DOI: 10.14744/ejmi.2019.74484
EJMI 2020;4(1):73–77

Research Article

Effects of Total and Subtotal Glial Tumor Resection on Survival

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Abstract

Objectives: Glial tumors are treated with a multidisciplinary team approach including specialists in brain surgery, radiology, pathology, radiation oncology and medical oncology. Surgery is one of the main treatment options. However, the effect of resection volume on prognosis is still uncertain. The aim of this study is to investigate the relationship between the residual tumor volume and survival of the patients who were operated with the diagnosis of intracranial glial tumor in the last 5 years.

Methods: Of 49 patients, 30 underwent total resection and 19 underwent subtotal resection.

Results: The average surveys of total resection were 13.6 (6-32 months) months. 4 of 6 patients with anaplastic astrocytoma survived and the mean survey was 26.5 (4-45) months. The survey of subtotal resection group was significantly shorter than the other TR group.

Conclusion: As a result, recovery was inversely increased with residual tumor volume.

Keywords: Glial tumor, residual tumor, surgery, survival, treatment options

Cite This Article: *Ercan S, Ataizi Z, Ataizi F, Bulduk EB. Effects of Total and Subtotal Glial Tumor Resection on Survival. EJMI 2020;4(1):73–77.*

Among brain tumors, glial tumors with distinct heterogeneity, which can develop from different cell types, are one of the most common types of primary intracranial tumors and include mainly astrocytoma, oligodendrogliomas, and ependymomas.[1, 2] Among these tumors, glioblastoma multiforme (GBM), classified by the World Health Organization as stage IV glioma, is a type of glioma that accounts for 80% of all primary malignant central nervous system tumors.[1] The average age at diagnosis is 64 years and is more common in men than women.[3] Among the developed countries, Australia, New Zealand, Europe and North America a highest incidence is seen while in regions such as Africa and the Pacific is rare.[4] In general, malignant gliomas are aggressive tumors with high morbidity and mortality rates. Although several treatment models have been developed in the last few decades, such as safe surgical resection, radiotherapy and chemotherapy, the overall survival rate of GBM for 5 years is still less than 5%.[5]

The mean overall survival for patients who are newly diagnosed GBM, underwent maximum surgical resection followed by radiotherapy and chemotherapy, is 12–18 months.[3, 6, 7] Ahmed et al.[8] reported that even with optimal treatment, the average survival was 12-15 months for GBM and 2-5 years for anaplastic glioma. Today, the only known risk factor for the development of GBM is the exposure to ionizing radiation, and no environmental risks such as cell phone use, infection or trauma have been shown to have an impact.[9] Genome studies have shown seven genomic variants with increased risk of glioma.[1]

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Submitted Date: September 10, 2019 **Accepted Date:** November 01, 2019 **Available Online Date:** January 17, 2020

Preoperative tumor volume is known to affect outcome.[10] Similarly, postoperative residual tumor volume has been also shown to affect survival of patients with GBM.[11, 12] Despite the studies on the residual tumor volume and survival after surgery, a complete consensus has not been established. Our aim is to find out how residual tumor volume affects well-being and survival after adjuvant chemotherapy and radiotherapy.

Methods

Ethical approval: Our study was approved by the Ethical Committee of Eskisehir Osmangazi University ,and all applicable international, national, and institutional guidelines for the care and use of human subjects were followed (Eskisehir Osmangazi University Ethical Commitee, Chairman: Dr. Muhammed E Karakilic, No: 25403353-050.99-E.76044, Date:02, July, 2019).

The patients who were admitted to our clinic between 2014 - 2019 and diagnosed as glial tumors were retrospectively analyzed. Inclusion criteria: 1. Complete clinical and radiological information in patient records. 2. Histologically, the molecular pattern of the tumors should be diagnosed. 3. Presence of measurable contrast uptake to calculate residual tumor volume on both CT and MR images. In all patients, surgical intervention was performed with the principle of tumor removal at the highest volume possible without damaging the functional sites. Tumor borders and functional areas were controlled by intraoperative neuronavigation.

Residual volume was calculated using OsiriX DICOM Processor (Pixmero SARL, 266 Rue de Bernex, CH-1233 Bernex, Switzerland) in postoperative contrast-enhanced brain tomography and MR images (Fig. 1). Standard descriptive statistical tools (mean, standard deviation) were used for demographic examination. Chi-square test was used to compare residual volume.

