



Strategies for the Prevention of Complications in Brain Glioma Surgery: A Case Series Analysis

¹⁻³ Krešimir Rotim

¹⁻⁴ Bruno Splavski

¹ Filip Vrbanić

¹ Ante Rotim

¹ Department of Neurosurgery, Sestre milosrdnice University Hospital Center, Zagreb, Croatia

² J. J. Strossmayer University School of Medicine, Osijek, Croatia

³ University of Applied Health Sciences, Zagreb, Croatia

⁴ J. J. Strossmayer University School of Dental Medicine and Health, Osijek, Croatia

and the extent of tumor resection complications, dichotomized as peri- and post-operative variables, were correlated with investigated parameters to find out their possible association.

Results: Transitory neurological deficit was the most common peri-operative complication. Seizures, meningitis, and permanent neurological deficit were commonly recorded among post-operative complications.

Conclusion: Patients' gender and age, and the extent of tumor resection were not influential to the development of brain glioma complications. Aggressive surgery requires the avoidance of complications by cautious patient selection, multidisciplinary preoperative planning, and scrupulous neurosurgical technique augmented by up-to-date armamentarium.

Abstract

Introduction: Brain glioma is the most common and lethal primary malignant intracranial tumor. Nonetheless, gross tumor resection remains the most successful treatment modality, which may prolong progression free survival of these patients. However, excessive surgery brings a danger of neurological, regional and systemic complications, which may be diminished/avoided by better pre- and intra-operative care and by modern neurosurgical techniques.

Aim: To analyze the incidence and type of peri- and post-operative complications in surgical brain glioma patients. Computing the results, advice on complication prevention was made.

Methods: A single institution series of brain glioma patients operated on during a two-year period was analyzed. The incidence, type and time of complications were observed, as well as the patients' gender and age,

Keywords: brain glioma's treatment, complications, prevention strategies

Article received: 05.12.2020.

Article accepted: 15.01.2021.

<https://doi.org/10.24141/1/7/2/1>

Corresponding author:

Bruno Splavski

A: Department of Neurosurgery, Sestre milosrdnice University Hospital Center, Vinogradska c. 29, 10 000 Zagreb, Croatia

E-mail: splavuno@gmail.com

T: +385 1 378 71 11

No sources of support in the form of grants or others were received. The authors report no potential conflicts of interest.

Introduction

Brain glioma is the most common and lethal primary malignant intracranial tumor with annual incidence of up to 9/100.000^{1,2}. In spite of the advances in diagnostics and therapy, overall survival continues to be poor. Gross tumor resection remains the most successful treatment modality regardless of the glioma malignancy grade and/or improvements in adjuvant therapies^{3,4}. Progression free survival in these patients is mainly related to the extent of tumor resection⁵, which may assure long-term glioma remission and provide disease control when combined with adjuvant therapy. However, surgery brings the danger of neurological, regional and systemic complications⁶, such as iatrogenic peri-operative cortical/vascular injury, surgical wound dehiscence, and various post-surgical medical obstacles. The risk for and development of such complications may be heavily influenced by certain parameters like tumor histopathology, age, and functional impairment score^{3,7}.

Complications are defined as any aberration from the ordinary post-operative course happening within 30 days post-surgery⁸. It is known that the brain glioma surgery carries an increased risk of complications, including iatrogenic stroke, intracranial hemorrhage, and meningitis as the most common ones⁶. Since such complications are more related to the procedure itself, they are considered life-threatening surgical complications⁸. Nonetheless, the complication rates became considerably diminished due to the advancements in pre- and intra-operative care and modern surgical techniques.

The aim of this article was to analyze the incidence and type of various peri- and post-operative complications appearing in surgical glioma patients. Computing the results of a single institution series, the advice on complication prevention methods was made.

Material and Methods

In a retrospective study, we analyzed a single institution series of brain glioma patients who were operated on during a two-year period (January 2019 - December 2020)

at the Department of Neurosurgery of Sestre milosrdnice University Hospital Center, Zagreb, Croatia, searching for various types of surgical/medical complications.

The investigated parameters were patients' gender and age, and the extent of tumor resection. Complications, dichotomized as peri- and post-operative variables were analyzed to find out possible correlation between the investigated parameters and incidence/type of complications.

