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Evaluation of the Efficiency of Neuronavigation in Patients with Glioblastoma

Bülent Gülensoy [1](ID)

[1]Department of Neurosurgery, Lokman Hekim University School of Medicine, Ankara, Turkey.

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Abstract

Objective: To investigate the effect of neuronavigation use on mortality in patients with glioblastoma.

Methods: For each of the 26 patients that underwent neuronavigation-assisted supratotal resection for glioblastoma between 2018 and 2020, one patient that underwent supratotal resection without navigation was selected.

Results: Radiographic radicality was observed in 35% of the cases in the neuronavigation-assisted surgery group and 29% of those in the conventional surgery group. Absolute and relative residual tumor volumes were significantly lower in the neuronavigation-assisted surgery group. Radical tumor resection was associated with a very significant increase in survival. There was no significant difference in the survival rates between the patients that underwent surgery with and without neuronavigation. This was attributed to the small number of participants and supratotal resection being performed in all statistically determined patients The low median survival period of glioblastoma may have also contributed to this finding.

Conclusions: Surgery plays an important role in the treatment of glioblastoma. A combination of techniques including intraoperative magnetic resonance imaging, neuronavigation, ultrasound, and fluorescence guidance allows for safe and maximum surgical resection, leading to better outcomes in terms of survival and postoperative functional recovery. However, despite maximal surgical resection and adjuvant chemotherapy-radiotherapy, most cases develop tumor recurrence within 10 months, which is considered to be due to established cancer stem cells. Therefore, there is an urgent need to develop more effective treatment strategies for glioblastoma.

Key words: Neuronavigation, Glioblastoma, Supratotal resection, Mortality

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Address for correspondence/reprints:

Bülent Gülensoy

Telephone number: +90 (312) 589 86 50

E-mail: bulentgulensoy@hotmail.com

INTRODUCTION

Gliomas are the most common tumors of the central nervous system (CNS). Glial cells in CNS are composed of oligodendrocytes, astrocytes, and microglia (1,2). There are three different types of gliomas, namely ependymomas originating from glial cells in the epithelial tissue of the brain and spinal cord, oligodendrogliomas originating from oligodendrocytes, and astrocytomas originating from astrocytes (3,4). GBM is the most aggressive intracranial malignancy due to the rapid growth, inevitable recurrence, and high mortality associated with these tumors (4). Among these tumors, astrocytomas are the most common gliomas in pediatric, adolescent, and adult patients. In adults, grade IV astrocytoma or glioblastoma multiforme (GBM) accounts for approximately 15.6% of all brain tumors and 45.2% of all primary malignant brain tumors (5). GBM is the most aggressive, highly malignant tumor of the astrocytic tumor type and usually diagnosed in elderly patients (median age at diagnosis: ≥65 years) (6).

Only a small portion of cases achieve long-term survival after surgical resection and chemotherapy-radiotherapy. In patients diagnosed with GBM, the median survival is approximately 12 to 15 months (7). Despite decades of research to improve patient outcomes, GBM is still a type of tumor that is incurable and very difficult to treat. Younger age, better performance status and higher resection grade are universally considered to be the predictors of better survival in GBM. One of the challenges in GBM treatment concerns the aggressive growth characteristics of tumors. The complete surgical resection of these tumors is not possible due to their infiltrative growth and microscopic spread, and the presence of multiple lesions. Therefore, there is a pressing need for new and effective GBM therapy.

Depending on the type of intracranial lesion, pathology, and surgical approach, some craniotomy procedures can be assisted with neuronavigation based on magnetic resonance imaging or computed tomographic scans to adapt the procedure to the size of the tumor using the smallest incision possible. Neuronavigation is a modern computerized technology that can help surgeons locate a pathology more precisely by combining a series of craniofacial points in patients. Neuronavigation provides better guidance, orientation, and localization. It also offers a higher level of confidence for the surgeon and better outcomes for the patient (8).

METHODS

For each of the 26 patients that underwent neuronavigation-assisted supratotal resection for glioblastoma between 2018 and 2020, one patient who underwent supratotal resection without neuronavigation was selected. The files of a total of 52 patients (37 male, 15 female) aged 29 to 89 years were retrospectively reviewed. The patients' demographic information (age, gender), pathology results, preoperative and follow-up magnetic resonance imaging (MRI) findings, and one-year follow-up results were recorded. The evaluation of the integrity of tumor resection, including volumetric analysis was performed with MRI in the early postoperative period. Recurrence and survival times were obtained for all the patients. The results were statistically analyzed using SSPI.

