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Research Article

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Exploring the Impact of Extent of Resection, MRI Findings and Genetic markers on Overall Survival in Low Grade Glioma Patients: Evaluation at the end of 1 year

Harsh Patel*, Preeti Singh, and Abhaya Kumar

Department *of Neurosurgery, Kokilaben Dhrirubhai Ambani Hosital and Medical Research Institute, Andheri (West), Mumbai – 400053*

***Corresponding author:**
Harsh Patel, Department of Neurosurgery, Kokilaben Dhrirubhai Ambani Hosital and Medical Research Institute, Andheri (West), Mumbai – 400053.

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Abstract

Background: *Diffuse low-grade glioma (LGG), i.e WHO grade II glioma, is a rare brain cancer, whose etiopathogenesis is poorly understood, making difficult the prediction of its natural course, especially at an individual level. LGG spontaneously exhibits different stages in its evolution, namely (i) a pre- symptomatic period in which the tumor is usually slow growing, as demonstrated in cases of incidental discovery (ii) a symptomatic period in which the glioma induces clinical consequences, usually seizures and/or mild cognitive impairments visible on neuropsychological assessment , while continuing to progress slowly but constantly (about 3 4 mm mean diameter per year) and (iii) a period of malignant transformation (MT) with acceleration of the growth rate, resulting in more severe neurological deficits and ultimately death .*

Aims and Objectives: *To evaluate the surgical effect on survival in patients with low-grade glioma (LGG). To identify factors that influence survival for patients that underwent surgical resection of LGGs.*

Materials and Methods: *Data of patients who underwent surgery for excision of LGGs during the years 2019 2023 in Koikilaben Dhirubhai Ambani Hospital & Research Institute will be collected from the Department of Neurosurgery database. Data of operated patient would be thoroughly examined, pre- and post- operative neurological status, size of the lesion would be measured volumetrically comparing the pre- and post-operative MRI imaging along with other features of lesion at interval of 1week, 3months, 6months and 1 year. The neurological deficits and progression free survival will be closely monitored.*

Results: *In this study, we evaluated the impact of extent of resection, MRI findings, and 1p/19q status on tumor progression in 78 patients with low-grade glioma (LGG) over a 12-month follow- up period. Our findings indicate that age under 40 years, IDH-mutant status, safe maximal surgical resection, and early initiation of chemotherapy and/or radiotherapy (CT/RT) for residual lesions were associated with better clinical outcomes. Among the 57 patients with IDH-mutant tumours, the lesion size remained stable over the 1-year follow-up period. In contrast, of the 21 patients with IDH-wildtype tumours, 6 showed an increase in residual lesion size, and 9 experienced tumour recurrence. Patients with 1p/19q codeletion responded more favourably to CT/RT compared to those with 1p/19q retention. Specifically, 56 patients with the 1p/19q codeleted status demonstrated stable residual lesions or no recurrence, indicating a better response to chemotherapy. On the other hand, in the 22 patients with 1p/19q retention, tumour progression or recurrence was observed despite early initiation of CT/RT. These findings underscore the importance of molecular markers (IDH and 1p/19q status) and extent of surgical resection in guiding treatment strategies and improving outcomes in LGG patients.*

Conclusion: *Our single-institution cohort of 78 patients confirmed that in lower-grade gliomas, the IDH mutation is the most significant predictor of clinical outcomes. Patients with IDH-wildtype tumors demonstrated significantly shorter progression-free survival compared to those with IDH-mutant tumors. Importantly, IDH mutation status appeared to outweigh traditional histological grading, as there was no significant difference in median overall or progression- free survival between IDH-mutant grade II and grade III tumours.*

The integration of molecular biomarkers particularly IDH mutation and 1p/19q codeletion into routine diagnostic workflows represents a major advancement in the field. This molecularly integrated approach is essential not only for accurate prognosis but also for the development of personalized treatment strategies. For example, identification of 1p/19q codeletion may guide clinicians toward more intensive chemotherapy regimens, whereas IDH-mutant, 1p/19q-retained tumours may benefit from alternative therapeutic approaches.

Our findings reinforce the growing importance of incorporating molecular diagnostics into glioma classification and treatment planning. This personalized, biomarker-driven strategy enhances our understanding of glioma biology and supports more precise, patient-centred care. Additionally, the study underscores the critical need for continued research into the molecular underpinnings of gliomas, as ongoing discoveries in tumour genetics will further refine how we classify, treat, and ultimately improve outcomes for patients with these tumours.

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Keywords: Low-grade Glioma, IDH Mutation, 1p/19q Codeletion, Extent of Resection, MRI Findings, Peritumoral edema.

Introduction

Diffuse low-grade glioma (LGG), i.e. WHO grade II glioma, is a rare brain cancer, whose etiopathogenesis is poorly understood, making difficult the prediction of its natural course, especially at an individual level. LGG spontaneously exhibits different stages in its evolution, namely (i) a pre- symptomatic period in which the tumor is usually slow growing, as demonstrated in cases of incidental discovery (ii) a symptomatic period in which the glioma induces clinical consequences, usually seizures and/ or mild cognitive impairments visible on neuropsychological assessment , while continuing to progress slowly but constantly (about 3 4 mm mean diameter per year) (iii) a period of malignant transformation (MT) with acceleration of the growth rate, resulting in more severe neurological deficits and ultimately death [1,2]. However, LGG represents a heterogeneous group of tumors with various courses, which are difficult to predict at the individual level and at each stage of the disease. In addition, due to its unknown origin and diffuse features within the central nervous system, this is an incurable tumoral disease [3].

The management of LGGs is primarily centred on surgical resection, as histological and molecular analyses are crucial for accurate diagnosis and prognostication. Needle biopsies have been associated with misdiagnosis rates exceeding 50%, making surgical resection the preferred method for tumour characterization [4]. Extensive surgical resection has been shown to improve overall survival (OS) and progression-free survival (PFS), with studies indicating that patients undergoing gross total resection (GTR) have significantly better outcomes compared to those with subtotal resection (STR). However, factors such as tumour location, involvement of critical brain structures, and histological subtype can influence the feasibility of achieving GTR [5, 6].

Molecular profiling has become integral in the management of LGGs, as it provides insights into tumour behaviour and potential therapeutic targets. Key molecular markers include mutations in the isocitrate dehydrogenase (IDH) gene and co-deletion of chromosomes 1p and 19q. IDH-mutant tumours, particularly those with 1p/19q co-deletion, generally have a more indolent course and better response to treatment compared to IDH-wild-type tumours, which tend to be more aggressive [7]. The identification of these molecular subtypes has led to more personalized treatment approaches, including tailored surgical strategies and adjuvant therapies. Despite advances in surgical techniques and molecular diagnostics, the prognosis for patients with LGGs remains variable [8]. Factors such as age, performance status, tumour volume, and molecular characteristics play significant roles in determining outcomes. For instance, younger patients with favourable performance status and IDH-mutant tumours tend to have better survival rates. Conversely, older patients and those with IDH-wild-type tumours often experience more aggressive disease progression and poorer outcomes [9, 10].

The treatment paradigm for LGGs has evolved to incorporate multimodal strategies, including surgery, radiation therapy, and chemotherapy. Early postoperative radiation has been associated with improved PFS, while chemotherapy has demonstrated benefits in both PFS and OS, particularly in patients with IDH1-mutant tumors. However, the optimal timing and combination of these therapies remain subjects of ongoing research and debate [11].

