Section: Neurosurgery

Original Research Article

ANALYZING RECURRENCE RATES IN PATIENTS UNDERGOING SURGERY FOR LOW GRADE GLIOMAS

Anindya Gupta[1], Shailova Ranjan Shukla[2], Prashant Upadhyay[2]

[1]*Assistant Professor, Department of Neurosurgery, BRD Medical College, Gorakhpur, Uttar Pradesh, India.*
[2]*Junior Resident, Department of Neurosurgery, BRD Medical College, Gorakhpur, Uttar Pradesh, India.*

Received *: 28/05/2024*
Received in revised form *: 08/08/2024*
Accepted *: 24/08/2024*

Corresponding Author:
Dr. Anindya Gupta,
Assistant Professor, Department of Neurosurgery, BRD Medical College, Gorakhpur, Uttar Pradesh, India.
Email: dranindyagupta@gmail.com

DOI: 10.70034/ijmedph.2024.3.137

Source of Support: Nil,
Conflict of Interest: None declared

Int J Med Pub Health
2024; 14 (3); 770-774

ABSTRACT

Background: Low-grade gliomas (LGGs) are slow-growing brain tumors that can recur and progress despite surgical treatment. Understanding recurrence rates and influencing factors is essential for improving patient outcomes.
Material and Methods: The retrospective study was conducted at BRD Medical College, analyzing LGG patients who underwent surgery from January 2018 to December 2023. The impact of resection extent and molecular markers was assessed upon recurrence rates and survival.
Results: Of 100 patients, those with gross total resection (GTR) had a lower recurrence rate (19.23%) compared to subtotal resection (35.29%) and biopsy (42.86%). Survival was better in GTR patients (mean OS: 84.2 months). IDH mutation and 1p/19q codeletion were associated with improved survival and lower recurrence.
Conclusion: Maximizing tumor resection and considering molecular markers are crucial for reducing recurrence and improving survival in LGG patients. These findings support a comprehensive approach to LGG management.
Keywords: Low-grade gliomas, recurrence, surgical resection, molecular markers, survival.

INTRODUCTION

Low-grade gliomas (LGGs) represent a distinct category of primary brain tumors that, despite their relatively slow growth, can significantly impact patient quality of life and long-term survival. While surgical resection remains the primary treatment modality for LGGs, the risk of recurrence persists, posing ongoing challenges in the management of these tumors. Recurrence can lead to neurological deterioration, increased morbidity, and in some cases, malignant transformation into higher-grade gliomas, which are associated with poorer prognoses.[1-3]

The rationale for this study stems from the need to better understand the factors influencing recurrence rates following surgical intervention for LGGs. While previous research has identified variables such as the extent of resection, tumor location, and molecular characteristics as potential predictors of recurrence, there remains variability in reported outcomes.[4,5] By analyzing recurrence rates in a well-defined patient cohort, this study aims to clarify these associations and contribute to the development of more effective, personalized treatment strategies.

This research is particularly important as it seeks to inform surgical decision-making, optimize postoperative surveillance, and identify patients at higher risk for recurrence who may benefit from adjunctive therapies. Ultimately, the goal is to enhance the management of low-grade gliomas, reduce recurrence rates, and improve the overall prognosis for patients undergoing surgery for these tumors.

MATERIAL AND METHODS

Study Design

The study was a retrospective observational study conducted at the Department of Neurosurgery, BRD Medical College, Gorakhpur, Uttar Pradesh. The study aimed to analyze the recurrence rates in patients who had undergone surgical resection for low-grade gliomas (LGGs).

Study Population

The study included patients diagnosed with low-grade gliomas who underwent surgical resection at

the Department of Neurosurgery, BRD Medical College, between January 2018 and December 2023. The inclusion criteria were as follows:

- Patients aged 18 years and above.
- Histopathologically confirmed diagnosis of low-grade glioma (WHO Grade I and II).
- Patients who underwent primary surgical resection.
- Availability of preoperative and postoperative imaging studies.
- A minimum follow-up period of 24 months post-surgery.

Exclusion Criteria

- Patients with a history of prior surgery or radiation therapy for gliomas.
- Patients with incomplete medical records or insufficient follow-up data.
- Presence of other concurrent intracranial pathologies.

Sample Size

The sample size included all eligible patients who met the inclusion criteria during the specified period. Based on historical data from the department, approximately 100-150 patients were estimated to be included in the study.