Statistical Analysis

Statistical analysis was performed by Statistical Package for Social Sciences (SPSS) 16.0 software. The results were given as means and standard deviations. Non-parametric tests, including the Mann-Whitney U test, Fisher's exact test, chi-square test, and Kruskal-Wallis test, were used to compare the groups. Since the p-value was greater than 0.05, it was not considered significant.

RESULTS

The mean operative times were similar in the two groups, but the mean preparation time was 30 minutes longer in the navigation-assisted surgery group. Radiological radicality was detected in 35% of the cases in the neuronavigation-assisted surgery group and 29% of those in the conventional surgery group.

Table 1. Results of the chi-square test

	Value	Df	Asymp. Sig. (two-tailed)	Tam Sig. (two-tailed)	Tam Sig. (one-tailed)
Pearson chi-square median	.171[a]]	1	.679		
Continuity	.005	1	.941		
Probability ratio	.171	1	.679		
Fisher's exact test				.743	.470
Number of patients	52				

[a]0 cells (0.0%) have an expected count of less than 5.]The minimum expected number is 5.39
[b]Only calculated for the 2x2 table

Absolute and relative residual tumor volumes were significantly lower in the neuronavigation-assisted surgery group. Radical tumor resection was associated with a very significant increase in survival. There was no significant difference in the survival rates of the patients that underwent surgery with and without neuronavigation. This was attributed to the small number of individuals participating in the study and supratotal resection being performed in all the patients during surgery. In addition, the low median survival time of patients with glioblastoma may have contributed to this finding (Table 1).

DISCUSSION

The current gold standard of treatment for GBM is surgical resection followed by adjuvant chemotherapy and radiotherapy. Given the poor prognosis of GBM, the surgical removal of the tumor mass is often performed to reduce the tumor burden and increase survival. It is necessary for neurosurgeons to evaluate the size and location of the tumor and the patient's functional status to determine the extent of resection (EOR) that prolongs overall survival (OS), improves the quality of life, and preserves neurological function (9). Neurosurgical options for GBM include biopsy, gross total resection (GTR), or subtotal resection (STR). GTR is defined as the maximum removal of the tumor observed on MRI. In contrast, STR refers to the removal of only a portion of the tumor, and therefore residual tumor lesions are seen on postoperative images. Han et al. showed that GTR significantly improved progression-free survival (PFS) and OS compared to STR in patients with GBM (10,11).

In recent studies, neuronavigation has been reported to help the surgeon orientate through adequate application accuracy. It facilitates the precise planning of craniotomy and the surgical vector in targeted small subcortical lesions and helps define the boundaries of the tumor and resection (12).

However, multiple tumor lesions, bilateral tumor involvement, and large-volume tumors pose clinical challenges and risks for total resection (13). STR is used as an alternative surgical approach because it is not clinically feasible. Although maximal surgical resection has been shown to improve the OS and quality of life of patients, recurrence is still inevitable.

Since the actual surgical position is related to preoperative images, a gradual recording error may be seen during intraoperative navigation due to brain shift. This situation may be further complicated by cerebral blood volume, the use of mechanical ventilators or diuretics, or retraction during surgery. Dorward et al. measured brain shift during open cranial surgery to assess the effect of post-imaging brain distortion on neuronavigation and reported a mean shift of 4.6 mm in the cortical surface after dural patency and 6.7 mm at the completion of tumor resection. This suggests that the use of more advanced navigation systems that calculate this shifting effect will make resection safer in the future.

However, there are still some uncertainties limiting the integration of augmented reality (AR) into daily practice. Currently, there is no prospective study showing a significant difference between AR-assisted and navigation-assisted procedures in terms of morbidity, mortality, and clinical efficacy.

In a study summarizing the cases in which navigation was used during various neurosurgery operations between 1996 and 2015, the rate of patients with glioblastoma was reported to be 7.17% (Table 2). This indicates that neuronavigation is used more in patients with glioblastoma than in those with other tumor types.