Quality of life (QoL) is a critical consideration in the management of LGG patients. While surgical resection can alleviate symptoms and improve neurological function, it may also lead to postoperative deficits, including cognitive impairments and fatigue. Studies have shown that patients often experience a decline in QoL following surgery, with issues such as fatigue, insomnia, and cognitive dysfunction persisting long-term. These factors underscore the importance of a multidisciplinary approach to care, focusing not only on survival but also on maintaining and improving patients' functional status and overall well-being [12-14].

In conclusion, the management of LGGs requires a comprehensive and individualized approach that considers the molecular characteristics, the patient's clinical status, and the potential impact on quality of life. Advancements in surgical techniques, molecular diagnostics, and adjuvant therapies have improved outcomes for many patients; however, challenges remain in optimizing treatment strategies and predicting disease progression. Ongoing research and clinical trials are essential to further refine management protocols and enhance the prognosis for individuals affected by these complex tumours [15].

The aim of this study is to evaluate the surgical effect on survival and to identify factors that influence survival for patients that underwent surgical resection of LGGs.

Review of Literature

Over the past decade, advances in molecular genetics have led to a paradigm shift in CNS tumor diagnostics. The 2016 WHO classification introduced molecular alterations into the diagnostic work-up of certain tumors, establishing an integrated diagnosis combining histopathology and molecular information. Building upon this foundation, the 2021 WHO CNS5 edition further emphasizes the role of molecular data, incorporating recent discoveries to refine tumor classification and guide clinical practice [2-4]. Primary central nervous system (CNS) tumors account for approximately 2 3% of all cancers. In Western countries, the annual incidence is about 15 cases per 100,000 people, with a prevalence of approximately 69 per 100,000. In children, CNS tumors are the second most common cancer after leukemia. Among these, gliomas, originating from glial cells, are the most prevalent type [3]. Gliomas are brain tumors classified by the World Health Organization (WHO) into four grades based on malignancy. Grade I tumors, like pilocytic astrocytomas, are benign and slow-growing, primarily affecting children. Grade II tumors are low- grade, often infiltrative, and may recur as higher-grade lesions. Grade III tumors are malignant and tend to recur aggressively. Grade IV tumors, such as glioblastomas, are the most aggressive and common in adults, with a peak incidence between 50 and 60 years [4, 5].

The histological classification and grading to date still represents the most reliable and meaningful indicator for the biological and clinical behavior of gliomas as well as patient outcome. Patients with WHO grade I tumors can usually be cured by surgical resection. WHO grade II tumors -though still exhibiting a rather slow growth- nearly invariably recur after resection and bear the inevitable tendency to progress to anaplastic gliomas of WHO grade III or secondary glioblastomas of WHO grade IV. Thus, median survival of patients with WHO grade II gliomas is in the range of only 5 8 years after diagnosis [5]. Anaplastic gliomas (WHO grade III) are rapidly growing malignant tumors that, in addition to surgery, require aggressive adjuvant treatment with radio- and/or chemotherapy. Median survival time is just 2 3 years after diagnosis, except for the subgroup of patients with anaplastic oligodendroglial tumors, who often do better, in particular when their tumors carry a prognostically favorable combined deletion of chromosomal arms 1p and 19q, as outlined below [6].

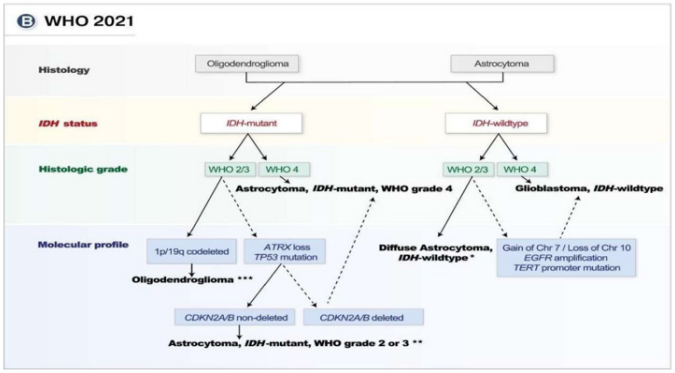

Figure 1: Classification and grading of the main glioma subtypes according to the WHO classification of tumors of the central nervous system.

Diffuse low-grade gliomas (DLGGs) are slow-growing, infiltrative brain tumors that often progress to higher-grade malignancies over time [3]. Incidentally discovered low-grade gliomas (iLGGs) are asymptomatic tumors found during imaging for unrelated reasons, representing a rare subset of DLGGs [4]. These tumors, though clinically silent, exhibit continuous growth along white matter pathways and have an intrinsic tendency for malignant transformation. The median interval from incidental detection to symptomatic progression is approximately 48 months. While traditional management favored a "wait and see" approach, recent trends advocate for early surgical intervention, even in asymptomatic cases, to reduce the risk of malignant progression and improve patient outcomes [5,6].

Due to the rarity of LGGs and difficulty in long-term follow-up, prospective and retrospective studies clarifying questions regarding optimal management for these tumors are lacking. Thus, we set out to identify the factors that influence outcome and survival for patients that underwent early surgery for LGGs [7,8].

Pathological Characterization of LrGGs the WHO Classification

The 2021 WHO Classification of Tumors of the Central Nervous System (CNS5) represents a significant evolution in glioma diagnosis, integrating molecular parameters alongside histopathological features. Building upon the 2016 edition, CNS5 emphasizes an "integrated diagnosis," where molecular alterations play a pivotal role in classification and prognostication. This approach aligns with the 2014 International Society of Neuropathology's Haarlem consensus guidelines, which advocated for incorporating molecular data into tumor classification to enhance diagnostic precision and therapeutic decision-making. Consequently, CNS5 has redefined entities such as glioblastoma and IDH-mutant gliomas, underscoring the necessity of molecular profiling in contemporary neuro-oncology practice [5,6]. The 2021 WHO Classification of Tumors of the Central Nervous System (CNS5) has revolutionized glioma diagnosis by integrating molecular profiling with traditional histopathology. This "integrated diagnosis" approach emphasizes molecular alterations such as IDH mutations, 1p/19q codeletions, and TERT promoter mutations over histological features alone, providing a more accurate reflection of tumor biology and behavior. Consequently, molecular characterization has become essential for classification, prognostication, and therapeutic decision-making in gliomas [7,8]. Tumor grading has become secondary to molecular profiling in glioma classification, with molecular alterations now taking precedence over histological features. A pivotal molecular marker in low-grade gliomas (LGGs) is the isocitrate dehydrogenase 1 (IDH1) mutation, specifically the R132H variant. This mutation, first identified through genome-wide sequencing efforts, leads to the production of the on-cometabolite D-2-hydroxyglutarate (2-HG), which disrupts normal celluler processes by inhibiting α-ketoglutarate dependent dioxygenases. Consequently, IDH1 mutations are associated with epigenetic alterations, including DNA hypermethylation, and are considered early events in glioma genesis. The presence of IDH1 mutations in LGGs is linked to improved prognosis and response to treatment, underscoring their clinical significance in neuro-oncology [9, 10]. The 2021 WHO CNS5 classification emphasizes molecular diagnostics over histology, integrating molecular alterations into glioma diagnosis and grading [22].

