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Prognostic Factors Analysis As Long Term Follow Up In Adult Patients With Low- Grade Glioma (WHO II) Postoperatively Irradiated

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Abstract

Aim: The purpose of this study was to evaluate the long-term survival in adult patients with LGG post-operatively irradiated in one institution, and to identify prognostic factors for progression free survival.

Background: Adult low-grade gliomas are a rare and aggressive pathology of the central nervous system. Some of their characteristics contribute to the patient's life expectancy and to their management. There is little consensus about the optimal treatment for low-grade glioma (LGG), Radiation therapy is one option for treatment of patients with LGG, whereas other options include postoperative observation, or chemotherapy or both.

Materials and methods: Total 90 patients with LGG (WHO II), between Jun 2010 to May, 2015 received non radical (subtotal or partial) excision followed by postoperative irradiation and close follow up. The five-year retrospective study statistically analyzed the demographic, imaging and morphogenetic characteristics of the patient group through appropriate parameters. Patients had to be 18 years of age or older, and have histologic proof of supratentorial fibrillary (FA), protoplasmic (PA) or gemistocytic astrocytoma (GA). Radiotherapy was given within 3–10 weeks after surgery. Treatment fields were localized and included the preoperative tumor volume, with a 1–2 cm margin, treated to a total dose of 50– 60 Gy in 25–30 fractions over 5–6 weeks.

Results: Actuarial seven-year progression free survival (APFS) in the whole group was 19%. The worse prognosis was observed in patients with GA. Seven-years APFS rates for GA, PA and FA were 10%, 18% and 22%, respectively. The presence of a residual tumor resulted in decreased survival and is an independent risk factor for mortality. We identified that a negative prognosis is influenced by the association of epilepsy with headache and tumor volume. Independent factors associated with mortality were midline shift and presence of tumor residue.

Conclusion: The findings from our long-term survival 90 patients with LGG confirmed by uni- and multivariate analysis demonstrated that only astrocytoma histology significantly determined the prognosis. The best survival was observed in patients with the fibrillary variant, and the worst for the gemistocytic one.

Keywords: Adult, combined modality, low grade glioma, radiation, surgery

Introduction

The low-grade gliomas(LGG) are primary brain tumors classified as grade I and II by the World Health Organization (WHO) grading system 1. This category includes both circumscribed and diffuse entities: fibrillary astrocytoma, protoplasmic astrocytoma, gemistocytic astrocytoma grade 2, and astrocytoma grade 2 (diffuse astrocytoma) 2,3. Their main characteristic is represented by a low

proliferative index1. They have an increased incidence in males between 35–44 years 3.

This terminology is helpful in differentiating LGG from lower or higher grade gliomas that have a significantly different prognosis. Patients with LGG may survive for relatively long periods, but often (60-70%) progress to higher-grade tumors which are invariably fatal to the patient 2,3,4,5 . Life expectancy is relatively good, with an average survival rate of 5.6 to 13.3 years 1.

The unpredictable behavior of the tumor makes it difficult to assess risk factors. However, to date, studies have only shown the following potential indicators of the promotion of malignancy: age of patient, presence of seizures, tumor volume, histology and method of treatment 6,7.

Radiation therapy is one option for treatment of patients with LGG, or postoperative observation accordingly .In general, treatment is reserved for patients with symptomatic residual disease despite optimal surgical resection or for patients who are suspected to have high risk features. The current hypothesis is that patients older than forty, with residual disease, should receive earlier intervention. The basis for these recommendations is three prospective studies done over the past ten years 43,44,45.

Aim

This study aimed to identify and characterize the main prognostic factors for progression free survival in low-grade gliomas at long term follow up.