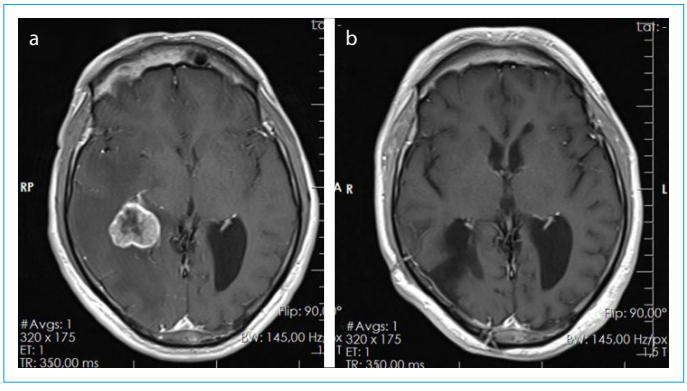

Figure 1. Brain MRI image. **(a)** It is observed that the pre-operative mass stained with contrast. **(b)** No postoperative residual tumor image.

Results

A total of 49 patients were evaluated according to age, sex, surgical resection, postoperative radiotherapy, chemotherapy, and disease surveillance. There were 31 men and 18 women. The age range was between 29 and 77 (mean 60.2). 22 (44.9%) patients were still alive and the remaining 27 (55.1%) patients died. Among these, the patients with the shortest 2-month survey were diagnosed with gliosarcoma and the longest with 62-month oligodendroglioma. In terms of tumor location, 28 (57.2%) of the supratentorial patients were located in the right hemisphere and 21 (42.8%) were in the left hemisphere. In the frontal region 23, temporal 9, parietal 10, occipital 4 and temporoparietal 3 patients were observed. Infratentorial settlement was not observed. Pathological diagnoses were named by direct microscopic diagnosis of surgical excised materials. In terms of the frequency of tumors, 51% (25 cases) GBM, 14.2% (7 cases) anaplastic astrocytoma, 10.2% (5 cases) astrocytoma, 8.1% (4 cases) gliosarcoma, 4.08% (2 cases) anaplastic oligoastrocytoma, 4.08% (2 cases) pilocytic astrocytoma, 4.08% (2 cases) oligoastrocytoma, 2% (1 case oligodendroglioma and 2% (1 case) papillary ependymoma were diagnosed (Table 1). Of these patients, 36 (73.4%) with malignant formation received radiotherapy and chemotherapy. Optimal dose of 60 Gy was given to tumor site as standard in radiotherapy. Also, temozolomide (TMZ) was given simultaneously.

Postoperative radiotherapy and adjuvant therapy (Temozolomide) were administered to all malignant glial tumors. Temozolomide was given at 75 mg/m^2 for 5/28 days. For the 200-2250 mg/mq RT plan, both computed tomography (CT) scan and MRI were used to determine tumor and residual amount after surgery.

Total resection (TR) was performed in 30 patients who underwent surgical operation with the diagnosis of glial tumor and 22 were still alive. 11 of them who underwent total resection were diagnosed GBM, and 6 survived. The average surveys were 13.6 (6-32 months) months. 4 of 6 patients with anaplastic astrocytoma survived and the mean survey was 26.5 (4-45) months. All 2 patients with anaplastic oligoastrocytoma continue to live. 10 patients had low grade glial tumors.

Subtotal resection (STR) was performed in 19 cases. The average survey of patients with GBM was 6.9 months (4-11) months. The survey of this group was significantly shorter than the other TR group ($p<0.005$). In 8 cases with TR, who died, we observe that the survey was longer than the cases with STR (Fig. 2).

Table 1. Demographic distribution of patients operated with glial tumor diagnosis

Demographic distribution of patients with glial tumors								
Tumors	**Number of patients, n (%)**	**Age (mean)**	**Sex**		**Location of tumor**			
			Male	**Female**	**Temporal**	**Frontal**	**Parietal**	**Occipital**
GBM	25 (51)	66.2	16	9	10	8	5	1
Astrocytoma	5 (10.2)	57.2	4	1	1	4	-	-
Anaplastic Astrocytoma	7 (14.2)	61.5	5	2	1	2	2	2
Pilocytic Astrocytoma	2 (4.08)	43	1	1	-	1	-	1
Oligoastrocytoma	2 (4.08)	38.5	0	2	-	2	-	-
Anaplastic Oligoastrocytoma	2 (4.08)	38.2	1	1	-	1	-	1
Gliosarcoma	4 (8.1)	72.2	3	1	1	2	1	-
Oligodendroglioma	1 (2)	41	1	0	-	1	-	-
Ependymoma	1 (2)	29	0	1	1	-	-	-

