# Role of Glioblastoma Craniotomy Related to Patient Survival: A 10-Year Survey in a Tertiary Care Hospital in Pakistan

Saman Shahid[1] Kamran Hussain[2]

[1] Department of Sciences and Humanities, National University of Computer and Emerging Sciences (NUCES), Foundation for Advancement of Science and Technology (FAST), Lahore, Pakistan
[2] Department of Neurosurgery, Federal Post Graduate Medical Institute, Shaikh Zayed Hospital, Lahore, Pakistan

**Address for correspondence** Saman Shahid, PhD, Department of Sciences and Humanities, National University of Computer and Emerging Sciences (NUCES) Foundation for Advancement of Science and Technology (FAST), Faisal Town, Lahore, Pakistan (e-mail: saman.shahid@gmail.com).

J Neurol Surg B 2017;78:132–138.

**Abstract**

A total of 270 glioblastoma patients were treated for tumor resection during 2004 to 2014. The following variables were examined: patient age group (PAG) and percent of the extent of resection (EOR) in four types of resections: gross total resection (GTR), subtotal resection (STR), partial resection (PR), and biopsy/decompression (BD). The Karnofsky performance scale (KPS) was used and the average survival time noted. The least survival time (7 months) was noticed in the patient age group 18 to 35 years with biopsy only, whereas, the maximum survival time (14.5 months) was noted with the patient age group 54 to 71 years by gross tumor resection. The largest number of ($n = 76$) patients had PR (80%) and these patients had an average survival time of 10.5 months. Total 190 patients out of 270, with EOR (100–80%) had a KPS score "0" (80 and above) and total 80 patients out of 270 patients, with EOR (50%) had a KPS score "1" (below 80). The correlation was statistically significant at ($p < 0.050$) for EOR (%) and KPS score (0/1) only. Correlation analysis showed that the maximum resection has a strong impact on the glioblastoma patient's survival. A lesser EOR correlated with poor quality of life and also a decreased survival of patients.

**Keywords**
- glioblastoma
- craniotomy
- patient survival
- extent of resection
- quality of life

## Introduction

Glioblastoma (the World Health Organization [WHO] grade IV) is the most common primary brain tumor. The standard treatment of glioblastoma involves surgical excision followed by radiation treatment. Malignant gliomas have an extremely poor prognosis in spite of surgery, radiotherapy, and chemotherapy. Aggressive surgical resection of malignant gliomas in neurosurgery is an issue, which has been debated. But recently, it is observed that the survival time in such patients has modestly increased because of advances in surgical and intraoperative imaging techniques.[1] To improve prognosis, the extent of resection (EOR) is an important factor in glioblastoma patients' survival assessment.[2,3] We operated on a total of 270 patients with glioblastoma in a period from 2004 to 2014 at a tertiary care hospital in Lahore, Pakistan. Here, we emphasized the EOR (%) and its bearing on patients' average survival time (AST). We analyzed glioblastoma craniotomy related to patient survival in our hospital with a discussion of previous studies.

Glioblastoma has a 5-year survival rate of less than 5%[3] with an incidence of 5 to 10 per 100,000[4] which accounts for approximately 2% of all cancer morbidity.[1,5,6] The median survival time is approximately 10 to 12 months or in some cases, it is up to 14 months.[1,4] These glioma tumors are considered to arise from glial, stem, or neuronal precursor cells.[1,7] Malignant gliomas show a diffuse infiltration and a high proliferation index.[1] Glioblastoma has a characteristic

**received**
April 7, 2016
**accepted after revision**
August 22, 2016
**published online**
October 10, 2016



**DOI** http://dx.doi.org/10.1055/s-0036-1593469.
**ISSN** 2193-6331.

rapid growth and infiltration properties, hence complete resection is near impossible due to its tissue infiltration. Craniotomy of a brain tumor with maximum EOR (%) is a good treatment to prolong a patient's survival time with an improved neurological status.[8] The goal of surgery is to establish a diagnosis of the lesion, reduction of mass effect, and to get a better response of adjuvant therapy such as radiation. Greater EOR gives a proportional improvement in medical outcome and reduction of morbidity.[9] Intraoperative techniques such as computed tomography (CT), ultrasound, 5-aminolevulinic acid fluorescence, and intraoperative magnetic resonance imaging (MRI) are in use to improve the percentage of EOR.[10] Recurrence is generally quick and there are limited studies regarding recurrent excisions and their effect on survival.