Materials and Methods

This study was a Retrospective trial conducted in the department of Neurosurgery at Patna Medical College ,Patna from Jun, 2010 to May 2015 over a period of 5 years. Total 90 patients were selected who fulfilled the following inclusion criteria are:

1. Age ≥18 years to 70 years
2. At Radiological diagnosis and Pathological diagnosis of WHO grade II gliomas.
3. On regular medical follow up 4. KPS >= 70

Exclusion criteria :

1. Oligodendrogliomas, mixed oligoastrocytomas and other variants .
2. Death not related to the tumor.

All patients signed an informed consent at the time of admission. An ethics opinion was obtained from the local ethics commission. Central pathology review was performed at the Department of pathology, PMCH, Patna or outside as per need. The oldest patient was 64, the youngest 19 years old (median 47 years). The distribution of patho-clinical characteristics is given in Table 1.

In surgery, gross total, subtotal and partial resection was defined by no residual tumor volume, residue ≤10 and ≥10 cm3 on flair-weighted MRI, respectively. Radiotherapy was given within 3–10 weeks after surgery. Some patients were treated with 2D technique and some by the 3D-Conformal technique as per the patients choice. The treatment fields were localized and included the preoperative tumor bed with a 1–2 cm margin treated to a total dose of 50–60 Gy (median 56 Gy) in 25–30 fractions over 5–6 weeks.

Follow up was done after the completion of therapy (every 3-4 months for 2 years, every 6 months for 3 years, and yearly thereafter), patients had a physical examination that included a neurologic examination and CT or MRI scan, or when clinically indicated.

Table 1 – Patho-clinical characteristics of 90 adult patients with LGG

Characteristics	**N**	**%**
Age (years)		
40 and less	40	44
More than 40	50	56
Gender		

Volume 6, Issue 1; January-February 2023; Page No 658-668

Male	48	53
Female	42	47
KPS		
60-70	41	46
More than 70	49	54
Seizure		
Yes	51	57
No	39	43
TCM		
Yes	30	33
NO	60	67
Extent of Surgery		
Gross total	15	17
Subtotal	48	53
Partial	27	30
Histology		
Fibrillary astrocytoma	50	56
Protoplasmic astrocytoma	18	20
Gemistocytic astrocytoma	22	24
Total Radiation dose		
50Gy	36	40
More than 50Gy	54	60
KPS-Karnofsky performance status		
TCM- Tumor crossing midline		

Statistical Analysis

Actuarial 7-year progression free survival (APFS) rates were calculated from date of surgery, and estimated using the Kaplan–Meier method and compared using one or two sided log rank tests 8,9 . Only variables that were identified as significantly ($p \leq 0.05$) associated with the end point (APFS) were considered valid prognostic parameters. The Cox proportional hazards model was used to assess the strengths of association of APFS with various histo-clinical characteristics10.

Results

Patient Characteristics

A total of 90 patients diagnosed were included. The median age was 48 years with a large part of patients diagnosed between 41 and 64 years. Epilepsy was the most common symptom leading to let on the lesion (83.2%), headache and neurological troubles revealed the tumor in 8.6% and 4.1% of cases, respectively. Incidental detection represented 4% of the cases. Concerning the radiological characteristics, the

Volume 6, Issue 1; January-February 2023; Page No 658-668

frontal lobe was invaded in 64% of cases, and the temporal lobe was invaded in 25% of the cases. Moreover, multiple lobes affected in 30% of patients, 56% of tumors were identified as fibrillary astrocytoma, 24% as protoplasmic astrocytomas and 20 % as gemistocytic astrocytoma.

Therapeutic Strategy

The first-line treatment consisted of surgery alone for a large number of patients (61%), and adjuvant radiotherapy in most of the cases. The first-line treatment has constantly evolved over time, and surgery has become the primary first-line treatment (from 33% in 1989–1996 to 62% in the last period 2013–2016). Gross total resection and subtotal resection were achieved in 15% and 48% of cases, respectively. Radiotherapy has been the mainstay of LGG therapy for decades, but much controversy has surrounded the radiation dose which should be delivered. Most of the histologically confirmed LGG received radiation dose post operatively with either 45Gy in 5 weeks (36%) or 59.4Gy in 6.6weeks (54%) @ 1.8 Gy or 2 Gy per fraction.

The treatment was generally well tolerated, signs and symptoms of increased intracranial pressure occurred in 21 patients (12%), and resolved with steroid administration. APFS for all 180 patients is presented in Fig. 1. The 10-yearAPFS was of 19%.