The peri-operative complications were defined as transient neurological deficit/temporary motor weakness, speech difficulties, and intracranial hematoma. The post-operative complications included seizures, infective complications (meningitis/pneumonia), and permanent neurological deficit/motor weakness, as well as cerebrospinal fluid (CSF) leak due to local wound dehiscence, and deep venous thrombosis.

Local ethics committee approval and informed consent from each patient were obtained before the beginning of the study.

Statistical analysis

The difference between investigated variables was statistically analyzed using the Chi-square test. The significance was set at Alpha = 0.05. The program SPSS for Windows, version 16.0 (SPSS Inc., Chicago, Illinois, USA) was used for statistical analysis of the published data.

Results

The total number of surgical glioma patients was 66 with male to female ratio of 32:34. The mean age of the group was 49.2 years. The most affected age group was that of 60-69 years, which included 22 (33.3%) patients, followed by 70-79 age group, which numbered 17 (25.7%) patients ($P < 0.001$) (Table 1).

Gross tumor resection was performed in 30 (45.5%), partial (subtotal) tumor resection in nine (13.5%), and stereotactic biopsy in 27 (41.0%) patients ($P = 0.003$) (Table 2), 21 (77.7%) of whom were older than 60 years.

Table 1. Age distribution of glioma surgical patients

Age group	N	%	P*
30-39 years	2	3.0	< 0.001
40-49 years	8	12.1	
50-59 years	13	19.7	
60-69 years	22	33.3	
70-79 years	17	25.8	
80-89 years	4	6.1	
Total	66	100	

*Chi-square Test

Table 2. Extent of tumor resection

Type of surgery	N	%	P*
gross total resection	30	45.5	0.003
subtotal resection	9	13.5	
stereotaxic biopsy	27	41.0	
Total	66	100	

*Chi-square Test

The incidence of overall complications following brain glioma surgery is depicted in Table 3. In the series of 66 surgical glioma patients, seven (10.6%) patients developed peri-operative complications, while post-operative complications were recorded in 21 (31.8%) of them (Table 3). Peri-operative complications included: transient neurological deficit together with temporary motor weakness, speech difficulties, and intracranial hematoma (Table 3). Among post-operative complications, there were seven (33.3%) patients with seizures, five (23.8%) patients with meningitis, and five (23.8%) with permanent neurological deficit (motor weakness), while two

(9.5%) patients developed CSF leak due to local wound dehiscence. Deep venous thrombosis and pneumonia were recorded in one (4.8%) patient each (Table 3).

The extent of tumor resection, as well as patients' gender and age were not correlated to the frequency and type of peri- and post-operative complications. The difference between the investigated variables was not statistically significant.

Most complications gradually subsided after symptomatic and/or antimicrobial treatment and during the in-hospital patients' stay, except seizures and permanent neurological deficit.

Discussion

Surgery is the preferred and primary method of choice in the treatment of brain glioma. However, it carries the risk for the development of various complications endangering the management outcome and functional recovery, as well as the quality of life of such patients.

The most affected age group in our series was that of 60-69 years old, followed by 70-79 years old (Table 1), what is consistent with the literature data indicating that the incidence of malignant brain glioma increases with age, being primarily identified in elderly patients with a median age of 64 at diagnosis⁹.

The infiltrative and aggressive nature of tumor growth is very well-established characteristic of brain glioma

Table 3. Type and incidence of complications

Type of complication	Overall		Peri-operative		Post-operative	
	N	%	N	%	N	%
seizures	7	25.0			7	33.3
transitional neurological deficit	6	21.4	6	85.7		
permanent neurological deficit	5	17.8			5	23.8
meningitis	5	17.8			5	23.8
CSF leak	2	7.2			2	9.5
intracranial hematoma	1	3.6	1	14.3		
pneumonia	1	3.6			1	4.8
deep venous thrombosis	1	3.6			1	4.8
Total	28	100	7	100	21	100