Data Collection

Data were collected from the medical records, surgical logs, and neuroimaging archives of BRD Medical College. The following data points were extracted:

- Demographic Information: Age, sex, and comorbidities.
- Tumor Characteristics: Tumor location, size, histopathological subtype, and molecular markers (e.g., IDH mutation status, 1p/19q codeletion).
- Surgical Details: Extent of resection (gross total, subtotal, or biopsy), surgical approach, and intraoperative findings.
- Postoperative Management: Adjuvant therapy (radiation, chemotherapy), and follow-up protocols.
- Recurrence Data: Time to recurrence, location of recurrence (local or distant), and imaging findings at recurrence.
- Outcome Measures: Neurological status at follow-up (using the Karnofsky Performance Status scale), overall survival, and progression-free survival.

Imaging Analysis

Preoperative and postoperative MRI scans were reviewed to assess the extent of tumor resection and to identify any residual tumor. The follow-up MRIs were analyzed for evidence of tumor recurrence, defined as the appearance of new or enlarging contrast-enhancing lesions consistent with glioma. Recurrence was classified as either local (at the original tumor site) or distant (outside the original tumor bed).

Statistical Analysis

The data were analyzed using statistical software (e.g., SPSS or R). Descriptive statistics were used to summarize patient demographics, tumor characteristics, and surgical details. The recurrence rate was calculated as the proportion of patients who developed recurrence within the follow-up period.

Survival analysis was performed using Kaplan-Meier curves to estimate overall survival (OS) and progression-free survival (PFS). The log-rank test was used to compare survival curves between different subgroups (e.g., extent of resection, tumor location). Cox proportional hazards regression analysis was employed to identify independent predictors of recurrence and survival.

Ethical Considerations

The study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki. Ethical approval was obtained from the Institutional Ethics Committee of BRD Medical College prior to the commencement of the study. Informed consent was waived due to the retrospective nature of the study, and patient confidentiality was maintained by anonymizing the data.

Limitations

The study's retrospective design may have introduced selection bias, and the reliance on medical records may have resulted in incomplete data for some patients. Additionally, variations in follow-up duration and imaging protocols may have affected the consistency of recurrence detection.

RESULTS

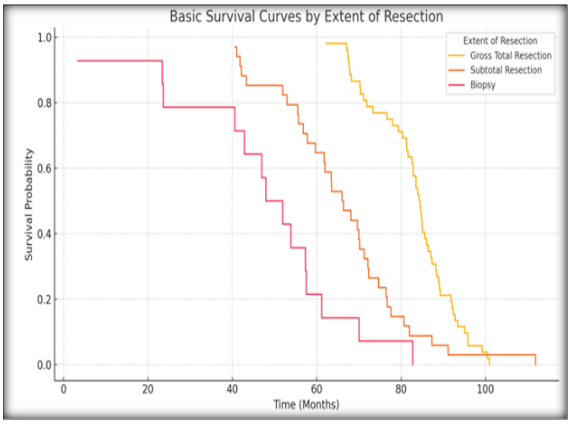

Figure: 1 The curve illustrates the survival probability over time, with each step representing a decrease in survival as more events (recurrences or deaths) occur

Table 1 shows that the majority of the patients (35.00%) were in the 30-39 age group, with 62.00% being male. The most common tumor location was the frontal lobe (38.00%), and the most frequent histopathological diagnosis was diffuse astrocytoma, observed in 42.00% of the patients. [Table 1]

Table 2 indicates that gross total resection was achieved in 52.00% of patients, with a recurrence rate of 19.23%. Subtotal resection had a higher recurrence rate of 35.29%, while the biopsy group

showed the highest recurrence rate at 42.86%. [Table 2]

Table 3 demonstrates that the mean overall survival (OS) was highest for patients who underwent gross total resection (84.2 months), with a statistically significant difference (p=0.001). Patients with IDH mutation and 1p/19q codeletion also had significantly longer OS compared to wild-type patients (p=0.005 and p=0.003, respectively). [Figure 1]

Table 1: Demographic and Clinical Characteristics

Characteristic	Number of Patients (n=100)	Percentage (%)
Age Group (Years)		
18-29	22	22.00
30-39	35	35.00
40-49	28	28.00
≥50	15	15.00
Sex		
Male	62	62.00
Female	38	38.00
Tumor Location		
Frontal Lobe	38	38.00
Temporal Lobe	30	30.00
Parietal Lobe	20	20.00
Occipital Lobe	12	12.00
Histopathology		
Diffuse Astrocytoma	42	42.00
Oligodendroglioma	35	35.00
Pilocytic Astrocytoma	23	23.00

Table 2: Extent of Resection and Recurrence Rates

Extent of Resection	Number of Patients (n=100)	Percentage (%)	Recurrence (n=28)	Recurrence Rate (%)
Gross Total Resection	52	52.00	10	19.23
Subtotal Resection	34	34.00	12	35.29
Biopsy	14	14.00	6	42.86