Kaplan–Meier estimates of survival by histology are given in Fig. 2. The 10-year APFS for FA, PA and GA was of 25%, 18% and 9%, respectively. The results of univariate and multivariate analysis are shown in Tables 2 and 3.

Fig. 1 – Actuarial progression-free survival (APFS) in 90 patients with low-grade gliomas (LGGs).

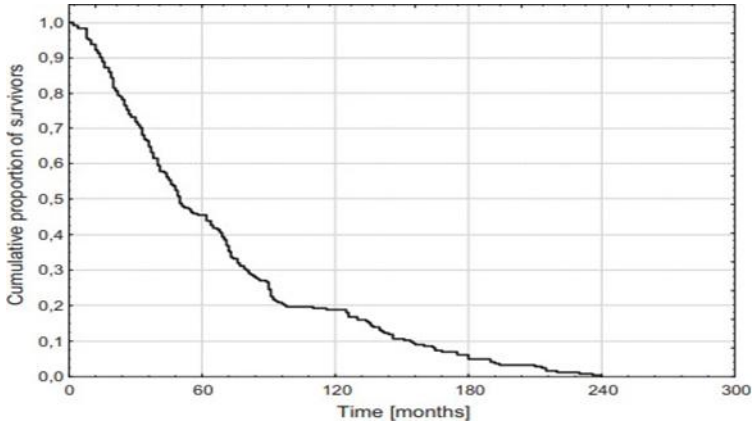


Table 2 – Univariate analysis of 90 adult patients with LGG

Characteristics	7 years APFS (%)	p
Age (years)		
40 and less	22	
More than 40	16	NS
Gender		
Male	19	
Female	19	NS
KPS		
60-70	17	
More than 70	23	NS

Volume 6, Issue 1; January-February 2023; Page No 658-668

Seizure		
Yes	20	
No	16	NS
TCM		
Yes	12	
NO	22	NS
Extent of Surgery		
Gross total	9	
Subtotal	25	NS
Partial	16	
Histology		
Fibrillary astrocytoma	22	
Protoplasmic astrocytoma	18	0.1387
Gemistocytic astrocytoma	10	0.0312
Total Radiation dose		
50Gy	20	
More than 50Gy	16	NS
KPS-Karnofsky performance status TCM- Tumor crossing midline NS- Not Significant		

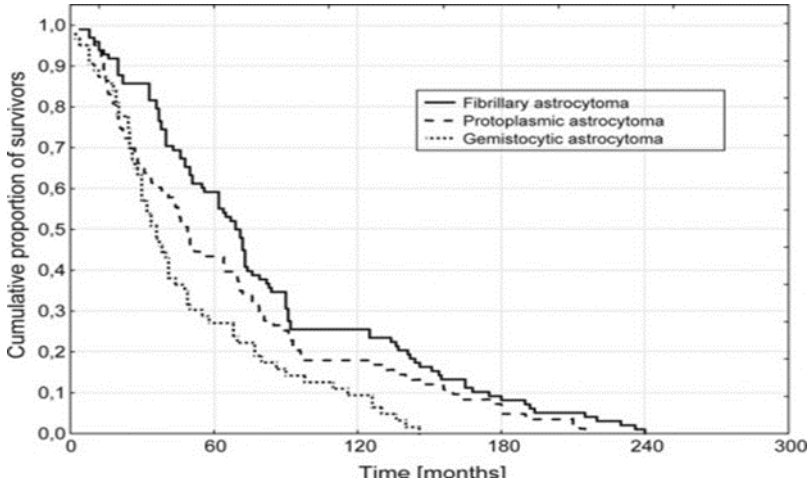
Table 3- Multivariate analysis (Cox s Model)

Characteristics	Relative Risk	p
Histology		
Fibrillary astrocytoma	1	0.52
Protoplasmic astrocytoma	1.16	0.020
Gemistocytic astrocytoma	2.92	

In our study of 90 patients with LGG , the patho-clinical features of the present material are similar to those reported by other author 5,6,7,14,24,25. More than 50% of patients had seizures at presentation, the majority of our population were in their fifth and sixth decades of age. The tumor was located predominantly in the frontal lobe in 41% of patients, in the temporal lobe in 39%, in the parietal lobe in 17%, and in the occipital lobe in 3%. Thirty percent of patients had bulky residual tumor after surgery, and 54%,had Karnofsky performance status more than seventy.

