Crude		Adjusted	
	OR (95% CI)	P	OR (95% CI)	P
Age	1.01 (0.98–1.03)	0.800	1.07 (1.02–1.13)	0.010
Gender				
Female	-	-	-	-
Male	6.25 (2.37–16.47)	< 0.001	5.52 (1.38–21.99)	0.010
Surgical resection				
Total	-	-	-	-
Partial	12.57 (1.49–106.02)	0.020	20.24 (1.21–337.51)	0.030
Treatment type				
Surgery	-	-	-	-
Surgery + chemotherapy	0.22 (0.04–1.16)	0.070	0.11 (0.01–1.05)	0.050
Surgery + radiotherapy	1.33 (0.09–20.12)	0.800	0.63 (0.01–30.05)	0.800
Surgery + radiotherapy + chemotherapy	0.13 (0.01-1.32)	0.080	0.07 (0.01–1.23)	0.070
Tumor location				
Infra tentorial	-	-	-	-
Supra tentorial	2.59 (0.75–8.96)	0.100	0.77 (0.17–3.57)	0.700
Tumor type				
Potentially low malignant tumors (Menengioma, Schwannoma, and others)	-	-	-	-
Potentially high malignant tumors (Glioblastoma, Astrocytoma, Ependymoma)	4.92 (1.91–12.68)	< 0.001	14.77 (4.85–45.02)	< 0.001

OR: Odds ratio; CI: Confidence interval

Reihani Kermani reported higher mortality rate for elderly patients.[7] Similar findings have also been reported in some studies;[12,13] for example, Tian et al. in a systematic review study indicated that higher age was a main risk factor for CNS cancers and its related death.[14] Age was also significantly associated with survival of patients in Stark et al. study.[15] Some studies have reported different results about the effect of patients' age on CNS surgery outcome, so in previous studies conducted on patients with glioblastoma, higher age was a prognostic factor for patients undergoing biopsy while not an effective factor in patients undergoing resection.[16,17]

According to the results, male gender was another significant factor for death in patients with CNS tumors undergoing surgery. Some previous studies support this finding.[1,3,18,19] In a study conducted by Villano et al., it was shown that male gender was a risk factor for death outcome from primary CNS lymphoma in patients with age less than 50 years. They also concluded that advanced age was only a significant risk factor for survival of these patients in +50 age groups.[20]

In addition to above mentioned demographic variables, two clinical factors including having tumors with high malignant potential and partial surgical resection of tumor were recognized as main risk factors for patient mortality after treatment. There are several studies about surgical resection type, partial or total resection, as predictor factor for treatment outcome in treated patients with CNS tumors. Johnson et al. showed that total resection was a positive prognostic factor.[21] Song et al. indicated that complete removal of tumor provided the best outcome. However, without complementary therapy, the outcome does not seem to be desirable.[22] The same conclusion about the association of total resection and 5-year survival of pineocytoma has also been reported by Clark et al.[23] In another study conducted by Chaichana et al., subtotal resections have been reported as independent risk factors for visual outcome and tumor recurrence in last follow-up of patients with

meningioma.[24] Oszvald et al. recommended total resection plus adjuvant therapy in elderly patients with malignant brain tumor.[25]

There are several earlier supportive studies regarding another significant clinical risk factor, i.e. tumors with high malignant potential, that had highest association (OR = 14.77) with patients' mortality in our study.[26-28] Our results showed that the chance of death in patients with high malignant potential tumors was approximately 15 times higher than patients with low malignant potential tumors. Higher mortality resulting from malignant versus benign CNS tumors has been reported as an acceptable issue in many previous studies.[29-31] Although, anatomical positions and specific conditions of the CNS tumors may lead to life threatening complications even in benign tumors,[32,33] our findings demonstrated that tumor malignancy was the strongest risk factor for death in patients with CNS tumors after modeling the data and controlling the potential confounders.

Location of tumor (infra or supra tentorial) and type of treatment (surgery or combination of surgery plus radiotherapy or/and chemotherapy) had no statistical association with mortality in our study; whereas, there is some evidence about the effect of these factors in the literature that is incompatible with our results. Bagley et al. demonstrated that patients with supratentorial tumors had shorter survival time than those with infratentorial tumors.[34] Two other studies advocated this finding.[15,35] In Stark et al. study, prolonged survival was associated with patients undertaking several treatments (radiotherapy, chemotherapy, and combined radio-/chemotherapy with temozolomide).[15] We did not observe any association between treatment type as a risk factor and mortality. The choice of the type of treatment by neurosurgeon depends on the clinical condition of the patient. Meeske and Nelson suggested combination treatment in patients with partial resection to remove residual tumor or tumor recurrence treatment.[10]

The main limitation of the present study was lack of full access to information on socioeconomic status (SES), body mass index (BMI), life styles, and geographic location of patients; whereas, some past studies have shown that these factors can play a significant role on post-surgery survival in both adults and children. Other limitations of the study were small sample size, cross-sectional analysis, and non-generalizability of the results.

Conclusion

In this study, we investigated the clinical outcome of treated patients with CNS tumors in six months after surgery in Sanandaj. The results showed that two demographic (advancing age and male gender) and two clinical factors (high malignant potential tumors and partial removal of tumor) were associated with higher mortality.

Conflict of Interests

Authors have no conflict of interests.

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