

# Incidence of Cerebrovascular Accidents Following Brain Tumor Surgery

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## ABSTRACT

**Background and Purpose:** Cancer and cerebrovascular accidents (CVA) are two most common causes of mortality and morbidity in the elderly. Patients with brain tumor can be highly affected by postsurgical stroke. CVA may be the first manifestation in these patients. Therefore, we aimed to assess the epidemiological factors affecting CVA after brain surgery.

**Methods:** In this cross-sectional study we enrolled 241 patients admitted for brain surgery due to a brain tumor during April 2009 to March 2013 in Tohid Hospital, Sanandaj, Iran, using the convenient sampling method.

**Results:** The mean±SD age of the patients was 48.1±21.3 years. 5 patients (2%) were complicated with CVAs (4 ischemic stroke and one haemorrhagic). The frequency of CVA was not different regarding age, sex, type of tumor, tumor site, hypertension, diabetes mellitus, smoking, and type of intervention. Type of tumor was meningioma in 2 patients, Oligodendroglioma in 2 patients, and metastatic cancer in 1 patient. Of the 5 patients with CVA, 2 were in middle fossa (1.9% of middle fossa tumors), 2 in anterior fossa (2.5%), and one in the meningeal membrane (3.3%).

**Conclusion:** Despite low incidence of stroke in this study, it seems there is a considerable rate of mortality and morbidity of cerebral vascular diseases, especially in people with underlying chronic medical conditions such as brain tumors necessitates regular follow-up of patients with brain tumors for assessing risk factors to be able to increase survival rate and reduce disease-related complications.

**Keywords:** Cerebrovascular Accidents; Brain Tumors; Surgery; Iran

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## INTRODUCTION

The prevalence of brain tumor is about 2.6-5.8 per 100,000 cases, which seems to be higher in developed countries and less in developing countries and is continuously increasing with advancing diagnostic technologies<sup>1-3</sup>. In addition, brain surgery with different modalities remain the gold standard of treatment<sup>4</sup>. Cerebrovascular accidents (CVAs), on the other hand, is a common cause of mortality and morbidity worldwide, especially in developing countries<sup>5</sup>. The association between CVA and brain malignancy has

been well established: On one hand, CVA can be the first presentation of brain malignancy<sup>6</sup> and, on the other hand, CVA is one of the growing postsurgical complications of brain surgery due to brain tumors<sup>7</sup>.

Increase in the prevalence of brain tumors, beside higher prevalence in Western countries, has been attributed to better diagnostic tools and higher elderly population<sup>1</sup>. Several risk factors have been identified for brain cancers, which has been established to include genetics, high dose radiation, male gender, ethnicity, and increasing age<sup>1</sup>.

The risk factors for CVA have also been clarified<sup>8</sup>, and anticoagulation have been suggested to prevent and treat CVA in high-risk patients<sup>9</sup>. Both CVA and brain tumor have a great impact on patients' quality of life and life expectancy and impairs functional outcome and return to community<sup>10</sup>. Few studies have evaluated the association between brain malignancy and CVA<sup>11</sup>, which might indicate common risk factors and mechanisms. Some have suggested the hypercoagulability state as a shared pathology<sup>12</sup>, yet, the factors affecting this association and the underlying mechanism have to be elucidated.

Therefore, we aimed to assess the epidemiological factors affecting CVA after brain surgery in patients with brain tumor, in order to assess prevalence and effective factors.

## MATERIALS AND METHODS

In this cross-sectional study, we enrolled 241 patients admitted for brain surgery due to a brain tumor during April 2009 to March 2013 in Tohid Hospital, Sanandaj, Iran, using the convenient sampling method. The protocol of the study was approved by the Kurdistan University of Medical Sciences. The researchers have considered all ethical consideration throughout the study.

The demographic characteristics, including age, sex, marital status, educational level, occupation, medical history, and the data regarding type of brain malignancy, size, and site of tumor, and treatments after surgery such as radiotherapy were collected. Data was collected from medical records of patients, and were completed and followed up by phone calls. Besides predisposing factors, including underlying diseases, smoking, and etc. were also recorded and were compared regarding the incidence of cerebrovascular accidents. All patients, primarily underwent CT scan and in case they needed a more accurate diagnosis, or upon tumor relapse or occurrence of complications, they underwent MRI. Surveillance on the occurrence of neurological symptoms was considered, and if the patients experienced on their acute neurological symptoms, they underwent reevaluation with imaging (CT SCAN OR MRI with contrast enhancement to rule out tumors, and to confirm the occurrence of stroke) were done.