Volume 6, Issue 1; January-February 2023; Page No 658-668

Fig. 2 – Actuarial progression-free survival (APFS) by histology



Our results with a 7-year APFS of 19% are close to or slightly worse than results achieved by other authors (Table 4). It must be emphasized, however, that the literature data presented in (Table 4) refer to patients after both radical and partial surgery, and that they include as well grade 2 astrocytomas as mixed forms of gliomas and oligodendrogliomas. We restricted our review only to adult patients with grade 2 astrocytoma, according to the WHO classification. This may pose certain interpretative difficulties in direct comparison of our results with those of other authors, including grade 1 glioma and mixed astro-oligodendroglioma variants. The notorious difficulties with respect to the histologic diagnosis of gliomas may also be an important cause for differences between study results. Interobserver variability in the diagnosis and grading of gliomas has been well documented 30,31,42,43,44. Coons et al. observed that even with well-defined criteria, expert observers and formal training, the maximal concordance rate achieved was 86%. Distinguishing between oligodendrogliomas and diffuse astrocytomas is particularly problematic, as is distinguishing between pure oligodendroglioma and mixed oligoastrocytoma. Entities that can confound low-grade classification include pilocytic astrocytoma, pleomorphic xanthoastrocytoma, ganglioglioma, and gliosarcoma33.

Table 4 –Results of postoperative irradiation of patients with LGG

Study	Median Follow up (years)	No. of Patients	PFS 5 year survival	OS 5 year survival
Shaw et al(NCCTG)	6.4	203	NR	NR
50.4GY		101	50	72
64.8Gy		102	50	65
Karim et al(EORTC 22844)	6.2	343	NR	NR
45Gy		171	47	58
59.4Gy		172	50	58
Karim et al and Van den Bent et al(EORTC 22845)	7.8	311	NR	NR

Volume 6, Issue 1; January-February 2023; Page No 658-668

Discussion

The indolent natural course of LGG has resulted in uncertainties and controversies regarding the role, timing and technique of both surgery and radiotherapy. LGG is a vexing problem. Some patients will enjoy years of freedom from tumor progression without intervention, whereas others progress rapidly with neurologic decompensation and death 11–14. Although these tumors are grouped together under the category of "low-grade glioma", they are actually an extremely heterogeneous group with a median survival time ranging from 5 to 10 year15–18. The best treatment policy for these tumors is still unclear. Some physicians advocate early and extensive surgery, while others tend to postpone treatment until functional deficits are present.

Surgery at the time of diagnosis provides tissue diagnosis in addition to a therapeutic debulking benefit. Our study displayed improved outcomes for patients who underwent more aggressive resections. However, GTR is often not possible without serious risk of neurologic injury because of tumour location or infiltration. We found that aggressive resection were more likely to have been performed in patients with more favorable tumor characteristic, like tumor size smaller than 5cm, lack of enhancement on CT scan, and lack of sensory motor symptoms. However, considering both retrospective and prospective data, many neurosurgeons favor maximally safe resection3,4,14,24,35,36,37,38. Although non randomised, three prospective studies correlate aggressive surgery and improved prognosis 3,4,34.

Radiotherapy is prescribed for most patients with LGG, only the timing of treatment is debated 19–23. Due to perceived toxicities with RT and the indolent nature , some advocate delaying RT until there is evidence of progression, symptoms, or high grade transformation 45,46. EORTC 22845 evaluated the timing of RT in a phase 3 trial of immediate RT or observation until progression 5,24,39,40,47. With follow up of 7 years, postop RT significantly prolonged the PFS without affecting the OS 5 . In addition, in the present study, the benefit of post op RT was most clearly seen , in terms of improved OS and PFS , in patients undergoing more limited resection.