pathophysiology. Hence, the debate and controversy over the extent of glioma surgical removal continue to influence the field of neurosurgical oncology with positive effects of gross total tumor resection documented in selected patients as the most important factor affecting the prognosis¹⁰⁻¹⁵. Accordingly, the majority of patients (45.5%) from this series underwent gross tumor resection as a surgical method of choice (Table 2). However, such a treatment strategy may not be always beneficial, especially in elderly patients, since it may bring a higher risk of complications, which may rule out satisfactory outcome¹⁶. Therefore, a stereotactic biopsy to provide tissue specimen for histopathological diagnosis should be performed in patients who would not tolerate a large cranial surgery due to their age, and/or unresectable tumors¹⁷. It appears that a stereotactic biopsy is well justified in strictly selected patients when the survival and the quality of life are concerned¹⁸. It was performed in substantial portion of patients (41%) from our series (Table 2), and the majority of these patients belonged to the elderly.

The development of peri-operative motor or language deficit was associated with decreased progression free survival¹⁹. The most frequent peri-operative complication in our series was a transient speech difficulty (Table 3), which did not affect in-hospital mortality at all.

Venous thromboembolism, including deep venous thrombosis (DVT), and pulmonary embolism, often complicate the post-operative course of brain glioma patients²⁰, primarily due to their prolonged immobility. Regardless of the lack of routine prophylactic anticoagulation therapy in the post-operative setting of patients in our series, the incidence of DVT was low (Table 3), and comparable to that observed in other institutional series²¹.

Approximately one third of glioma patients experience a seizure during the post-treatment period, regardless of previous history of epi attacks^{22, 23}. Seizures were observed as the most frequent post-operative complication in our series too (Table 3).

Patients with surgical complications experience longer hospitalization and a significantly increased risk of in-hospital mortality⁶. Therefore, to rise the efficacy and safety of brain glioma surgery, an assortment of state-of-the-art techniques has been developed including intra-operative ultrasound, computed tomography (CT) and magnetic resonance imaging (MRI), neuronavigation, brain mapping, cortical stimulation, fluorescence-guided tumor resection, etc.²⁴. Thorough knowledge

of the surgical anatomy and mindfulness of possible neurosurgical drawbacks are also extremely helpful in reducing the rate of complications and maximizing tumor resection²⁵. A substantial amount of complications in glioma surgery may be avoided by using standardized operative protocols, and improved teamwork²⁶. We have followed the above postulates while performing surgery on our patients.

Considering the results of this paper, patients' gender and age, and the extent of tumor resection were not influential to the development of glioma complications. In general, an acceptable proportion of glioma surgery complications was recorded in our series. Non-life-threatening complications that were treated without invasive procedures were mostly observed. Complications requiring invasive management, as well as life-threatening complications were encountered rarely. No in-hospital deaths as a result of complications were documented in our series at all. Nevertheless, one has to always be mindful of possible complications and has to be particularly cautious while performing glioma surgery using the state-of-the-art armamentarium to prevent them.

At the end of this paper, it is compulsory to address certain study limitations generating from its retrospective character and the fact that only in-hospital complications could be identified, since most of the patients were lost to follow up after discharge due to subsequent oncological treatment.

Conclusion

Our results may be helpful to assist treatment strategies in the diminishment of operative risks and prevention of post-operative complications in patients undergoing surgery for brain glioma, regardless of their age. Prospective, randomized studies on a broader material are needed to corroborate our results.