Table 1: Classification of Diffuse gliomas as per WHO CNS5 classification

2021 WHO CNS5 Classification of Tumours of the Central Nervous System
Adult-type diffuse gliomas
Astrocytoma, IDH-mutant
Oligodendroglioma, IDH-mutant and 1p/19q-codeleted
Glioblastoma, IDH-wildtype
Pediatric-type diffuse low-grade gliomas
Diffuse astrocytoma, *MYB- or MYBL1-altered*
Angiocentric glioma
Polymorphous low-grade neuroepithelial tumour of the young
Diffuse low-grade glioma, MAPK pathway-altered
Pediatric-type diffuse high-grade gliomas
Diffuse midline glioma, H3 K27-altered
Diffuse hemispheric glioma, H3 G34-mutant
Infant-type hemispheric glioma

Figure 2: Classification of Diffuse gliomas as per WHO CNS5 classification 2021

IDH1 mutations are prevalent in diffuse lower-grade gliomas (LGGs) and secondary glioblastomas (GBMs), but rare in primary GBMs and absent in pilocytic astrocytomas, ependymomas, or medulloblastomas [11]. The most common mutation is a missense change at codon 132 (R132H), which impairs enzymatic activity and leads to the production of 2-hydroxyglutarate, a metabolite associated with tumorigenesis.

IDH1 mutations serve as strong prognostic markers, correlating with improved survival outcomes, particularly when combined with 1p/19q co-deletion. This co-deletion is nearly exclusive to IDH-mutant tumours and is associated with better overall survival and responsiveness to chemotherapy [30]. The WHO CNS5 classification integrates these molecular features, categorizing gliomas into subgroups such as "Astrocytoma, IDH-mutant" and "Oligodendroglioma, IDH-mutant and 1p/19q-codeleted," each with distinct prognostic implications. This molecular stratification enhances diagnostic precision and guides therapeutic decisions [12-14].

Diffuse low-grade gliomas (LGGs) are a heterogeneous group of intrinsic brain tumors characterized by initially indolent growth and a significant tendency for recurrence and malignant transformation. Incidentally discovered LGGs (iLGGs) are rare, asymptomatic tumors identified during imaging for unrelated reasons. Due to their rarity and challenges in long-term follow-up, there is limited data on the management of iLGGs. While early and maximal safe resection is the first-line treatment for symptomatic LGGs (sLGGs), the optimal management approach for iLGGs remains under investigation.[15]

Related Factors

Glioma Tumoral Volume

Diffuse low-grade gliomas (LGGs) exhibit variable volumes at diagnosis, ranging from 0.39 to 386cm^3. While a size ≥ 6cm was traditionally considered an adverse prognostic factor, recent studies indicate that larger tumor volumes are significantly associated with a higher risk of malignant transformation (MT) and shorter overall survival (OS). Interestingly, incidental LGGs (iLGGs), which are asymptomatic and detected incidentally, tend to have smaller volumes at discovery and exhibit slower growth compared to symptomatic LGGs. Despite their smaller size, iLGGs still carry a risk of progression and MT, emphasizing the need for early diagnosis and intervention. Consequently, a screening policy has been proposed to diagnose and treat LGGs earlier, optimizing the opportunity to understand the origin of these tumors and potentially improving patient outcomes [16,17].

Growth Rate

Tumor growth velocity, measured as the rate of change in mean glioma diameter over time, is a significant prognostic factor in diffuse low-grade gliomas (LGGs) [18]. is associated with a higher risk of malignant transformation (MT) and shorter overall survival (OS). This marker is independent of molecular profiles, including IDH status, and can aid in identifying tumors at higher risk of progression during the pre-therapeutic period. Monitoring growth velocity through regular MRI assessments (every 3 6 months) is recommended for early intervention and to guide treatment decisions, even in asymptomatic patients [19,20].

Pattern of Migration versus Proliferation and Tumor Location

Gliomas preferentially invade along white matter (WM) tracts, a pattern evident both radiologically and pathologically. Tumor cells often migrate along the periphery of these tracts, with myelin status influencing this behavior. In regions where myelin is intact, glioma cells encounter inhibitory molecules that restrict migration. Conversely, in areas of demyelination, these inhibitory effects are diminished, facilitating tumor spread. This dynamic is particularly relevant in adolescents, as the maturation of WM tracts during this period may influence both the onset and progression of glioma [21].

The Peritumoral Zone

Low-grade gliomas (LGGs) are heterogeneous and poorly defined neoplasms, with isolated tumor cells (ITCs) extending beyond the MRI-visible lesion core. Biopsy samples have identified ITCs up to 10 20 mm from the tumor core, particularly at the periphery, where the cycling tumor cell fraction is higher in 62.5% of patients. This peripheral distribution of ITCs contributes to the high risk of recurrence even after extensive resection. The peritumoral zone (PTZ), defined as the region surrounding the contrast-enhancing tumor core, exhibits inter individual variability, with ITCs detected up to 20 mm away. Understanding the PTZ is crucial for improving surgical strategies and therapeutic approaches to reduce recurrence rates [22-23].

Metabolic Changes

Recent advancements in multimodal MRI and PET imaging, particularly using tracers like F- DOPA, have enhanced the detection of glioma progression and recurrence. F-DOPA PET, in particular, has shown increased sensitivity in identifying areas of malignant transformation within low-grade gliomas (LGGs) before conventional MRI enhancement becomes apparent. This capability allows for earlier intervention, potentially improving patient outcomes. Additionally, integrating machine learning classifiers with longitudinal MRI data can predict glioma behavior changes, offering a non-invasive method to monitor tumor dynamics and inform timely treatment decisions [24].

Multicentric LGG and Leptomeningeal Dissemination

Multicentric low-grade gliomas (LGGs) are rare, accounting for 2 10% of cases, and present as multiple, spatially separated lesions without anatomical continuity. These tumors may arise synchronously or metachronously, even in the absence of local recurrence. The pathophysiology remains poorly understood, but factors such as IDH-wildtype status and PDGFRA amplification have been implicated in more aggressive tumor behavior and earlier recurrence. Despite their rarity, multicentric LGGs can be safely resected, often through single or staged surgeries, with favorable functional outcomes. Adjuvant therapies, including chemotherapy, may be considered, especially when high-grade transformation occurs. Similarly, leptomeningeal dissemination (LMD) of LGGs, previously uncommon, is increasingly recognized due to advancements in imaging and prolonged survival. LMD can manifest even without local tumor progression, underscoring the need for a comprehensive treatment approach that considers potential global dissemination of the disease [25].

Histomolecular Profile and Intratumoral Heterogeneity

Molecular profiling has significantly advanced the classification and prognostication of low- grade gliomas (LGGs), moving beyond traditional histological assessments. Key genetic markers such as IDH mutation, 1p/19q codeletion, MGMT methylation, and TERT promoter mutations are integral to the

2021 WHO classification, offering insights into tumor behavior and therapeutic responses. However, these markers may not always predict individual outcomes accurately; for instance, IDH-mutant LGGs can exhibit aggressive progression, while IDH- wildtype tumors may demonstrate prolonged survival, especially following extensive surgical resection. Moreover, intratumoral heterogeneity is common in LGGs, with distinct histomolecular components observed within the same tumor, potentially influencing treatment efficacy and necessitating caution in therapeutic decision-making [26-28].

External Factors Neurocognitive Assessment

A comprehensive assessment of neurocognitive function (NCF) is essential in evaluating patients with low-grade gliomas (LGGs), as these tumors can disrupt multiple brain networks. Neurological examinations often appear normal, making NCF testing through detailed neuropsychological assessments crucial. Such evaluations can identify subtle cognitive deficits, provide accurate estimates of symptom burden, and guide therapeutic strategies, including rehabilitation efforts targeting language, memory, and executive functions. Notably, baseline cognitive function may be significantly affected even before surgical intervention, emphasizing the importance of early and thorough assessment [29-30].