Several studies have attempted to identify prognostic factors in LGG. A number of patient and tumor characteristics, such as age at diagnosis, performance status, histology subtype, presence of seizures at diagnosis and extent of resection, have been proposed as prognostic factors14,28.

In our group, only the histologic subtype was most consistently and significantly associated with survival in univariate and multivariate analysis. The outcome of patients with gemistocytic astrocytomas was slightly worse than that of those with protoplasmic and fibrillary variants, with seven year APFS rates of 10%, 18% and 22%, respectively. Hazard ratio for gemistocytic vs. fibrillary variant being of 2.92 means that death rate of patients presenting with GA was about three times higher in comparison with fibrillary variant. Better prognosis for fibrillary astrocytoma was confirmed by Durmaz, and Piepmeir 17,20 Gemistocytic astrocytomas and a high MIB labeling index have also been related to poor prognosis in LGG 29,32

We found that seven year APFS was 12% and 22% for TCM (+) and TCM (−) patients, respectively. Our findings do not consist with the results of the EORTC 22845 trial, in which a median survival time for TCM (+) and TCM (−) characteristics was 3.6 years and 7.9 years, respectively, with a hazard ratio of 1.43 15. Thus TCM has not significantly influenced the prognosis.

In the univariate analysis, the extent of surgery in our material reached the borderline of significance, with a p-value of 0.0579. There was no statistical difference in survival between patients who had been treated with subtotal resection and those who had undergone a partial one. The 7-year APFS for the former group was of 25% compared to 16% for the latter. The role of surgical resection in management of patients with LGG has remained controversial. The theoretical goals of surgical resection in LGG are to improve neurologic deficits and to minimize the risk of recurrence, or malignant transformation. The literature is replete with retrospective series analyzing the impact of surgical resection on patient outcome 3,18,19,26. Keles et al. identified 30 articles on LGG published between 1970 and 2000 that incorporated statistical analyses and addressed the issue of resection. In order to reduce known biases, they eliminated studies that included pediatric

Volume 6, Issue 1; January-February 2023; Page No 658-668

patients, contained WHO grade 1 astrocytoma, or evaluated small numbers of patients (less than 75). They were left with only five articles that they deemed as valid studies, all of which demonstrated that extent of resection was a statistically significant variable in univariate analysis, and in four out of the five studies it was a significant factor in multivariate analysis 23. Pignatti et al. argued that good prognosis of LGG patients having undergone an extensive resection may not be due to the resection itself but to the limited size and superficial site of the tumor (thus being accessible to more extensive surgery) 14. Based on our own experience, we think that then impact of extent of surgery is difficult to ascertain due to the inadequate terminology used in surgical reports, which vary from surgeon to surgeon14.

Age is a well-established prognostic factor for survival in LGG, the prognosis being worse for older patients 16,17,18,25. The present series has failed to show any significant survival benefits for younger patients. A cut-off point at 40 years was chosen, but in clinical practice, this should not be interpreted as an absolute cut-off value.

A number of studies concerning LGG found some association between prognosis and signs and symptoms at presentation. One series observed a favorable outcome in patients presenting with seizures, other found the performance status to be of prognostic significance 4,16,17,18,25,27,30 . The present study did not reveal a significant association between the described parameters and patient survival.

Radiotherapy has been a mainstay of LGG therapy for decades, but much controversy has surrounded the radiation dose which should be delivered 46,47. The EORTC 22844 trial randomly assigned 379 patients with histologically confirmed LGG to receive irradiation postoperatively (or post biopsy) with either 45 Gy in 5 weeks or 59.4 Gy in 6.6 weeks. The minimum length of follow-up was 54 months. The conclusion of this study was that there was no significant difference between the low-dose and high-dose radiation groups as their 5-year progression-free survival (PFS) values were 47% and 50% 42. In a similar trial, the North Central Cancer Treatment Group (NCCTG), the Radiation Therapy Oncology Group (RTOG), and the Eastern Cooperative Oncology Group (ECOG) randomly assigned 211 patients to two groups. One hundred and eight patients received 50.5 Gy in 28 fractions and one hundred and three patients received 64.8 in 36 fractions. There was no difference in survival or PFS between the two groups. The 2- and 5-year survival in the low-dose radiation group was 94% and 72%, respectively. The 2- and 5-year survival in the high-dose radiation group was 85% and 64%. Likewise, the PFS at 5 years was 55% and 52%, respectively 15,34,41,43,44 .In our study, the total dose was not a prognostic factor for the 7-year APFS, as in the described trials.