Being a very aggressive tumor, the cells of glioblastoma invade local tissues beyond the detectable reach of the radiographic imaging techniques.[10,11] The microscopic invasion makes curative surgical resection almost impossible and recurrence is almost inevitable, even though postoperative imaging may suggest a complete resection of the tumor.[11,12] Patients with glioblastoma usually fall prey to relapses and recurrences; hence, the idea of repeated resections is often not embraced by many surgeons. A study, however, showed the significant prolongation of survival in patients who underwent resections more than four times for glioblastomas, but this was independent of the age of the patient or functional status. Repeated resections did not increase the morbidity of the patients.[13] Although, a poor evidence available about the relationship between resection extent and mean survival times[11,13,14]; any surgery with 98% or greater resection and preservation of normal parenchyma along with neurological function was shown to have a greater improvement in the survival of the patients.[10]

## Patients and Methods

### Patient Admission and Surgery

Total 270 histologically confirmed glioblastoma patients (►**Fig. 1**) were treated during the years 2004 to 2014 at the Neurosurgical Unit of Shaikh Zayed Hospital, Lahore, Pakistan. The demographic data on the patients were collected on a designated proforma. Brain tumor grades were identified according to the WHO classification system. Glioblastoma patients' tumors either had a burr-hole biopsy (freehand or with stereotaxy) or craniotomy and excision/biopsy with and without stereotaxy. Tumors considered suitable for either gross total resection (GTR), subtotal resection (STR), partial resection (PR), or biopsy/decompression (BD) was decided on preoperative imaging by the neurosurgeons. Patients were screened through an outpatient clinic or emergency department of the hospital and admitted on the basis of neurosurgical indications or from workup of a diagnosis. After a careful history and examination, probable patients were admitted for imaging and other laboratory tests. Once the patients were admitted, a steroid therapy (dexamethasone 4 mg intravenously 6 hourly) and other medications were prescribed for symptomatic relief. Neuro-

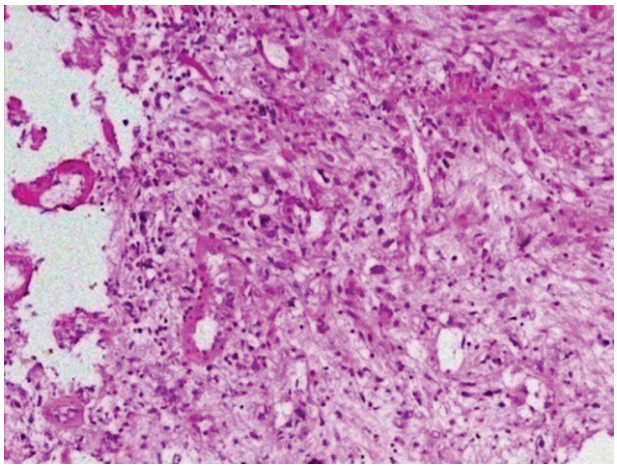

**Fig. 1** Glioblastoma-WHO grade IV. (Photo Magnification: ×20). WHO, World Health Organization.

navigation was used in most cases for the biopsy and excision of the lesions to help in aggressive resection, if so desired. A piecemeal excision of the tumor is generally preferred by the primary surgeon with an internal cavitation of the lesion being done first, and the excision being extended to the periphery of the lesion until normal tissue (►**Fig. 2**). Excision may be stopped before a complete macroscopic removal if deemed too near vital areas by the surgeon intraoperatively or in case of adverse events, such as excessive bleeding. Once the tumor margins are excised, the extent of excision again checked using image-guided surgery (IGS) probe. This prohibits the surgeon from damaging any surrounding normal brain tissue and this is the benefit of using IGS. A postoperative CT scan with contrast is done to see the EOR, bleeding, or any other abnormal development in the brain within 24 to 48 hours.

### Statistical Analysis

A bivariate linear correlation was conducted to see the correlation between average survival time (AST) in months by the following predictors: patient age group (PAG), EOR %

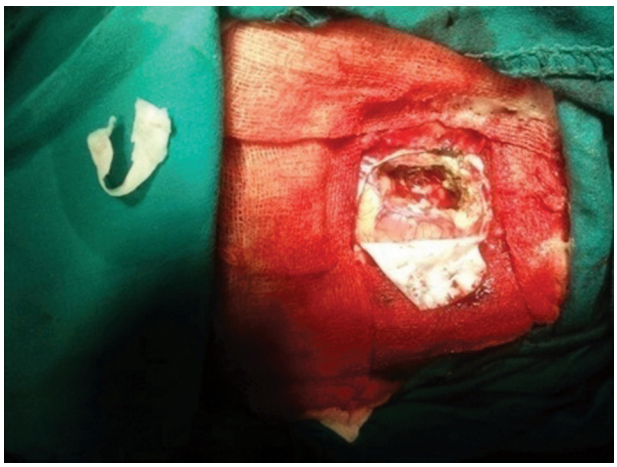

**Fig. 2** Craniotomy for excision glioblastoma of frontal lobe.

and Karnofsky performance status (KPS) scale.[15,16] The *r*-values (Pearson coefficients) were obtained and analyzed to observe the strength and direction (±) of the correlation. The *p*-values obtained were checked for the significance or non-significance of AST with the independent/predictor parameters, that is, PAG, EOR (%), and KPS score. A score of "0" was assigned to those patients who had KPS of equal to or greater than 80, whereas, a score of "1" was assigned to those patients who had KPS less than 80. The KPS scale and corresponding scores have been assigned to quantify patients' quality of life (QOL).