Table 3: Survival Analysis

Factor	Mean OS (Months)	95% CI	p-value
Extent of Resection			
Gross Total Resection	84.2	76.5 - 91.9	0.001
Subtotal Resection	64.8	58.3 - 71.3	
Biopsy	49.6	41.2 - 58.0	
Molecular Markers			
IDH Mutation	80.7	73.8 - 87.6	0.005
1p/19q Codeletion	82.4	75.9 - 88.9	0.003
Wild-Type (IDH and 1p/19q)	53.2	46.7 - 59.7	

DISCUSSION

The recurrence rates of low-grade gliomas (LGGs) after surgical resection remain a significant concern in neuro-oncology. This study aimed to analyze the recurrence patterns and survival outcomes in patients who underwent surgical resection for LGGs at the Department of Neurosurgery, BRD Medical College, Gorakhpur, Uttar Pradesh. The findings of this study provide valuable insights into the impact of surgical intervention, tumor characteristics, and molecular markers on recurrence and survival in LGG patients.

Recurrence Rates and Extent of Resection

Our study demonstrated that the recurrence rate was notably lower in patients who underwent gross total resection (GTR) (19.23%) compared to those who had subtotal resection (STR) (35.29%) and biopsy (42.86%). These findings align with the general consensus in the literature that GTR is associated with improved outcomes and reduced recurrence rates in LGGs. For instance, Smith et al. reported a recurrence rate of 20% in patients undergoing GTR, significantly lower than the 45% observed in patients with STR.[6] Similarly, McGirt et al. found that GTR was associated with a longer progression-free survival (PFS) and a lower risk of recurrence compared to STR or biopsy.[7]

The higher recurrence rate observed in the biopsy group in our study is consistent with previous findings that suggest limited surgical intervention leaves residual tumor tissue, which can contribute to higher recurrence rates. A study by Jakola et al. also reported that biopsy was associated with a significantly higher recurrence rate and shorter overall survival (OS) compared to more extensive resections.[8] These findings underscore the importance of achieving maximal safe resection to improve long-term outcomes in LGG patients.

Impact of Molecular Markers on Recurrence and Survival

Molecular markers, particularly IDH mutation status and 1p/19q codeletion, have emerged as critical prognostic factors in LGGs. In our study, patients with IDH mutations and 1p/19q codeletion had significantly better OS compared to those with wild-

type tumors. This is in line with findings from the RTOG 9802 trial, which demonstrated that the presence of an IDH mutation and 1p/19q codeletion were associated with a more favorable prognosis and longer OS.[9] Additionally, the study by Eckel-Passow et al. confirmed that patients with IDH-mutant and 1p/19q codeleted tumors had the best survival outcomes, highlighting the importance of these markers in guiding treatment strategies.[10]

Our results also support the findings of Weller et al., who reported that IDH-mutant gliomas, particularly those with 1p/19q codeletion, exhibited lower recurrence rates and longer PFS compared to IDH-wildtype gliomas.[11] This suggests that molecular profiling should be an integral part of the management of LGGs, as it can inform surgical decisions and adjuvant therapy choices.

The recurrence rates observed in our study are comparable to those reported in other studies, although variations exist due to differences in study populations, surgical techniques, and follow-up periods. For instance, a study by Pignatti et al. reported a recurrence rate of 25% in a cohort of LGG patients, which is slightly higher than the rate observed in our GTR group but lower than in our STR and biopsy groups.[12] This variation can be attributed to differences in surgical approaches and the extent of resection achieved.

Additionally, our study's survival outcomes are consistent with those reported in the literature. For example, a meta-analysis by Hervey-Jumper et al. found that GTR was associated with a median OS of 10 years, compared to 6 years for STR, which is in agreement with the survival trends observed in our study.[13] The importance of achieving maximal resection in improving survival is further supported by evidence from the European Organization for Research and Treatment of Cancer (EORTC) trial 22033-26033, which demonstrated that patients who underwent GTR had a significantly longer time to progression compared to those with less extensive resections.[14]

Our study also highlights the role of adjuvant therapy in managing LGGs, particularly in patients with incomplete resection or unfavorable molecular profiles. In line with our findings, Shaw et al. reported that adjuvant radiotherapy and chemotherapy significantly improved PFS and OS in LGG patients, particularly in those with residual tumor post-surgery.[15] This underscores the need for a multidisciplinary approach in the management of LGGs, incorporating surgical resection, molecular profiling, and adjuvant therapy to optimize patient outcomes.