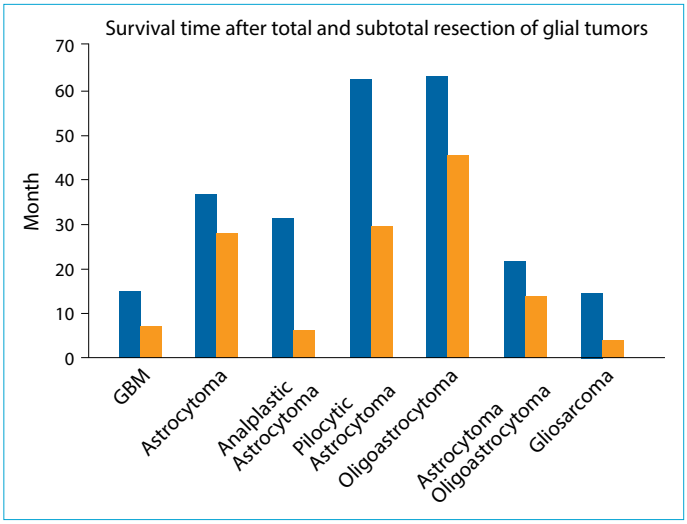

Figure 2. Survival relationship in total and subtotal excised cases according to tumor pathological diagnoses.

Discussion

The most common types of primary intracranial tumors are glial tumors, astrocytoma, oligodendrogliomas and ependymomas. Among these glial tumors with distinct heterogeneity, which may develop from different cell types, glioblastoma multiforme constitutes the most common, aggressive and mortal subgroup.[1] In contrast to previous classifications, the World Health Organization (WHO) classified central nervous system tumors according to their epigenetic and genetic characteristics in 2016.[13] In this classification, the coding of oligodendroglioma, mutation in astrocytoma, histopathological evaluation, pleomorphism, nuclear atypia, intense mitotic activity, necrosis and microvascular proliferation for GBM are identified.[14]

Glial tumors are treated with a multidisciplinary team approach including specialists in brain surgery, radiology, pathology, radiation oncology and medical oncology. Surgery is one of the main treatment options. However, the effect of the degree of resection on prognosis is still uncertain. The aim of glial tumor surgery is to remove tumor tissue at the highest possible volume without causing morbidity and to provide more benefit from adjuvant chemoradiotherapy to be applied to the patient.[15] The previous studies show that minimizing the postoperative tumor volume both supports healing and prolongs the average survival. Total resection has been reported to increase survival by 2-8 months compared to subtotal resection (50-98%).[11, 15, 16]

Mc Girit et al.[17] Have shown that TR has a better survival in 451 newly diagnosed GBM patients than in patients with STR. The mean survival for TR, near total resection and STR patients was found to be 13, 11, and 8 months, respectively. It is possible to measure residual volume rates after surgery and compare survival times. Lacroix et al.[18] found a 98% resection needed for higher survival. Average survival for resection more than 98% was found 13.3 months, while lesser was 8.8 months. Orringer et al.[19] found in their GBM study with 46-case, 1-year survival was associated with patients with more than 90% resection. Since resection cannot be performed safely in deeply located tumors, these studies are still limited, although guiding the relationship between wide resection and survival. For instance, deep-located tumor rates were reported by Sanai and Orringer as 69% and 39%, respectively. These deep-located tumors make it difficult to determine whether more extensive resection is independently associated with long-term survival.[20]

However, regardless of the residual tumor volume and the amount of tumor resection, each is independently associated with long-term survival and delayed recurrence. This reduction in residual tumor volume may increase the effectiveness of adjuvant therapies.[21–23] Passina et al. confirmed the hypothesis that the residual tumor volume of 3 cm3 and below should be considered as affecting the survival of the tumor.[24]

Conclusion

In conclusion, surgical intervention is one of the first options in the treatment of glial tumors. Adjuvant chemotherapy and radiotherapy should be planned according to the morphological diagnosis of the tumor. Total removal of the tumor or small amount of residual tumor volume positively affects survival. During tumor surgery, it is crucial that the tumor is resected in total or subtotal with minimal morbidity.

Disclosures

Ethics Committee Approval: The Ethics Committee of Eskisehir Osmangazi University provided the ethics committee approval for this study (June 2, 2019, 25403353.050.99-E.76044).

Peer-review: Externally peer-reviewed.

Conflict of Interest: None declared.

Authorship Contributions: Concept – S.E., E.B.B.; Design – Z.S.A., F.A.; Supervision – E.B.B., F.A.; Materials – Z.S.A., S.E.; Data collection &/or processing – Z.S.A., F.A.; Analysis and/or interpretation – E.B.B., S.E.; Literature search – Z.S.A., F.A.; Writing – S.E., E.B.B.; Critical review – Z.S.A., F.A.

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