Further, linear regression analyses were performed and R (square) (coefficient of determination) values were observed for the analysis of the preparation of variance in the dependent variable (AST), which can be subjected to be predicted from statistically significant independent variables: EOR (%) and KPS. The measure of the strength of AST's association was analyzed with statistically significant independent variables: EOR (%) and KPS. Further, R (square) values, model's coefficients, and *p*-values analyzed to estimate AST. Finally, regression equations were developed between independent variables (EOR and KPS) and the dependent variable (AST).

## Results

### Patients' Information and Histopathology

Total 270 glioblastoma patients were treated for the tumor resection during the years 2004 to 2014 with a follow-up of 2 years at the neurosurgical department of the Shaikh Zayed Hospital, Lahore, Pakistan. ►**Fig. 1** shows WHO grade IV glioblastoma. This represents high endothelial proliferation with necrosis and cellular mitosis.[17] The pattern shows high endothelial proliferation with a showing of necrosis and cellular mitosis.[17] ►**Fig. 2** shows the craniotomy for glioblastoma excision of the frontal lobe. There were 50 patients whose tumor was less than 2 cm, 150 patients' tumor was 2 to 4 cm, and there were 70 patients whose tumor was greater than 4 cm. ►**Fig. 3** shows the preoperative localization of tumor. ►**Fig. 4a–c** shows CT and MRI of glioblastoma. The MRI postoperative scan (►**Fig. 5**) showing residual tumor with surrounding edema and areas of infarcts. Decompression has somewhat restored the ipsilateral ventricle. ►**Figs. 5** and **6** are postoperative scans of the excised tumor showing areas of infarcts and edema and some reversal of left lateral ventricular horn (►**Fig. 5**).