Familial Predisposition

Familial low-grade gliomas (LGGs) are rare, accounting for approximately 5 10% of all glioma cases [31-32]. While some familial gliomas are linked to high-penetrance mutations in syndromic genes like TP53 and POT1, most cases lack identifiable single-gene causes. Genome-wide association studies have identified several low-penetrance single nucleotide polymorphisms (SNPs) associated with glioma risk, including rs55705857 near CCDC26 at 8q24.21, which is more prevalent in individuals with IDH-mutant gliomas. Despite these genetic associations, the molecular profiles of familial and sporadic LGGs are largely similar, suggesting that familial gliomas share common pathways with their sporadic counterparts. Screening first-degree relatives of glioma patients for these genetic variants may aid in early detection and intervention [34-35].

Age

Age is a significant prognostic factor in low-grade glioma (LGG) patients. Studies indicate that older age correlates with poorer outcomes, with survival rates decreasing as age increases. For instance, a study found that older patients with LGG had a median overall survival of 2.7 years, compared to younger patients who had a median survival of 4.1 years. Additionally, older patients are more likely to present with multifocal tumors, higher-grade histology, and more neurological deficits, which contribute to worse prognoses. These findings underscore the importance of considering age in the management and treatment planning for LGG patients [36].

Pregnancy

Pregnancy may influence the progression of low-grade gliomas (LGGs). A cohort study found that 43.7% of women with stable LGGs experienced tumor behavior changes during or within three months after pregnancy, including increased growth rate and contrast enhancement. The median overall survival from delivery was 5.7 years, with a median time to death of 3.9 years. Factors such as postoperative tumor residual volume and pre-pregnancy tumor growth rate were significant predictors of post-pregnancy survival. These findings underscore the importance of careful monitoring and pre-pregnancy counseling for women with LGGs considering motherhood [37-38].

Therapeutic Factors and LGG

Type of Resection

Early maximal resection is the preferred initial treatment for low-grade gliomas (LGGs), as it is associated with improved overall survival (OS). A meta-analysis has shown that gross total resection (GTR) significantly reduces mortality and progression risk compared to subtotal resection (STR) at all time points. Achieving a "supra-complete" resection, which extends beyond the MRI-defined tumor margins into the peritumoral zone (PTZ), may further decrease recurrence rates and delay malignant transformation. Long-term follow-up indicates that such extensive resections can lead to prolonged survival while maintaining quality of life. Therefore, systematic assessment of residual tumor volume post-surgery and consideration of early reoperation at relapse are recommended strategies to optimize patient outcomes [39-40].

Adjuvant Medical Treatments

Chemotherapy is a viable initial treatment for low-grade gliomas (LGGs), particularly in oligodendrogliomas. A systematic review indicates that chemotherapy is associated with decreased mortality at 5 and 10 years. Early radiation therapy (RT) was not associated with decreased mortality, although progression-free survival (PFS) was improved compared with patients receiving delayed or no radiation. Combining RT with procarbazine, CCNU (lomustine), and vincristine (PCV) resulted in prolonged overall survival (OS) compared with RT alone. Biomathematical modeling might also be helpful to simulate and compare the activity of different chemo- radiotherapy strategies in silico. However, LGGs may acquire chemoresistance, and temozolomide can induce hypermutation in a subset of tumors. Identifying factors that predict such mutational changes is crucial for selecting the appropriate treatment at the optimal time for each patient [41-42]. Study done by Pallud et al in 47 patients showed iLGGs have a female predominance ($P = .05$), smaller initial tumor volumes ($P < .001$), lower incidence of contrast enhancement ($P = .009$), and are more likely to undergo gross total surgical removal ($P < .001$) [12].

Study done by Potts et al in 37 patients showed iLGGs have a significantly lower preoperative tumor volumes than sLGGs(20.2 vs 53.9 cm^3, $P = .001$), less likely to have tumors in eloquent locations (14.3% vs 61.9%, $P = .001$), and a higher prevalence of females (57.1% vs 36%, $P = .02$). In addition, patients with LGGs were also more likely to undergo gross total resection (60% vs 31.5%, $P = .001$) and had improved overall survival on Kaplan- Meier analysis ($P = .039$).[13]

Study done by Zhang et al in 23 patients showed LGGs had higher preoperative KPS ($P < .001$), smaller tumor volume ($P = .014$), lower frequency of eloquent areas involvement ($P < .001$) and higher rate of complete resection ($P = .037$) comparing to those with sLGGs.[14]

Study done by Ius et al in 34 patients showed LGGs had higher preoperative Karnofsky performance scale (KPS) (P = .003), smaller tumor volume (P = .0001), lower frequency of eloquent areas involvement (P = .0001), and higher rate of complete resection (P = .0001) compared to those with sLGGs [15].

Study done by Gogos et al in 113 patients showed Complete resection of the FLAIR abnormality was achieved in 57% of patients with incidental lesions but only 23.8% of symptomatic lesions (P < .001), and the residual volumes were smaller for LGGs (2.9 vs 13.5 cm3, P < .0001). Overall survival was significantly longer for patients with incidental tumors (median survival not reached for patients with iLGGs vs 14.6 yr for those with sLGGs, P < .0001) [16].

Lacunae in Literature
In this review we have summarized that LGG is a disease with low malignant potential and slow progression. If the calculation of survival of LGG patients takes into account the silent phase of the disease, then surgical timing (namely, whether surgery was performed before or after symptom occurrence) has no significant effect on survival, but other factors (namely, total resection and the pathology of oligodendroglioma) are significantly positively correlated with PFS and OS. Total resection can also significantly prolong MPFS. Thus, in the clinical practice, if an initial imaging diagnosed LGG shows slow growth behavior during follow-up, the diagnosis of LGG should be highly suspected, and surgical planning should be performed accordingly.

Research Question
How fast will a low-grade glioma grow?

How should low grade gliomas be monitored after treatment?

Aims & Objectives
Primary Objectives: To evaluate the effect of surgical excision, MRI findings and genetic markers on survival in patients with low-grade glioma (LGG) at the end of one year.

Secondary Objectives: To identify factors that influence survival for patients that underwent surgical resection of LGGs which includes secondary treatment radiotherapy and chemotherapy

Material and Methods
Study Area: Study was conducted at Kokilaben Dhirubhai Ambani Hospital and Medical Research Institute.

Study Population: All patients diagnosed with Primary CNS Glioma admitted in Neurosurgery department of Kokilaben Dhirubhai Ambani Hospital and Medical Research Institute during year January 2019 - December 2023 post IEC approval.

Sample size: Based on literature, the prevalence of CNS tumors is 2-3%. Sample size was calculated considering 3% prevalence, 99% confidence level to achieve 5% confidence limits and design effect of 1. Sample size was calculated to be 78.
Sample size n=[DEFF*Np (1-p)]/ [(d2/Z21-α/2*(N-1) +p*(1-p)]

n==1*((1000000*0.03*0.97)/(((0.05^2)/(2.575^2))*(1000000-1)) + (0.03*0.97)) n= 77

where p = proportion of affected population = 3% =0.03 1-p = 1-0.03 = 0.97

d is confidence limit = 5% = 0.05
Z = confidence level = 99% = 2.575
N = population size = 1000000 DEFF - Design effect = 1

Statistical methods: Data would be analysed using SPSS software for Windows. Data would be presented as Mean/ SD or frequency (%). Crocs tabulations would be computed and compared using chi-square test. p <0.05 would be considered statistically significant.