Table 2: Neurosurgical lesions treated with the aid of Augmented Reality

Pathology	# Lesions	% Lesions
Neoplastic lesions	**75**	**38.46**
Glioma/GBL* supratentorial	14	7.17
Glioma/GBL* infratentorial	0	0
Meningioma/supratentorial	12	6.15
Meningioma/infratentorial-skull base	7	3.58
Pituitary adenoma	12	6.15
Metastasis	11	5.64
Schwannoma, vestibular	2	1.02
Ependymoma	1	0.51
Oligodendroglioma	1	0.51
Hemangioblastoma	1	0.51
Neuroepitelial tumors	1	0.51
Other neoplastic lesions	13	6.66
Vascular lesions	**77**	**39.48**
Aneurysm ant.circul.	39	20.00
post.circul.	4	2.05
Cavernoma	20	10.25
AVM	8	4.10
Moya-Moya disease (by-pass)	3	1.53
Stroke	2	1.02
Arterial dissection (By-pass)	1	0.51
Non-neoplastic, non vascular	**1**	**0.51**
Hydrocephalus	1	0.51
Undetermined	**42**	**21.53**
Epileptogenic lesions	40	20.51
Others	2	1.02
Total	**195**	**100**

* (14)

Glioblastoma can occur in different places and in patients of different ages. For tumors located in the brainstem or adherent to supratentorial functional regions, the goal of surgery should be to maximize tumor resection while preserving important neurological functions. Therefore, it is essential to separate the tumor margin from the surrounding normal tissue for the safe removal of the lesion.

Glioblastoma surgery means striking a balance between maximizing the extent of resection and preventing postoperative neurological complications. Various surgical techniques and adjuvants can be used to identify areas of the brain that are significant either to detect tumor tissue (residual) and increase EOR (reduce residual volume) or maintain functionality. In recent years, considerable progress has been made for both ends, with numerous scientific efforts. Neurosurgeons can choose their preferred preoperative and intraoperative modalities from a wide variety of possibilities. Different modalities may be used for the same purpose, often with comparable results or without strong, prospective evidence for one modality in particular. The clinical impact for some of these modalities and patient subgroups is not always based on high-level evidence. Thus, rather large prospective studies, such as RCTs or multicenter cohort studies, are needed to compare various modalities in a multimodal setting to determine which modality is most appropriate for which patient (grade, location, etc.).

CONCLUSION

The small number of patients is a limitation of our study. The effectiveness of neuronavigation can be better evaluated in a study to be conducted with a larger number of patients. In addition, the contribution of neuronavigation to radical resection and reduction of recurrence rates in deeply located tumors present as important topics of research.

In this study, some applications, and limitations of neuronavigation were reviewed. Advances in technology will increase the cost-benefit ratio and user-friendliness of the system and may help achieve the goal of complete cytoreductive surgery with minimal morbidity in the near future. However, considering the current state of knowledge, neuronavigation can only assist surgeons and cannot replace their experience and knowledge in neuroanatomy.

Since first developed and reported by Roberts et al. in 1986, neuronavigation has been frequently used during brain tumor resection surgery. One of the advantages of neuronavigation over glioma surgery is that it provides assistance in preoperative planning, allowing neurosurgeons to identify nuclei and white matter fibers that are not visible under a microscope, thus leading to better neurological outcomes. However, neuronavigation also has the primary disadvantage of brain shift.

In older series, it was reported that this shift was more than 10 mm (15). The range of system errors can be reduced through upgraded navigation equipment.

Recent studies have shown that neuronavigation is more effective when combined with sodium fluorescein.

Surgery plays an important role in the treatment of glioblastoma. A combination of techniques including intraoperative MRI, neuronavigation, ultrasonography, and fluorescence guidance will allow for safe and maximum surgical resection, resulting in better outcomes in terms of survival and postoperative functional recovery. However, despite maximal surgical resection and adjuvant chemotherapy-radiotherapy, tumor recurrence occurs in many cases within 10 months, which is due to established cancer stem cells. Therefore, there is a compelling need for the development of more effective treatment strategies for glioblastoma.

Ethics Committee Approval: This prospective study was approved by the ethical review committee of Lokman Hekim University Ethics Committee dated 18.10.2021 and numbered 2021/0127.

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