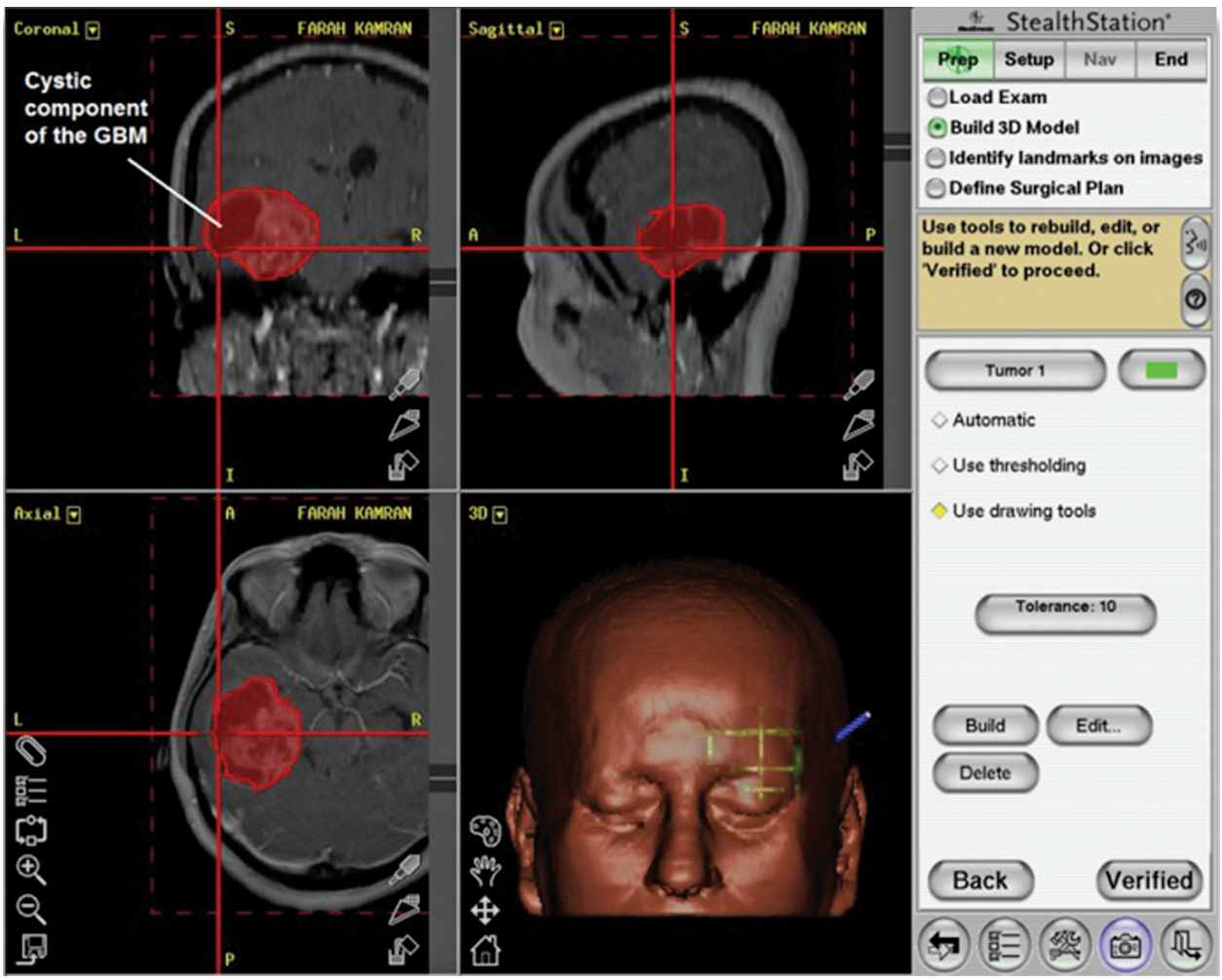


**Fig. 3** Tumor as localized on IGS (preoperative) probe. IGS, image-guided surgery.

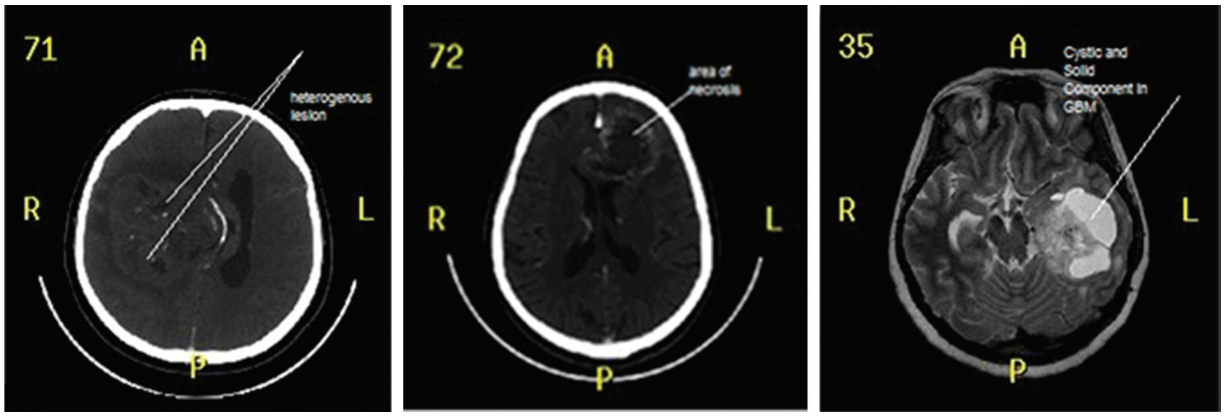


**Fig. 4** (**A–C**) Various preoperative glioblastoma images, (**C**) preoperative MRI showing a glioblastoma. MRI, magnetic resonance imaging.

### Number of Resections, Radiotherapy, and Chemotherapy Status

The 2% of the glioblastoma patients' tumors were resected three times and 15% of tumors were resected twice. The 95% patients had fractioned radiation with a dose of 60 Gy. Total 130 patients had a craniotomy and excision/biopsy of gliomas without stereotaxy, while 92 patients had a stereotactic craniotomy with excision or biopsy. The 42 patients had a free hand burr-hole biopsy and 6 patients had a frontal or temporal lobectomy. Patients were followed up for 2 years at 6-month intervals with clinical evaluation (KPS scale). Only 20% of these patients also received adjuvant therapy with temozolomide which is a standard effective chemotherapy and the average survival increased from 4 to 7 months in glioblastoma patients.