References

1. Dolecek TA, Propp JM, Stroup NE, Kruchko. CCBTRUS statistical report: primary brain and central nervous system tumors diagnosed in the United States in 2005-2009. *Neuro Oncol* 2012; 14(Suppl 5):1-49.
2. Zhang AS, Ostrom QT, Kruchko C, Rogers L, Peereboom DM, Barnholtz-Sloan JS. Complete prevalence of malignant primary brain tumors registry data in the United States compared with other common cancers, 2010. *Neuro Oncol* 2017; 19(5):726-35.
3. Jackson C, Westphal M, Quiñones-Hinojosa A. Complications of glioma surgery. *Handb Clin Neurol* 2016; 134:201-18.
4. Sherman JH, Hoes K, Marcus J, Komotar RJ, Brennan CW, Gutin PH. Neurosurgery for brain tumors: update on recent technical advances. *Curr Neurol Neurosci Rep* 2011; 11(3):313-9.
5. Chaichana KL, Cabrera-Aldana EE, Jusue-Torres I, Wijesekera O, Olivi A, Rahman M, et al. When gross total resection of a glioblastoma is possible, how much resection should be achieved? *World Neurosurg* 2014; 82(1-2):e257-65.
6. De la Garza-Ramos R, Kerezoudis RP, Tamargo RJ, Brem H, Huang J, Bydon M. Surgical complications following malignant brain tumor surgery: An analysis of 2002–2011 data. *Clin Neurol Neurosurg* 2016; 140:6-10.
7. Álvarez de Eulate-Beramendi S, Álvarez-Vega MA, Balbin M, Sanchez-Pitiot A, Vallina-Alvarez A, Martino-González J. Prognostic factors and survival study in high-grade glioma in the elderly. *Br J Neurosurg* 2016; 30(3):330-6.
8. Landriel Ibañez FA, Hem S, Ajler P, Vecchi E, Ciraolo C, Baccanelli M, et al. A new classification of complications in neurosurgery. *World Neurosurg* 2011; 75(5-6):709-715.
9. Ostrom QT, Gittleman H, Farah P, Ondracek A, Chen Y, Wolinsky Y, et al. CBTRUS statistical report: Primary brain and central nervous system tumors diagnosed in the United States in 2006–2010. *Neuro Oncol* 2013; 15(Suppl 2):iii1-56.
10. Buckner JC. Factors influencing survival in high-grade gliomas. *Semin Oncol* 2003; 30:10-4.
11. Koc K, Anik I, Cabuk B, Ceylan S. Fluorescein sodium-guided surgery in glioblastoma multiforme: a prospective evaluation. *Br J Neurosurg* 2008; 22:99-103.
12. Rahman M, Abbatematteo J, De Leo EK, Kubilis PS, Vaziri S, Bova F, et al. The effects of new or worsened postoperative neurological deficits on survival of patients with glioblastoma. *J Neurosurg* 2017; 127:123-131.
13. Shinoda J, Sakai N, Murase S, Yano H, Matsuhisa T, Funakoshi T. Selection of eligible patients with supratentorial glioblastoma multiforme for gross total resection. *J Neurooncol* 2001; 52:161-71.
14. Stummer W, Reulen HJ, Meinel T, Pichlmeier U, Schumacher W, Tonn JC, et al. Extent of resection and survival in glioblastoma multiforme: identification of and adjustment for bias. *Neurosurgery* 2008; 62:564-76.
15. Wolbers JG. Novel strategies in glioblastoma surgery aim at safe, supra-maximum resection in conjunction with local therapies. *Chin J Cancer* 2014; 33(1):8-15.
16. Dobran M, Nasi D, Della Costanza M, Gladi M, Iacoangeli M, Rotim K, et al. Characteristics of treatment and outcome in elderly patients with brain glioblastoma: a retrospective analysis of case series. *Acta Clin Croat* 2019; 58:221-8.
17. Young RM, Jamshidi A, Davis G, Sherman JH. Current trends in the surgical management and treatment of adult glioblastoma. *Ann Transl Med* 2015; 3(9):121.
18. Lakičević G, Splavski B, Brekalo Z. The value of stereotactic biopsy in improving survival and quality of life for malignant brain glioma patients. *Coll Antropol* 2010; 34(Suppl 1):93-7.
19. McGirt MJ, Mukherjee D, Chaichana KL, Than KD, Weingart JD, Quinones-Hinojosa A. Association of surgically acquired motor and language deficits on overall survival after resection of glioblastoma multiforme. *Neurosurgery* 2009; 65:463-9.
20. Senders JT, Goldhaber NH, Cote DJ, Muskens IS, Dawood HY, De Vos FYFL, et al. Venous thromboembolism and intracranial hemorrhage after craniotomy for primary malignant brain tumors: a National Surgical Quality Improvement Program analysis. *J Neurooncol* 2018; 136(1):135-45.
21. Rinaldo L, Brown DA, Bhargav AG, Rusheen AE, Naylor RM, Gilder HE, et al. Venous thromboembolic events in patients undergoing craniotomy for tumor resection: incidence, predictors, and review of literature. *J Neurosurg* 2019; 4:1-12.
22. Sizoo EM, Braam L, Postma TJ, Pasman HR, Heimans JJ, Klein M, et al. Symptoms and problems in the end-of-life phase of high-grade glioma patients. *Neuro Oncol* 2010; 12(11):1162-6.
23. Sizoo EM, Koekkoek JA, Postma TJ, Heimans JJ, Pasman HR, Deliens L, et al. Seizures in patients with high-grade glioma: A serious challenge in the end-of-life phase. *BMJ Support Palliat Care* 2014; 4(1):77-80.
24. Diez Valle R, Tejada Solis S, Idoate Gastearena MA, et al. Surgery guided by 5-aminolevulinic fluorescence in glioblastoma: volumetric analysis of extent of resection in single-center experience. *J Neurooncol* 2011; 102:105-13.
25. Lang FF, Olansen NE, DeMonte F, Gokaslan ZL, Holland EC, Kalhorn C, et al. Surgical resection of intrinsic insular tumors: complication avoidance. *J Neurosurg* 2001; 95:638-50.
26. Wong JM, Panchmatia JR, Ziewacz JE, Bader AM, Dunn IF, Laws ER, et al. Patterns in neurosurgical adverse events: intracranial neoplasm surgery. *Neurosurg Focus* 2012; 33(5):E16.