Continuous variables are presented as mean±standard deviation and qualitative variables are reported through frequency and percentage. Comparison between variables was performed through chi-square and Fisher exact tests and logistic regression. Statistical analysis was performed using STATA software, version 12. P-values less than 0.05 were considered statistically significant.

## RESULTS

The mean±SD age of the patients was 48.1±21.3 years and 114 (47.5%) were men and 52.5% were female, 63% were living in urban areas and 37% in rural areas, 76.7% had less than high-school education, 19.1% were high school graduates and 4.2% had an academic degree.

Among the 241 patients, 5 cases had experienced CVA (2%), 4 cases were ischemic and one haemorrhagic. The frequency of CVA was not different regarding age ( $P=0.29$ ) and sex ( $P=0.73$ ). Type of tumor was meningioma in 2 patients, Oligodendroglioma in 2 patients, and metastatic cancer in 1 patient, and CVA did not occur in other types (OR=0.98, CI 95%: 0.69-1.42,  $P=0.97$ ). Tumor site was in the median cavity in 2 patients, anterior cavity in 2 patients, and in the meningeal membrane in 1 patient (OR=1.32, CI 95%: 0.73-2.40,  $P=0.34$ ). The prevalence of tumor's type and site and their association to CVA is demonstrated in table 1.

Regarding tumor's size, 93.2% were smaller than 5 cm and 6.7% greater than 5 cm. All the 5 cases of CVA had a tumor of smaller than 5 cm. Besides, 22.5% had a history of radiation and 77.5% did not. Regarding the underlying diseases, 22 (9.2%) patients had hypertension, 2 of whom had CVA ( $P=0.067$ ); 13 (5.4%) patients had diabetes mellitus, but none had CVA ( $P=0.072$ ); 52 (21.7%) patients were smokers, but none had CVA ( $P=0.58$ ); and 8.7% suffered from other diseases.

Regarding type of intervention, 226 patients underwent craniotomy and microscopic resection with 2.2% prevalence of CVA and 14 underwent brain endonasal endoscopy, none of whom had CVA, but the prevalence of CVA was not different between them ( $P=0.79$ ). Information on the technique of intervention, did not exist in one patient.

## DISCUSSION

In the current study, 2% of the patients were complicated with CVA, but the frequency of CVA was not different regarding age, sex, type of tumor, tumor site, hypertension, diabetes mellitus, smoking, and type of intervention. Type of tumor was meningioma in 2 patients, Oligodendroglioma in 2 patients, and metastatic cancer in 1 patient. The tumor's site was middle fossa in 2 patients, anterior fossa in 2, and meningeal membrane in 1.

Similarly, other studies have assessed CVA after brain surgery due to brain malignancy. Sughru and colleagues assessed 705 patients undergoing craniotomy for meningioma. Similar to the results of the present study, they reported the incidence of CVA to be 2%. However, they have reported bifrontal craniotomy as the independent factor of venous infarction on CT imaging<sup>13</sup>.

**Table 1.** Location and type of tumors and their association to CVA.

| Type of tumor  | Total prevalence, No. (%) | Positive CVA, No. (%) | Negative CVA, No. (%) | Odds Ratio of positive vs. negative cases (confidence interval 95%) | P-value |
|--|---------------------------|-----------------------|-----------------------|---|---------|
| Glioblastoma Multiform                                   | 59 (24.6)                 | 0                     | 59 (100)              | 0.98 (0.69-1.42)  | 0.97    |
| Meningioma   | 64 (26.7)                 | 2 (3.1)               | 62 (96.9)             |   |         |
| Oligodendroglioma  | 26 (12.1)                 | 2 (6.9)               | 27 (93.1)             |   |         |
| Astrocytoma  | 44 (18.3)                 | 0                     | 44 (100)              |   |         |
| Pituitary Adenoma  | 14 (5.8)                  | 0                     | 14 (100)              |   |         |
| Metastatic cancer  | 11 (4.6)                  | 1 (9)                 | 10 (91)               |   |         |
| Ependymoma   | 2 (0.8)                   | 0                     | 2 (100)               |   |         |
| Medulloblastoma  | 2 (0.8)                   | 0                     | 2 (100)               |   |         |
| Choroid Papilloma  | 1 (0.4)                   | 0                     | 1 (100)               |   |         |
| Cystic Mass  | 2 (0.8)                   | 0                     | 2 (100)               |   |         |
| Lymphoma   | 9 (3.7)                   | 0                     | 9 (100)               |   |         |
| Schwannoma   | 3 (1.2)                   | 0                     | 3 (100)               |   |         |
| Unclassified & uncertain origin (e.g: haemangioblastoma) | 4 (1.6)                   | 0                     | 4 (100)               |   |         |
| <b>Tumor site</b>  |                           |                       |                       |   |         |
| Skull base   | 4 (1.7)                   | 0                     | 4 (100)               |   |         |
| Posterior cavity   | 31 (12.8)                 | 0                     | 31 (100)              |   |         |
| Median cavity  | 102 (42.3)                | 2 (1.9)               | 100 (98.1)            |   |         |
| Anterior cavity  | 40 (16.6)                 | 1 (2.5)               | 40 (97.5)             |   |         |
| Perivascular   | 3 (1.2)                   | 0                     | 3 (100)               |   |         |
| Meningeal membrane                                       | 61 (25.3)                 | 2 (3.3)               | 59 (96.7)             |   |         |