Study Design: Single center retrospective observational study.

Study Criteria
Inclusion Criteria:
1. Age between18 -80 years.
2. Patients with low-grade gliomas diagnosed histopathologically.
3. Patients with lesions in the supratentorial region.
4. No previous surgery.
5. No preoperative chemo- or radiotherapy.
6. Availability of data about post-surgery neurological and clinical status

Exclusion Criteria:
1. Patients were pathologically diagnosed as high-grade gliomas
2. Patients with pediatric gliomas or subtentorial gliomas

Study detail and intervention: This is single center retrospective exploratory study. No intervention will be done.

Study Methodology/Procedure: Data of patients who underwent surgery for excision of LGGs during the years 2019 2023 in Kokilaben Dhirubhai Ambani Hospital & Medical Research Institute will be collected from the Department of Neurosurgery database. Data of operated patient would be thoroughly examined, pre- and post-operative, neurological status, size of the lesion would be measured volumetrically comparing the pre- and post-operative MRI imaging along with other features of lesion at interval of 1week, 3months, 6months and 1 year. The percentage of excision was estimated. The neurological deficits were stated as occurred or not as regard the motor, sensory, and speech systems. Resolution of neurological deficits and other treatment modalities such as radiation, chemotherapy in patients on subsequent follow- up examinations will be documented.

Study Duration: Data of patients diagnosed with Primary CNS low-grade Glioma admitted in Neurosurgery department of Kokilaben Dhirubhai Ambani Hospital and Medical Research Institute during academic year January 2019 - December 2023, will be collected post IEC approval.

Method of measurement of outcome of interest: Based on extent of resection calculated from pre and post operative MRI findings outcome will be measured in terms of neurological deficits and progression free survival/overall survival.

Data Collection Methods: Patients will be enrolled only if a patient qualifies for the study. performa /case record form. The data will be cross checked with source data.

Statistical Method

Data would be analyzed using SPSS software for Windows. Data would be presented as Mean/ SD or frequency (%). Crocs tabulations would be computed and compared using chi-square test. $p<0.05$ would be considered statistically significant.

Ethical Consideration

kept entirely confidential and privacy of the data will be maintained. In order to ensure confidentiality and privacy, we will codify and anonymize the data and collected data will be secured in order to restrict the access to study team members, Institutional Ethics Committee Academics and representatives of national and local health authorities only.

Patient's name will be replaced with a special code called that identifies the patient. This code, along with Study Information, will be used for the study purposes as mentioned in the study protocol.

Patient name will be available only to the following people or agencies: the Study Doctor and staff; and authorized representatives of the Study Doctor; Institutional Ethics Committee Academics, health authority inspectors, such as (but not limited to) the Drug Controller General of India, designated study monitors and auditors.

Study will be initiated only post IEC-A approval. All retrospective data will be analyzed. Application for wavier of Consent.

Results

Table 1: Clinical and Tumor Characteristics of the Sample Set According to IDH Mutation Status

Characteristic	Total (n=78)	IDH Mutant (n=60)	IDH Wild Type (n=18)	p-value
Age, Median (IQR)	41.5 (35.75-63.25)	37.5 (32.25-43.75)	51 (39.75-61.5)	0.078
Gender				0.243
- Male	44 (56.4)	36 (60.0)	8 (44.4)	
- Female	34 (43.6)	24 (40.0)	10 (55.6)	
Histologic Type and Grade				0.423
- Oligodendroglioma Grade II	27 (34.6)	22 (36.7)	5 (27.8)	
- Oligodendroglioma Grade III	5 (6.4)	4 (6.7)	1 (5.6)	
- Oligoastrocytoma Grade II	1 (1.3)	0 (0.0)	1 (5.6)	
- Oligoastrocytoma Grade III	2 (2.6)	1 (1.7)	1 (5.6)	
- Ganglioma Grade I	2 (2.6)	1 (1.7)	1 (5.6)	
- Astrocytoma Grade II	9 (11.5)	6 (10.0)	3 (16.7)	
- Astrocytoma Grade III	21 (26.9)	16 (26.7)	5 (27.8)	
- Other	11 (14.1)	10 (16.7)	1 (5.6)	
Extent of Resection				0.153
- Total Resection (TR)	30 (38.4)	28 (35.8)	2 (2.56)	
- Sub Total Resection (GTR)	48 (61.53)	29 (37.17)	19 (24.35)	
Tumor Location				0.833
- Frontal lobe	39 (50.0)	31 (51.7)	8 (44.4)	
- Parietal lobe	15 (19.2)	11 (18.3)	4 (22.2)	
- Temporal lobe	9 (11.5)	6 (10.0)	3 (16.7)	
- Other	15 (19.2)	12 (20.0)	3 (16.7)	
Eloquent Area Involved				0.395
- Yes	24 (30.8)	17 (28.3)	7 (38.9)	
- No	54	43 (71.7)	11	
	(69.2)		(61.1)	
First Presenting Symptoms				
- Seizure	22	18	04	
- Headache	78	68	10	
- Mental Change	12	02	10	
- Motor/Movement	24	09	15	
- Speech	05	03	02	
- Visual	04	02	02	
- Incidental	01	01	00	
Type of Surgery				0.049
- Awake	33 (42.3)	29 (48.3)	4 (22.2)	
- Asleep	45 (57.7)	31 (51.7)	14 (77.8)	
1p 19q Status				0.057
- Codeleted	56 (71.79)	54 (69.23)	02 (2.56)	
- Retained	22 (28.20)	2 (2.5)	20 (25.64)	

Data presented as median (IQR) and number (%).

This table presents a comparison of clinical characteristics between IDH mutant and IDH wild-type patients with low-grade gliomas (LGGs). The p-values indicate the statistical significance of differences between these two groups.

1. Age at Diagnosis

In our cohort, the median age at diagnosis was 41.5 years. Notably, patients with IDH-wildtype tumours were significantly older, with a median age of 51 years, compared to a median age of 37.6 years in patients with IDH-mutant tumours. This age disparity further supports the biological and clinical differences between IDH-wildtype and IDH-mutant lower-grade gliomas.

2. Gender Distribution

Males comprised the majority of the overall cohort (56.4%). When stratified by IDH status, 60% of patients with IDH-mutant tumors were male, compared to 44.4% in the IDH-wildtype group. Conversely, females represented 55.6% of the IDH-wildtype group and 40% of the IDH-mutant group. Despite these observed differences, the variation in gender distribution between IDH-mutant and IDH-wildtype patients was not statistically significant ($p = 0.243$), indicating no meaningful gender-based disparity between the groups.

3. Histologic Type and Grade

The most common histologic subtype in our cohort was Oligodendroglioma Grade II, accounting for 34.6% of cases, followed by Astrocytoma Grade III at 26.9%.

When stratified by IDH status:

- IDH-mutant tumours were more frequently classified as Oligodendroglioma Grade II (36.7%) and Astrocytoma Grade III (26.7%).
- In contrast, IDH-wildtype tumours displayed a more even distribution across various histologic subtypes, without a dominant pattern.

These findings highlight the histologic and molecular correlations that may guide more tailored diagnostic and therapeutic decisions.