### Statistical Inferences

►**Table 1** shows the number of patients resected for a respective surgery procedure. ►**Table 2** shows the glioblastoma PAG, EORs, that is, GTR, STR, PR, and BD and respective patients' AST. The neurosurgical record shows that 10% of glioblastoma patients were from the age group 18 to 35 years, 20% were from the age group 36 to 53 years, and 70% were from the age group 54 to 71 years. The least survival time (7 months) has been noticed in the PAG 18 to 35 years by BD resection, whereas, the maximum survival time (14.5 months) has been noticed by the PAG 54 to 71 years by GTR. Maximum number ($n = 76$) of patients had been resected with PR, having AST of 10.5 months. A second maximum number ($n = 56$) of patients has been treated with BD and they were having the AST of 8 months. Total 190 patients

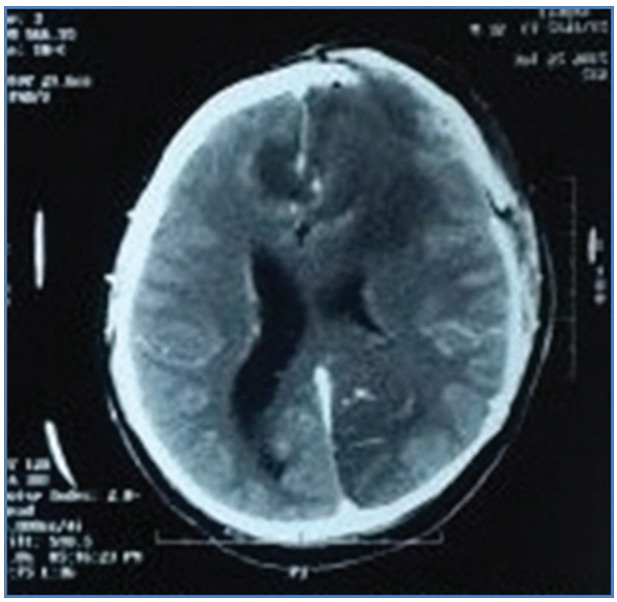

**Fig. 5** Contrasted postoperative axial CT image showing residual tumor and an occipital infarct. CT, computed tomography.

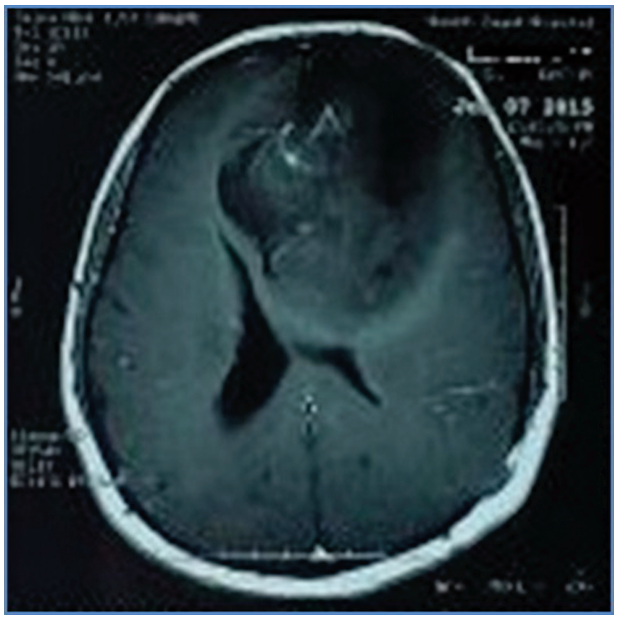

**Fig. 6** T1-weighted contrasted axial MRI scan showing a large heterogeneous left frontal glioma with contrast enhancement, significant mass effect, and invasion across midline. MRI, magnetic resonance imaging.

**Table 1** Surgical procedures performed for 270 glioblastoma patients

| Number of glioblastoma patients (*N*) | Surgical procedure performed |
|---|---|
| 130 | Craniotomy and excision/biopsy of gliomas without stereotaxy |
| 92 | Stereotactic craniotomy and excision/biopsy of all brain tumors |
| 42 | Free hand craniotomy/burr hole biopsy |
| 6 | Craniotomy and frontal/temporal lobectomy |

out of 270, with EOR (100–80%) had a KPS score "0" (80 and above) and total 80 patients out of 270 patients, with EOR (50%) had had a KPS score "1" (below 80).

►**Table 3** shows a correlation analysis between patients' AST in months with the EOR (50–100%), PAG in years, and KPS score. Correlation analysis was performed for the AST to see the strength of association with patients' age groups, EOR done and KPS score. The correlation is statistically significant at ($p < 0.050$) for EOR (%) and KPS score (0/1). The correlation is nonsignificant for a PAG ($p > 0.050$). It is observed that EOR (50–100%) has a positive strong relationship with the patients' AST (months); whereas, KPS has a strong negative relationship with the patients' AST (months). It means that maximum resection has a strong impact on the glioblastoma patient's survival; whereas a lesser EOR (%) correlated with poor QOL, leading a decreased survival of patients.