Conclusion

The findings from our study confirmed by univariate and multivariate analysis, demonstrated that only astrocytoma histology is an important, statistically significant prognostic factor for progression free survival. The best prognosis is for patients with the fibrillary variant, and the worst for the gemistocytic one.

References

1. Brown, T.J.; Bota, D.A.; van Den Bent, M.J.; Brown, P.D.; Maher, E.; Aregawi, D.; Liau, L.M.; Buckner, J.C.; Weller, M.; Berger, M.S.; et al. Management of low-grade glioma: A systematic review and meta-analysis. Neurooncol. Pract. 2019, 6, 249–258.
2. Greuter, L.; Guzman, R.; Soleman, J. Pediatric and Adult Low-Grade Gliomas: Where Do the Differences Lie? Children 2021, 8, 1075.
3. Pouratian, N.; Schiff, D. Management of Low-Grade Glioma. Curr. Neurol. Neurosci. Rep. 2010, 10, 224–231.
4. Onder, H.; Kanyilmaz, G.; Aktan, M.; Karahacioglu, E. Prognostic factors for survival in adult patients with grade II glial tumors. J. Turgut Ozal. Med. Cent. 2018, 25, 105–111.
5. Tom, M.C.; Park, D.Y.J.; Yang, K.; Leyrer, C.M.; Wei, W.; Jia, X.; Varra, V.; Yu, J.S.; Chao, S.T.; Balagamwala, E.H.; et al. Malignant Transformation of Molecularly Classified Adult Low-Grade Glioma. Int. J. Radiat. Oncol. Biol. Phys. 2019, 105, 1106–1112.
6. Satar, Z.; Hotton, G.; Samandouras, G. Systematic review—Time to malignant transformation in low-grade gliomas: Predicting a catastrophic event with clinical,