4. Extent of Resection

Total resection (TR) was achieved in 30 patients across the cohort. When stratified by IDH status:

1. 83.3% of IDH-mutant patients underwent total resection.
2. In contrast, 55.6% of IDH-wildtype patients were more likely to undergo subtotal resection.

This difference was statistically significant ($p < 0.05$), suggesting that IDH-mutant tumours may be more amenable to complete surgical removal.

5. Tumor Location

The frontal lobe was the most common site of tumour origin, observed in 50% of cases, followed by the parietal lobe (19.2%) and temporal lobe (11.5%).

1. IDH-mutant tumours were slightly more likely to occur in the frontal lobe (51.7%).
2. IDH-wildtype tumours were more evenly distributed across different lobes.

However, the difference in tumour location distribution between IDH-mutant and IDH-wildtype groups was not statistically significant ($p = 0.833$), indicating no strong association between IDH status and tumour location.

6. Eloquent Area Involvement

Overall, 30.8% of patients had tumours located in eloquent brain regions (areas critical for language, motor, or sensory function).

- IDH-wildtype tumours were more frequently located in eloquent areas (38.9%).
- IDH-mutant tumours showed slightly less involvement, with 28.3% located in these regions.

However, this difference was not statistically significant ($p = 0.395$), indicating that tumor location in eloquent regions does not strongly correlate with IDH mutation status.

7. First Presenting Symptoms

- Headache was the most common presenting symptom, reported in 78 patients.
- This was followed by motor/movement deficits in 24 patients and seizures in 22 patients.

When stratified by IDH status:

- Seizures were more frequent among IDH-mutant patients (18 cases) compared to IDH-wildtype patients (4 cases).
- Mental status changes were more common in the IDH-wildtype group (10 cases), while only 2 cases were observed in the IDH-mutant group.

While statistical significance was not established due to the absence of p-values, these trends suggest a potential association between symptom profile and IDH mutation status, warranting further investigation.

8. Type of Surgery

Awake surgery was performed in 42.3% of cases, while the remaining 57.7% underwent asleep surgery.

9. 1p/19q Co-deletion

- 71.79 % of patients in our cohort had 1p/19q co-deletion.
- This was significantly more common in the IDH-mutant group (96%), compared to the IDH- wildtype group (3.57%).
- 1p/19q retention was more prevalent in IDH-wildtype patients (90.9%).

The difference approached statistical significance ($p = 0.057$), suggesting a potential correlation between IDH mutation and 1p/19q co-deletion status.

Overall Summary

1p/19q Co-deletion:

- 71.79% of patients in our cohort had 1p/19q co-deletion.
- This was significantly more common in the IDH-mutant group (96%), compared to the IDH- wildtype group (3.57%).
- 1p/19q retention was more prevalent in IDH-wildtype patients (90.9%).

The difference approached statistical significance ($p = 0.057$), suggesting a potential correlation between IDH mutation and 1p/19q co-deletion status, although a larger sample size may be necessary for more definitive conclusions.

The bar chart represents the percentage distribution of male and female patients across different genetic subtypes of low-grade glioma. Males are more prevalent in the 1p/19q co-deleted (58.2%) and IDH mutant (60%) groups, while females are more prevalent in the 1p/19q retained (54.5%) and IDH wild-type (55.6%) groups. Overall, the study cohort consists of 56.4%

males and 43.6% females. This suggests possible sex-based differences in genetic profiles of gliomas, warranting further investigation.

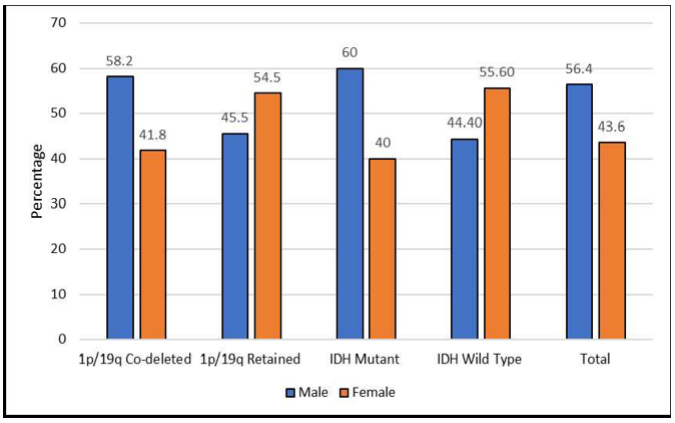

Figure 3: Sex Distribution by 1p/19q and IDH Mutation Status in Low-Grade Glioma Patients

Table 2: Clinical Characteristics of the Sample According to 1p/19q Co-Deletion Status

Characteristic	1p/19q Co-deleted (n=67)	1p/19q Retained (n=11)	p-value
Age, Median (IQR)	55 (41-62)	60 (39-66)	0.556
Gender			0.429
- Male	39 (58.2)	5 (45.5)	
- Female	28 (41.8)	6 (54.5)	
Histologic Type and Grade			0.520
- Oligodendroglioma Grade II	23 (34.3)	4 (36.4)	
- Oligodendroglioma Grade III	5 (7.5)	0 (0)	
- Oligoastrocytoma Grade II	1 (1.5)	0 (0)	
- Oligoastrocytoma Grade III	2 (3.0)	0 (0)	
- Ganglioma Grade I	1 (1.5)	1 (9.1)	
- Astrocytoma Grade II	7 (10.4)	2 (18.2)	
- Astrocytoma Grade III	17 (25.4)	4 (36.4)	
- Other	11 (16.4)	0 (0)	
Extent of Resection			0.317
- Total Resection (TR)	28 (49.12)	2 (0.09)	
- Sub Total Resection (STR)	29 (50.8)	18 (85.71)	
- Biopsy	0	1 (0.047)	
Tumor Location			0.906
- Frontal lobe	34 (50.7)	5 (45.5)	
- Parietal lobe	13 (19.4)	2 (18.2)	
- Temporal lobe	7 (10.4)	2 (18.2)	
- Other	13 (19.4)	2 (18.2)	
Eloquent Area Involved			0.786
- Yes	21 (31.3)	3 (27.3)	
- No	46 (68.7)	8 (72.7)	
Type of Surgery			0.081
- Awake	31 (46.3)	2 (18.2)	
- Asleep	36 (53.7)	9 (81.8)	
IDH Status			0.057
- Mutant	54 (80.6)	6 (54.5)	
- Wild Type	13 (19.4)	5 (45.5)	

This table compares clinical characteristics between patients with 1p/19q co-deletion (n=67) and those with retained 1p/19q status (n=11). The p-values indicate whether the differences between the groups are statistically significant.

Age and Gender Distribution

The median age for diagnosis in our cohort is 41.5 years, with those harboring IDH-wildtype tumors being significantly older (median age 51 years) compared to those with IDH-mutant tumors (median age 37.6 years) ($p < 0.05$)

Gender distribution was also similar ($p = 0.429$), with 58.2% males in the co-deleted group compared to 45.5% in the retained group.

Histologic Type and Grade

Oligodendrogliomas were more frequent in the co-deleted group (41.8% combined Grade II and III) compared to the retained group (36.4% Grade II only, none were Grade III).

Astrocytomas were more common in the retained group (Grade II: 18.2%, Grade III: 36.4%) than in the co-deleted group (Grade II: 10.4%, Grade III: 25.4%).

Gangliomas were rare, with one case in each group.

No statistically significant difference was observed in histologic type and grade ($p = 0.520$), though the trend suggests that astrocytomas are more frequent in 1p/19q retained cases.