Two regression models were developed to estimate the effect of an independent variable AST (months) on respective two independent parameters, that is, EOR (%) and KPS score, which were found statistically significant in the correlation analysis. ►**Table 4** shows two regression models for the statistically significant predictors (EOR and KPS score) and related statistics. For every unit increase in EOR (%) there is a 0.113 unit increase in an AST of a patient and for every unit decrease in KPS score, there is a 3.811 increase in AST for a patient. The regression equations are as follows:

$$Y\,(AST) = 2.102 + (0.113)\,x_1$$
$$Y\,(AST) = 11.831 + (-3.811)\,x_2;\ \text{where}$$

$x_1$ is EOR (%) and $x_2$ is KPS

## Discussion

Glioblastoma is the most common and aggressive primary brain tumor, which is prone to recur.[13–15] Malignant glioblastoma (WHO grade IV) represents one of the most calamitous diseases. It appears to be a common sense that increasing resection would benefit patient survival. While this is established that for a total or near-total resection of less than 80% has not been correlated with a progressively decreasing survival. This study has analyzed the role of maximum surgical resection of malignant gliomas. Studies have found that a tumor resection of 98% or more is an independent variable correlated with longer survival in glioblastoma patients.[16,17] There is a debate in the neurosurgery related to the efficacy of maximum resection of malignant gliomas, because malignant gliomas are invasive to the surrounding tissues of the brain, therefore, sometimes wide resections are not possible because of the close vicinity of eloquent areas of the brain. Some prospective studies are also available that have reported a favorable relationship between the EOR of gliomas and survival time.[18] It was identified that a maximum resection has a strong association with the glioblastoma patient's survival. Studies[19,20] have shown that patients, whose brain tumors had previously been resected completely, acquired greater benefit from temozolomide as part of the adjuvant treatment, compared with those patients whose

**Table 2** Patients' ($n = 270$) average survival time with the respective extent of resection (EOR %)

| PAG | Number of glioblastoma patients (*N*) | GTR EOR = 100% | STR EOR = 90% | PR EOR = 80% | BD EOR = 50% |
|---|---|---|---|---|---|
| 18–35 (10%) | 27 | 5[a] (13 mo) | 3 (12 mo) | 11 (10 mo) | 8 (7 mo) |
| 36–53 (20%) | 54 | 11 (13.5 mo) | 5 (10 mo) | 22 (12 mo) | 16 (8.5 mo) |
| 54–71 (70%) | 189 | 38 (14.5 mo) | 19 (12 mo) | 76 (10.5 mo) | 56 (8 mo) |

Abbreviations: BD, biopsy/decompression; EOR, extent of resection; GTR, gross total resection; mo, months; PAG, patients' age group; PR, partial resection; STR, subtotal resection.
[a]Number of patients.
Note: The average survival time is mentioned within the parenthesis.

**Table 3** Correlation analysis between patients' average survival time in months with the EOR (50–100%), PAG in years, and KPS score

| | | PAG (y) | EOR (%) | KPS |
|---|---|---|---|---|
| AST (mo) | Pearson correlation | $r = 0.025$ | 0.941[a] | −0.778[a] |
| | $p$ Value ($< 0.050$) | 0.685 | 0.000 | 0.000 |

Abbreviations: EOR, extent of resection; KPS, Karnofsky performance scale; PAG, patients' age group.
[a]Correlation is significant at the 0.050 level (two-tailed).

**Table 4** Regression analyses between two statistically significant ($p < 0.050$) predictors: EOR, KPS (score), and AST

| Regression analysis of AST (mo) and EOR (%) | | | | | |
|---|---|---|---|---|---|
| Model | Coefficients | | | *t* | *p* Value (< 0.05) |
| | Unstandardized coefficients | | Standardized coefficients | | |
| | | Standard error | Beta | | |
| Constant (%) | 2.102 | 0.195 | 0.941 | 10.752 | 0.000 |
| | 0.113 | 0.002 | | 45.415 | 0.000 |
| **Model summary** | | | | | |
| Model | *r* | $r^2$ | Adjusted $r^2$ | Standard error of the estimate | |
| | 0.941[a] | 0.885 | 0.885 | 0.75566 | |
| **Regression analysis of AST (mo) and KPS Score** | | | | | |
| Model | Coefficients | | | *t* | *p* Value (< 0.05) |
| | Unstandardized Coefficients | | Standardized Coefficients | | |
| | | Standard error | Beta | | |
| Constant | 11.831 | 0.101 | −0.778 | 117.128 | 0.000 |
| | −3.811 | 0.188 | | −20.282 | 0.000 |
| **Model summary** | | | | | |
| Model | *r* | $r^2$ | Adjusted $r^2$ | Standard error of the estimate | |
| | 0.778[b] | 0.606 | 0.604 | 1.39959 | |