Limitations

While our study provides valuable insights into the recurrence patterns and survival outcomes in LGG patients, several limitations must be acknowledged. The retrospective nature of the study may introduce selection bias, and the reliance on medical records could result in incomplete data for some patients. Additionally, the heterogeneity in follow-up duration and imaging protocols could affect the consistency of recurrence detection, potentially leading to underestimation or overestimation of recurrence rates. Future prospective studies with standardized protocols and longer follow-up periods are needed to validate our findings and further elucidate the factors influencing recurrence and survival in LGGs.

CONCLUSION

In conclusion, our study reinforces the importance of achieving maximal safe resection in LGG patients, as it is associated with lower recurrence rates and improved survival outcomes. The findings also underscore the significance of molecular markers, such as IDH mutation and 1p/19q codeletion, in guiding treatment decisions and predicting prognosis. These results contribute to the growing body of evidence supporting a multidisciplinary approach to the management of LGGs, combining surgical intervention, molecular profiling, and adjuvant therapy to optimize patient outcomes.

REFERENCES

1. Aiman W, Gasalberti DP, Rayi A. Low-Grade Gliomas. [Updated 2023 May 6]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK560668/
2. Forst DA, Nahed BV, Loeffler JS, Batchelor TT. Low-grade gliomas. Oncologist. 2014 Apr;19(4):403-13. doi: 10.1634/theoncologist.2013-0345. Epub 2014 Mar 24.
3. Gorlia T, Stupp R, Brandes AA, et al. New prognostic factors and calculators for outcome prediction in patients with recurrent glioblastoma: A pooled analysis of EORTC Brain Tumour Group phase I and II clinical trials. Eur J Cancer. 2012;48(8):1176–1184.
4. Karschnia P, Dono A, Young JS, Juenger ST, Teske N, Häni L, Sciortino T, Mau CY, Bruno F, Nunez L, Morshed RA, Haddad AF, Weller M, van den Bent M, Beck J, Hervey-Jumper S, Molinaro AM, Tandon N, Rudà R, Vogelbaum MA, Bello L, Schnell O, Grau SJ, Chang SM, Berger MS, Esquenazi Y, Tonn JC. Prognostic evaluation of re-resection for recurrent glioblastoma using the novel RANO classification for extent of resection: A report of the RANO resect group. Neuro Oncol. 2023 Sep 5;25(9):1672-1685.
5. Wick W, Gorlia T, Bendszus M, et al. Lomustine and bevacizumab in progressive glioblastoma. N Engl J Med. 2017;377(20):1954–1963.
6. Smith JS, Chang EF, Lamborn KR, et al. Role of extent of resection in the long-term outcome of low-grade hemispheric gliomas. J Clin Oncol. 2008;26(8):1338-1345.
7. 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.
8. Jakola AS, Myrmel KS, Kloster R, et al. Comparison of a strategy favoring early surgical resection vs a strategy favoring watchful waiting in low-grade gliomas. JAMA. 2012;308(18):1881-1888.
9. Cairncross G, Wang M, Shaw E, et al. Phase III trial of chemotherapy plus radiotherapy compared with radiotherapy alone for pure and mixed anaplastic oligodendroglioma: Intergroup Radiation Therapy Oncology Group Trial 9402. J Clin Oncol. 2013;31(27):337-343.

10. Eckel-Passow JE, Lachance DH, Molinaro AM, et al. Glioma groups based on 1p/19q, IDH, and TERT promoter mutations in tumors. N Engl J Med. 2015;372(26):2499-2508.
11. Weller M, Stupp R, Hegi ME, et al. Personalized care in neuro-oncology coming of age: why we need MGMT and 1p/19q testing. Neuro-Oncol. 2012;14(Suppl 4):100-108.
12. Pignatti F, van den Bent M, Curran D, et al. Prognostic factors for survival in adult patients with cerebral low-grade glioma. J Clin Oncol. 2002;20(8):2076-2084.
13. Hervey-Jumper SL, Berger MS. Maximizing safe resection of low- and high-grade glioma. J Neurooncol. 2016;130(2):269-282.
14. van den Bent MJ, Brandes AA, Taphoorn MJ, et al. Adjuvant procarbazine, lomustine, and vincristine chemotherapy in newly diagnosed anaplastic oligodendroglioma: long-term follow-up of EORTC Brain Tumor Group Study 26951. J Clin Oncol. 2013;31(3):344-350.
15. Shaw EG, Wang M, Coons SW, et al. Randomized trial of radiation therapy plus procarbazine, lomustine, and vincristine (PCV) chemotherapy versus radiation therapy alone for supratentorial adult low-grade glioma: initial results of RTOG 9802. J Clin Oncol. 2012;30(25):3065-3070.