Extent of Resection

Total resection (TR) was more common in the co-deleted group (93.3%) than in the retained group (6.6%), while subtotal resection was more frequent in the retained (86.36%) compared to the deleted group (33.9%).

The difference was statistically significant ($p = 0.056$).

Tumor Location

The frontal lobe was the most common tumour location in both groups, with 50.7% of 1p/19q co- deleted tumours and 45.5% of 1p/19q retained tumours located there.

The parietal lobe was the second most common location, observed in 19.4% of co-deleted tumours and 18.2% of retained tumours.

There was no significant difference in tumour location between the two groups ($p = 0.906$), indicating that 1p/19q co-deletion status does not strongly influence tumour localization.

Eloquent Area Involvement
Tumors involved eloquent areas in 31.3% of co-deleted cases and 27.3% of retained cases (p = 0.786), indicating no statistically significant association.

Type of Surgery
Awake surgery was more commonly performed in the co-deleted group (46.3%), whereas asleep surgery was more frequent in the retained group (81.8%).

Awake craniotomy under neuro-monitoring and functional cortical mapping was performed in majority of cases with eloquent area involvement.

This difference approached statistical significance (p = 0.081), suggesting a potential trend where awake craniotomy with cortical mapping led to good functional outcome.

IDH Mutation Status
The majority of co-deleted tumors were IDH mutant (96.42%), whereas only 9.09% of the retained tumors were IDH mutant.

The association between 1p/19q status and IDH mutation was significant (p = 0.087), suggesting a trend where IDH mutations are more frequent in 1p/19q co-deleted tumors, consistent with known molecular glioma classifications.

Summary
No significant differences were observed between 1p/19q co-deleted and retained groups in terms of age, gender, tumor location, eloquent area involvement, or extent of resection.

Histologic trends suggest that oligodendrogliomas are more frequent in co-deleted cases, while astrocytomas are more common in 1p/19q retained cases.

Awake surgery appears more common in co-deleted cases, while asleep surgery is more frequent in retained cases, though not statistically significant.

IDH mutations are more prevalent in co-deleted tumors, with a borderline significant association.

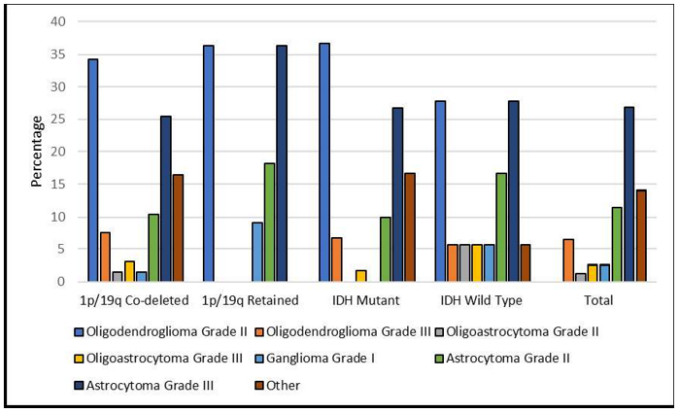

Figure 4: Distribution of Tumor Types by 1p/19q and IDH Mutation Status in Low-Grade Glioma Patients

The bar chart illustrates the percentage distribution of different glioma subtypes across genetic profiles.

Oligodendroglioma Grade II is the most prevalent histological type, particularly in the 1p/19q co- deleted and IDH mutant groups. Astrocytoma Grade II is more common in 1p/19q retained and IDH wild-type groups. Higher-grade tumors, including Astrocytoma Grade III and Oligoastrocytoma Grade III, appear in smaller proportions across all genetic subtypes. These patterns align with known correlations between genetic markers and glioma classification.

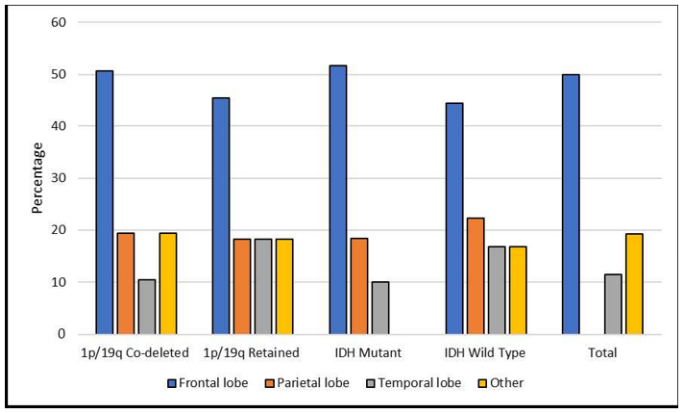

Figure 5: Lobar Distribution of Low-Grade Gliomas by 1p/19q and IDH Mutation Status

The bar chart illustrates the distribution of gliomas across different brain lobes based on 1p/19q co- deletion status and IDH mutation status. The frontal lobe is the most commonly affected region across all genetic subtypes, with over 50% of cases. The parietal and temporal lobes show relatively lower involvement, with a slightly higher proportion of IDH wild-type gliomas in the parietal lobe. The "Other" category, which includes less common tumor locations, has a nearly equal distribution across genetic groups. This pattern aligns with existing literature, where frontal lobe dominance is a well-established feature of low-grade gliomas.

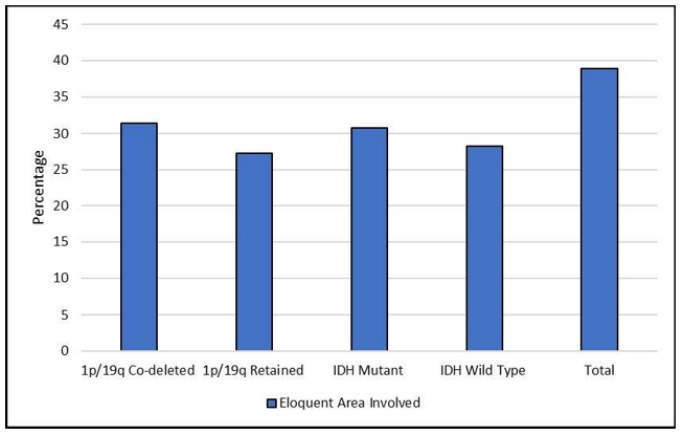

Figure 6: Eloquent Brain Area Involvement in Low-Grade Gliomas Based on Genetic Markers

The chart illustrates the percentage of low-grade glioma cases involving eloquent brain areas across different genetic subtypes. Eloquent areas, which control critical functions like speech,

motor skills, and vision, were affected in approximately 30% of cases across all genetic groups (1p/19q co- deleted, retained, IDH mutant, and IDH wild type). The total percentage of involvement appears slightly higher, nearing 40%. There is no significant variation between genetic subgroups, suggesting that tumor location in eloquent regions is not strongly associated with 1p/19q status or IDH mutation.