Abbreviations: AST, average survival time; EOR, extent of resection; KPS, Karnofsky performance scale.
Note: Coefficients: Dependent variable, AST.
[a]Predictors: Constant (%).
[b]Predictors: Constant.

tumor resection was less. In the current study, only 20% of patients were treated with temozolomide due to cost and affordability reasons. If all glioblastoma patients had been receiving temozolomide therapy then survival time would have been increased 3 to 7 months on average. For a multiplicity of reasons, only 20% of glioblastoma patients achieved a complete resection of the tumor.[20,21]

A retrospective study was conducted on anaplastic astrocytomas and glioblastoma patients' with following parameters: location of the tumor, EOR, performance status, and radiotherapy treatments.[22] This study believed neurological improvements through radiotherapy and the researchers concluded that young age and a good performance (postoperative) status were linked with longer survival in anaplastic astrocytomas but not in glioblastomas.[22] In both, anaplastic astrocytomas and glioblastoma patients, an extensive surgery was associated with improved postoperative conditions.[22] Another previous study was conducted on glioblastoma patients and analyzed patient survival time with respect to some already known prognostic factors, including KPS, age, EOR, and site & size of the tumor.[23] The patients who underwent total resection had an average survival of 11.3 months as compared with those patients, who were treated only with a biopsy.[23] There is also a debate in literature as to whether overall patient survival can be prolonged if GTR is performed at the recurrence, regardless of the previous EOR, as some authors coming out in favor of reoperation.[2] Another study has also shown that patients with recurrent glioblastoma can have an improved life expectancy by repeated surgical resections.[13,14] It was reported that the sole potential adjustable risk factor is associated with a survival time of glioblastoma patient is EOR of the tumor. While there are other studies which demonstrated an association between GTR and a prolonged survival for glioblastoma. However, it is also known that GTR is not always possible. A maximal EOR and minimal residual volume were independently correlated with a prolonged survival time and a slowed tumor recurrence.[13,14] Several studies have favored a maximum EOR which is associated with longer survival.[10] A retrospective study of glioblastoma patients identified patients' age $< 60$ years and KPS score $\geq 70$ as significant positive prognostic factors.[24] Older patients with glioblastoma are considered to have poor prognoses and are therefore rarely treated with aggressive resection. Some neuro-oncologists favor aggressive surgery, which may protract survival time for older glioblastoma patients. Other studies report older patients with aggressive resection and tumor size larger than 4 cm may not be getting much benefit from aggressive surgery.[13,14] It was reported that survival has significantly been improved to an EOR greater than 98%.[10] A study had identified that those patients whose tumors were resected experienced a median survival of 5.7 months, whereas, those patients who were treated with a needle biopsy, experienced 4 months of median survival time.[25]

## Concluding Remarks

Even with modern neurosurgical advances, the survival of glioblastoma patients has not improved significantly. Our observation regarding correlation with the survival time with EOR and KPS score is consistent with the international data on glioblastoma. The identification of these factors may provide an insight into which patients would benefit most from aggressive surgery.

Conflict of Interest
Authors report no conflict of interest.

Acknowledgment
We are thankful to Dr. Muhammad Abid (Shaikh Zayed Hospital, Lahore, Pakistan) and Dr. Nauman Ahmad (Shaikh Zayed Hospital, Lahore, Pakistan) who provided us all of the relevant data used in this study.