CVA: Cerebrovascular Accidents

But the type of intervention was not associated with CVA in the present study, which might be due to different details of procedures and postsurgical care, which indicates the need for reconsideration in surgical methods and techniques and postsurgical follow-up of patients.

Bekelis et al investigated 1834 patients in a retrospective cohort and reported no association between sex and CVA<sup>14</sup>, which is consistent with the results of the current study. Moreover, they also reported meningioma as the most common brain tumor (25%), which is in line with the results of the present study (26.7%), although they found a higher rate of higher meningioma in women. Kreisl et al have reported a prevalence of 1.3% for CVAs in 5132 patients undergoing brain surgery, 48.5% of which were postoperative and have concluded that operation might have intensified the pre-existing factors underlying stroke<sup>7</sup>. They reported glioma as the most common type of tumor and meningioma as the second cause. Kamiya-Matsuoka evaluated the prevalence of CVA in 6500 cases of glioma and reported a prevalence of 0.1% for CVA, 53% of which were postoperative<sup>15</sup>. Therefore, as the results of the present study indicate, consistent with the above-mentioned studies, postsurgical CVA is of great importance after craniotomies for brain malignancies, which might reveal a common pathology. Studies have

established different mechanisms for cancer-related CVA, such as embolism, atherosclerosis, and treatment-related mechanisms(iatrogenic), although they have not focused the brain tumors<sup>11,16,17</sup>. Therefore, patients with brain malignancy undergoing surgery are at a higher risk for CVA, which should be considered by physicians, in order to be able to reduce its risk by controlling the risk factors.

Sughru et al reported history of radiation in 9% of the studied patients and found no association between radiation and CVA<sup>13</sup>, which is similar to the statistics of the current study. Campen and colleagues have reported a 4.5% incidence for CVA and found that radiation was a strong risk factor for CVA in pediatric patients with primary brain tumor<sup>18</sup>, although the patients of their study did not undergo brain surgery, high prevalence of radiation (61.5%) in their investigation might play a role in the discrepancy of the results of this study with the present study, reporting 22.5% of patients with a history of radiation. Nevertheless, the study by van Alkemade et al showed the late effects of radiation and CVA<sup>19</sup>, in addition, Bowers et al have also established late occurrence of CVA in brain tumor survivors<sup>20</sup>; therefore, long follow-up of patients is suggested.

Regarding tumor's site, Kamiya-Matsuoka have also reported middle, anterior, and posterior fossa as the

most prevalent sites<sup>15</sup>, which were also common sites in the present study, but the most common tumor sites was middle and anterior fossa and meningeal membrane in the present study, which has not been separated in some studies, like the study by Kamiya-Matsuoka and colleagues.

The strengths of the present study include assessing multiple variables with details and their association in a fair number of samples, considering the low frequency of cases with a brain tumor. The current study also had some limitations, including lack of follow-up for indicating the outcome of patients in long-term, inability to perform modern surgical techniques, such as microsurgery, in our center and incapability to assess its efficacy on patients' prognosis.

## CONCLUSION

On the basis of the present study indicated that, in spite of low incidence of stroke after brain tumor surgery there is a high rate of mortality and morbidity of cerebral vascular diseases, especially in people with underlying chronic medical conditions such as brain tumors, regular follow-up of patients with brain tumors are necessary for assessing risk factors to be able to increase survival and reduce complications related to the disease.

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