Volume 6, Issue 1; January-February 2023; Page No 658-668

neuroimaging, and molecular markers. Neuro Oncol. Adv. 2021, 3, 1–12.
7. Murphy, E.S.; Leyrer, C.M.; Parsons, M.; Suh, J.H.; Chao, S.T.; Yu, J.S.; Kotecha, R.; Jia, X.; Peereboom, D.M.; Prayson, R.A.; et al. Risk Factors for Malignant Transformation of Low-Grade Glioma. Int. J. Radiat. Oncol. Biol. Phys. 2018, 100, 965–971.
8. Kaplan ME, Meier P. Non parametric estimation from incomplete observations. J Am Stat Assoc 1958;53: 457–83.
9. Mantel N. Evaluation of survival data and two new rank order statistics arising in its consideration. Cancer Chemother Rep 1996;20:163–70.
10. Cox DR. Regression models and life tables. J R Stat Soc B 1971;34:187–220.
11. Schiff D, Brown PD, Giannini C. Outcome in adult low-grade glioma: the impact of prognostic factors and treatment. Neurology 2007;69:1366–73.
12. Pouchieu, C.; Gruber, A.; Berteaud, E.; Ménégon, P.; Monteil, P.; Huchet, A.; Vignes, J.R.; Vital, A.; Loiseau, H.; Baldi, I. Increasing incidence of central nervous system (CNS) tumors (2000–2012): Findings from a population based registry in Gironde (France). BMC Cancer 2018, 18, 653.
13. Freyschlag, C.F.; Krieg, S.M.; Kerschbaumer, J.; Pinggera, D.; Forster, M.T.; Cordier, D.; Rossi, M.; Miceli, G.; Roux, A.; Reyes, A.; et al. Imaging practice in low-grade gliomas among European specialized centers and proposal for a minimum core of imaging. J. Neurooncol. 2018, 139, 699–711.
14. Pignatti F, vandenBent M, Curran D, et al. Prognostic factors for survival in adult patients with cerebral low-grade glioma. J Clin Oncol 2002;20:2076–84.
15. van den Bent MJ, Afra D, de Witte O, et al.; EORTC Radiotherapy and Brain Tumor Groups and UK Medical Research Council. Long-term efficacy of early versus delayed radiotherapy for low-grade astrocytoma and oligodendroglioma in adults: the EORTC 22845 randomised trial [published correction appears in Lancet. 2006;367:1818]. Lancet. 2005;366: 985-990.
16. Chang EF, Clark A, Jensen RL, et al. Multiinstitutional validation of the University of California at San Francisco low-grade glioma prognostic scoring system. Clinical article. J Neurosurg 2009;111(2):203–10.
17. Durmaz R, Vural M, Isildi E, et al. Efficacy of prognostic factors on survival in patients with low-grade glioma. Turk Neurosurg 2008;18:336–44.
18. Leighton C, Fisher B, Bauman G, et al. Supratentorial low-grade glioma in adults: an analysis of prognostic factors and timing of radiation. J Clin Oncol 1997;15:1294–301.
19. Xia, L.; Fang, C.; Chen, G.; Sun, C. Relationship between the extent of resection and the survival of patients with low-grade gliomas: A systematic review and meta-analysis. BMC Cancer 2018, 18, 48.
20. Piepmeier J, Crostopher S, Spencer D, et al. Variations in the natural history and survival of patients with supratentorial low-grade astrocytomas. Neurosurgery 1996;38:872–9.
21. Tunthanathip, T.; Sangkhathat, S.; Kanjanapradit, K. Risk Factors Associated with Malignant Transformation of Astrocytoma: Competing Risk Regression Analysis. Asian J. Neurosurg. 2021, 16, 777–784.
22. Papagikos MA, Shaw EG, Stieber VW. Lessons learned from randomized clinical trials in adult low grade glioma. Lancet Oncol 2005;6:240–4.
23. Keles GE, Lamborn KM, Berger MS. Low-grade hemispheric gliomas in adults: a critical review of extent of resection as a factor influencing outcome. J Neurosurg 2001;95:735–45.
24. Yeh SA, Ho JT, Lui CC, et al. Treatment outcomes and prognostic factors in patients with supratentorial low-grade gliomas. Br J Radiol 2005;78:230–5.
25. Lote K, Egeland T, Hager B, et al. Survival, prognostic factors, and therapeutic efficacy in low-grade glioma: a retrospective study in 379 patients. J Clin Oncol 1997;17:3129–40.
26. Acharya, S.; Lavrador, J.P.; Sekhon, P.P.; Visagan, R.; Jung, J.; Gullan, R.; Vergani, F.; Bhangoo, R.; Ashkan, K. Low-Grade Glioma Case Series: Lessons Learned from an Evolving 10- Year Single-Institution Multidisciplinary