## References

1 Eyüpoglu IY, Buchfelder M, Savaskan NE. Surgical resection of malignant gliomas-role in optimizing patient outcome. Nat Rev Neurol 2013;9(3):141–151
2 Bloch O, Han SJ, Cha S, et al. Impact of extent of resection for recurrent glioblastoma on overall survival: clinical article. J Neurosurg 2012;117(6):1032–1038
3 Grabowski MM, Recinos PF, Nowacki AS, et al. Residual tumor volume versus extent of resection: predictors of survival after surgery for glioblastoma. J Neurosurg 2014;121(5):1115–1123
4 Hassaneen W, Levine NB, Suki D, et al. Multiple craniotomies in the management of multifocal and multicentric glioblastoma. Clinical article. J Neurosurg 2011;114(3):576–584
5 Ohgaki H, Kleihues P. Population-based studies on incidence, survival rates, and genetic alterations in astrocytic and oligodendroglial gliomas. J Neuropathol Exp Neurol 2005;64(6):479–489
6 Kohler BA, Ward E, McCarthy BJ, et al. Annual report to the nation on the status of cancer, 1975-2007, featuring tumors of the brain and other nervous system. J Natl Cancer Inst 2011;103(9):714–736
7 McLendon R, Friedman A, Bigner D, et al; Cancer Genome Atlas Research Network. Comprehensive genomic characterization defines human glioblastoma genes and core pathways. Nature 2008; 455(7216):1061–1068
8 Sawaya R, Hammoud M, Schoppa D, et al. Neurosurgical outcomes in a modern series of 400 craniotomies for treatment of parenchymal tumors. Neurosurgery 1998;42(5):1044–1055, discussion 1055–1056
9 American Association of Neuroscience Nurses. Guide to the care of the patients with craniotomy post-brain tumor resection. 2006. Available at: https://www.scribd.com/document/232382883/Guide-to-the-Care-of-the-Patient-With-Craniotomy-Post-Brain-Tumor-Resection. Accessed September 22, 2016
10 Kuhnt D, Becker A, Ganslandt O, Bauer M, Buchfelder M, Nimsky C. Correlation of the extent of tumor volume resection and patient survival in surgery of glioblastoma multiforme with high-field intraoperative MRI guidance. Neuro-oncol 2011;13(12): 1339–1348
11 Genc M, Zorlu AF, Atahan IL. Accelerated hyperfractionated radiotherapy in supratentorial malignant astrocytomas. Radiother Oncol 2000;56(2):233–238
12 McGirt MJ, Chaichana KL, Gathinji M, et al. Independent association of extent of resection with survival in patients with malignant brain astrocytoma. J Neurosurg 2009;110(1):156–162
13 Chaichana KL, Jusue-Torres I, Navarro-Ramirez R, et al. Establishing percent resection and residual volume thresholds affecting survival and recurrence for patients with newly diagnosed intracranial glioblastoma. Neuro-oncol 2014;16(1):113–122
14 Chaichana KL, Zadnik P, Weingart JD, et al. Multiple resections for patients with glioblastoma: prolonging survival. J Neurosurg 2013;118(4):812–820
15 Hentschel SJ, Sawaya R. Optimizing outcomes with maximal surgical resection of malignant gliomas. Cancer Contr 2003; 10(2):109–114
16 Lacroix M, Abi-Said D, Fourney DR, et al. A multivariate analysis of 416 patients with glioblastoma multiforme: prognosis, extent of resection, and survival. J Neurosurg 2001;95(2):190–198
17 Kumar V, Abbas AK, Fausto N, et al. Robbins and Cotran Pathologic Basis of Disease, Professional Edition: Expert Consult-Online. Philadelphia, PA: Elsevier Health Sciences; 2009
18 van den Bent MJ, Dubbink HJ, Marie Y, et al. IDH1 and IDH2 mutations are prognostic but not predictive for outcome in anaplastic oligodendroglial tumors: a report of the European Organization for Research and Treatment of Cancer Brain Tumor Group. Clin Cancer Res 2010;16(5):1597–1604
19 Stummer W, Pichlmeier U, Meinel T, Wiestler OD, Zanella F, Reulen HJ; ALA-Glioma Study Group. Fluorescence-guided surgery with 5-aminolevulinic acid for resection of malignant glioma: a randomised controlled multicentre phase III trial. Lancet Oncol 2006; 7(5):392–401
20 Albert FK, Forsting M, Sartor K, Adams HP, Kunze S. Early postoperative magnetic resonance imaging after resection of malignant glioma: objective evaluation of residual tumor and its influence on regrowth and prognosis. Neurosurgery 1994;34(1):45–60, discussion 60–61
21 Barker FG II, Prados MD, Chang SM, et al. Radiation response and survival time in patients with glioblastoma multiforme. J Neurosurg 1996;84(3):442–448
22 Vecht CJ, Avezaat CJ, van Putten WL, Eijkenboom WM, Stefanko SZ. The influence of the extent of surgery on the neurological function and survival in malignant glioma. A retrospective analysis in 243 patients. J Neurol Neurosurg Psychiatry 1990;53(6):466–471
23 Simpson JR, Horton J, Scott C, et al. Influence of location and extent of surgical resection on survival of patients with glioblastoma multiforme: results of three consecutive Radiation Therapy Oncology Group (RTOG) clinical trials. Int J Radiat Oncol Biol Phys 1993;26(2):239–244
24 Tait MJ, Petrik V, Loosemore A, Bell BA, Papadopoulos MC. Survival of patients with glioblastoma multiforme has not improved between 1993 and 2004: analysis of 625 cases. Br J Neurosurg 2007;21(5):496–500
25 Chaichana KL, Garzon-Muvdi T, Parker S, et al. Supratentorial glioblastoma multiforme: the role of surgical resection versus biopsy among older patients. Ann Surg Oncol 2011;18(1): 239–245