STRATEGIJE U PREVENCIJI KOMPLIKACIJA KIRURŠKOG LIJEČENJA GLIOMSKIH TUMORA MOZGA: ANALIZA SKUPINE SLUČAJEVA

¹⁻³ Krešimir Rotim

¹⁻⁴ Bruno Splavski

¹ Filip Vrbanić

¹ Ante Rotim

¹ Klinika za neurokirurgiju KBC „Sestre milosrdnice“, Zagreb, Hrvatska

² Medicinski fakultet, Sveučilište J. J. Strossmayer u Osijeku, Osijek, Hrvatska

³ Zdravstveno veleučilište Zagreb, Zagreb, Hrvatska

⁴ Fakultet za dentalnu medicinu i zdravstvo, Sveučilište J. J. Strossmayer u Osijeku, Osijek, Hrvatska

Sažetak

Uvod: Gliomi mozga najučestaliji su smrtonosni primarni intrakranijski tumori. Unatoč tomu, njihovo radikalno kirurško uklanjanje i nadalje ostaje najuspješnija metoda liječenja kojom se može usporiti napredovanje bolesti i donekle produljiti život ovakvih bolesnika. Međutim, agresivno kirurško liječenje može povećati opasnost nastanka neuroloških, regionalnih i sustavnih komplikacija, koje se može pokušati izbjeći boljom pripremom prije i tijekom operacije, kao i uporabom suvremenih neurokirurških tehnika.

Cilj: Analizirati učestalost i vrstu perioperacijskih i poslijeoperacijskih komplikacija u kirurški liječenih bolesnika s gliomom mozga. Na temelju obrade rezultata, uspostaviti preporuke za sprječavanje nastanka komplikacija.

Metode: Analizirana je skupina bolesnika operiranih zbog glioma mozga tijekom dvogodišnjeg razdoblja. Promatrana je učestalost i vrsta komplikacija, kao i vrijeme njihova nastanka. Također su zabilježeni podaci o dobi i spolu bolesnika te stupnju tumorske resekcije. Komplikacije su dihotomizirane kao perioperacijske i poslijeoperacijske varijable čija je moguća povezanost uspoređivana s istraživanim pokazateljima.

Rezultati: Tranzitorni neurološki deficit bio je najučestalija perioperacijska komplikacija. Epileptički napadaj, meningitis i trajni neurološki ispad zabilježeni su kao najčešća poslijeoperacijska komplikacija.

Zaključak: Spol i dob bolesnika, kao i stupanj tumorske resekcije nisu utjecali na nastanak komplikacija kirurškog liječenja glioma mozga, koje je moguće izbjeći pažljivim odabirom bolesnika, multidisciplinarnim preoperacijskim planiranjem i primjenom obzirne neurokirurške tehnike poduprte uporabom najsuvremenije operacijske opreme.

Ključne riječi: gliom mozga, kirurško liječenje, komplikacije, strategija prevencije