Volume 6, Issue 1; January-February 2023; Page No 658-668

Team Practice. World Neurosurg. 2021, 151, 47–57
27. Zhao, Y.Y.; Chen, S.H.; Hao, Z.; Zhu, H.X.; Xing, Z.L.; Li, M.H. A Nomogram for Predicting Individual Prognosis of Patients with Low-Grade Glioma. World Neurosurg. 2019, 130, 605– 612.
28. Janny P, Cure H, Mohr M, et al. Prognostic parameters in benign astrocytomas. Cancer 1994;73:1937–45.
29. Grabenbauer GG, Roedel CM, Paulus W, et al. Supratentorial low-grade glioma: results and prognostic factors following postoperative radiotherapy. Strahlenther Onkol. 2000;176: 259-264.
30. Bauman G, Fisher B, Watling C, et al. Adult supratentorial low-grade glioma: long-term experience at a single institution. Int J Radiat Oncol Biol Phys 2009;5:1401–9.
31. Schomas DA, Laack NN, Brown PD. Low-grade gliomas in older patients: long-term follow- up from Mayo Clinic. Cancer 2009;17:3969–78.
32. Kerkhof, M.; Vecht, C.J. Seizure characteristics and prognostic factors of gliomas. Epilepsia 2013, 54, 12–17.
33. Coons SW, Johnson PC, Scheithauer BW, et al. Improving diagnostic accuracy and interobserver concordance in the classification and grading of primary gliomas. Cancer1997,79;1381-93.
34. Shaw EG, Berkey B, Coons SW, et al. Initial report of Radiation Therapy Oncology Group (RTOG) 9802: prospective studies in adult low-grade glioma (LGG) [abstract]. J Clin Oncol. 2006;24(suppl.): 58s.
35. Berben DMMJ. 33Y: follow-up of post-op irradiation for low-grade gliomas: results [abstract]. Neuro-Oncology. 2006;8: 43-44.
36. Claus EB, Horlacher A, Hsu L, et al. Survival rates in patients with low-grade glioma after intraoperative magnetic resonance image guidance. Cancer. 2005;103: 1227-1233.
37. Keles GE, Lamborn KR, Berger MS. Low-grade hemispheric gliomas in adults: a critical review of extent of resection as a factor influencing outcome. J Neurosurg. 2001;95: 735-745.
38. Smith JS, Chang EF, Lamborn KR, et al. The role of extent of resection in the long-term outcome of low-grade hemispheric gliomas [abstract]. Neuro-Oncology. 2007;9: 599-600.
39. Reijneveld JC, Sitskoorn MM, Klein M, Nuyen J, Taphoorn MJ. Cognitive status and quality of life in patients with suspected versus proven low-grade gliomas. Neurology. 2001;56: 618-623.
40. Piepmeier J, Christopher S, Spencer D, et al. Variations in the natural history and survival of patients with supratentorial low-grade astrocytomas. Neurosurgery. 1996;38: 872-878.
41. Hanzely Z, Polgar C, Fodor J, et al. Role of early radiotherapy in the treatment of supratentorial WHO grade II astrocytomas: long-term results of 97 patients. J Neurooncol. 2003;63: 305-312.
42. Karim ABMNF, Maat B, Hatlevol R, et al. A randomized trial on dose–response in radiation therapy of low-grade cerebral glioma: European Organization for Research and Treatment of Cancer (EORTC) Study 228444. Int J Radiat Oncol Biol Phys 1996;36:549–56.
43. Karim ABMF, Afra D, Cornu P, et al. Randomized trial on the efficacy of radiotherapy for cerebral low-grade glioma in the adult: European Organization for Research and Treatment of Cancer Study 22845 with the Medical Research Council Study BR04: an interim analysis. Int J Radiat Oncol Biol Phys 2002;52:316–24.
44. Shaw E, Arusell B, Scheithauer B, et al. Prospective randomized trial of low- versus high dose radiation therapy in adults with supratentorial low-grade glioma: initial report of a North Central Cancer Treatment Group/Radiation Therapy Oncology Group/Eastern Cooperative Oncology Group Study. J Clin Oncol 2002;20:2267–76.
45. Schultheiss TE, Kun LE, Ang KK, Stephens LC. Radiation response of the central nervous system [published correction appears in Int J Radiat Oncol Biol Phys. 1995;32:1269]. Int J Radiat Oncol Biol Phys. 1995;31: 1093-1112.
46. Mulhern RK, Ochs J, Kun LE. Changes in intellect associated with cranial radiation therapy. In: Gutin PH, Leibel SA, Sheline GE,

Volume 6, Issue 1; January-February 2023; Page No 658-668

eds. Radiation Injury to the Nervous System. New York: Raven Press; 1991: 325-340.

47. Jubelirer SJ, Rubin M, Shim C. An analysis of 38 cases of low-grade cerebral astrocytoma in adults. W V Med J. 1993;89: 102-105.

Volume 6, Issue 1; January-February 2023; Page No 658-668