Table 3A: Preoperative and Early Postoperative (3-Month) Characteristics

Variable	Total (n=78)	1p/19q Co-deleted (n=67)	1p/19q Retained (n=11)	p- value
Preoperative Variables				
Pre Op Tumor Size (Max mm)	28.0 (24.0-32.0)	30.0 (26.0-32.0)	25.0(18.75-33.5)	0.0313
Pre Op eritumoral Edema	77 (98.7)	66 (98.5)	11 (100.0)	0.683
Pre Op Enhancement Pattern	75 (96.2)	64 (95.5)	11 (100.0)	0.474
Early Postoperative (3- Month) MRI Findings				
Post Op 3-Month Resection Cavity	30 (38.5)	30 (44.8)	0 (0.0)	0.005
Post Op 3-Month Altered Signal	9 (11.5)	9 (13.4)	0 (0.0)	0.196
Post Op 3-Month Enhancement	4 (5.1)	4 (6.0)	0 (0.0)	0.405
Post Op 3-Month Residual Tumor	29 (37.2)	24 (35.8)	5 (45.5)	0.54
Post Op 3-Month Edema	13 (16.7)	12 (17.9)	1 (9.1)	0.467
Post Op 3-Month Post-Op Changes	42 (53.8)	33 (49.3)	9 (81.8)	0.045

This table compares preoperative and early postoperative (3-month) MRI findings between 1p/19q co-deleted and 1p/19q retained patients.

Preoperative Characteristics

- Tumor Size: The median preoperative tumor size was significantly larger in the 1p/19q co-deleted group (30 mm) compared to the 1p/19q retained group (25 mm) ($p = 0.0313$), suggesting a possible association between 1p/19q co-deletion and larger tumor size.
- Peritumoral Edema: Nearly all patients (98.7%) exhibited peritumoral edema, with no significant difference between the two groups ($p = 0.683$).
- Enhancement Pattern: The majority (96.2%) of tumors showed enhancement preoperatively, with no significant difference between groups ($p = 0.474$).

Early Postoperative (3-Month) MRI Findings

- Resection Cavity Presence: A significantly higher proportion of 1p/19q co-deleted patients had a visible resection cavity on 3-month MRI (44.8% vs. 0%, $p = 0.005$), possibly indicating differences in surgical approach or response to surgery.
- Altered Signal & Enhancement: While altered signal ($p = 0.196$) and enhancement ($p = 0.405$) were seen only in the 1p/19q co-deleted group, the differences were not statistically significant.
- Residual Tumor: Residual tumor at 3 months was observed in 37.2% of patients, with no significant difference between groups ($p = 0.54$).
- Postoperative Edema: Postoperative edema was seen in 16.7% of patients, with a slightly higher proportion in the 1p/19q co-deleted group, though this was not statistically significant ($p = 0.467$).
- Postoperative Changes: The presence of postoperative changes was significantly higher in the 1p/19q retained group (81.8%) compared to the 1p/19q co-deleted group (49.3%) ($p = 0.045$), suggesting possible differences in healing response or treatment effects.

Key Points

- 1p/19q co-deleted tumors were significantly larger preoperatively.
- Resection cavity was significantly more common in the 1p/19q co-deleted group.
- Postoperative changes were more frequent in the 1p/19q retained group.
- Other MRI findings (residual tumor, enhancement, and edema) did not significantly differ between groups.

These findings may indicate distinct tumor biology and post-surgical response patterns between 1p/19q co-deleted and 1p/19q retained gliomas.

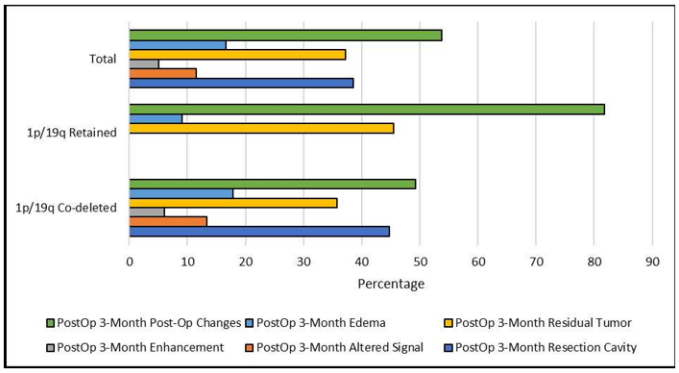

Figure 7: Early Postoperative (3-Month) MRI Findings Based on 1p/19q Status

This bar graph illustrates the distribution of early postoperative (3-month) MRI findings in patients with low-grade gliomas, categorized by 1p/19q co-deletion and retention status. The most frequent finding was postoperative changes, particularly in the 1p/19q retained group (81.8%). Residual tumor was more common in the retained group (45.5%) compared to the co-deleted group (35.8%). Resection cavity was observed only in the co-deleted group (44.8%), while altered signal and enhancement were absent in the retained group.

These findings suggest differences in postoperative imaging characteristics based on genetic subtypes.

Table 3B: Long-Term Postoperative Outcomes (6-Month to 12-Month Follow-Up)

Variable	Total (n=78)	1p/19q Co-deleted (n=67)	1p/19q Retained (n=11)	p- value
6-Month MRI Findings				
Residual Tumor	1 (1.3%)	0 (0.0%)	1 (9.1%)	0.013
Post-Treatment Changes	64 (82.1%)	55 (82.1%)	9 (81.8%)	0.983
Edema	1 (1.3%)	0 (0.0%)	1 (9.1%)	0.013
Enhancement	7 (9.0%)	6 (9.0%)	1 (9.1%)	0.988
Progression	4 (5.1%)	3 (4.5%)	1 (9.1%)	0.52
12-Month MRI Findings				
Tumor Status (Stable/Change)				0.085
Stable	73 (93.6%)	64 (95.5%)	9 (81.8%)	
Change	5 (6.4%)	3 (4.5%)	2 (18.2%)	
Residual Lesion	73 (93.6%)	64 (95.5%)	9 (81.8%)	0.085
Enhancement	0 (0.0%)	0 (0.0%)	0 (0.0%)	NA
Edema	0 (0.0%)	0 (0.0%)	0 (0.0%)	NA
Progression	0 (0.0%)	0 (0.0%)	0 (0.0%)	NA

6-Month MRI Findings

- Residual Tumor was observed in 1.3% (n=1) of the total patients, and it was exclusively present in the 1p/19q Retained group (9.1%), while none of the 1p/19q Co-deleted patients had residual tumors (p = 0.013, statistically significant).
- Post-Treatment Changes were commonly seen in both 1p/19q Co-deleted (82.1%) and 1p/19q Retained (81.8%) groups, with no significant difference (p = 0.983).
- Edema was seen in 1.3% (n=1) of the total population, exclusively in the 1p/19q Retained group (9.1%), with none in the 1p/19q Co-deleted group (p = 0.013, statistically significant).
- Enhancement was observed in 9.0% of patients, with a nearly identical distribution between 1p/19q Co-deleted (9.0%) and 1p/19q Retained (9.1%) groups (p = 0.988, not significant).
- Tumor Progression at 6 months was observed in 5.1% of patients, with a higher proportion in the 1p/19q Retained group (9.1%) compared to the 1p/19q Co-deleted group (4.5%), but the difference was not statistically significant (p = 0.52).

12-Month MRI Findings

Tumor Stability (Stable vs. Change)

- 93.6% of total patients had stable tumor status, with a higher proportion in the 1p/19q Co-deleted group (95.5%) than in the 1p/19q Retained group (81.8%).
- Tumor change was more frequent in the 1p/19q Retained group (18.2%) compared to the 1p/19q Co-deleted group (4.5%), the difference was statistical significance (p = 0.055).

Residual Lesion

- 48 patients (61.5%) had stable size residual lesion at 12 months.
- The 1p/19q Co-deleted group had a higher proportion (95.5%) compared to the 1p/19q Retained group (81.8%), but this was not statistically significant (p = 0.085).

Key Takeaways

Significant Findings

- Residual tumor and edema at 6 months were significantly more frequent in the 1p/19q Retained group compared to the 1p/19q Co-deleted group (p = 0.013).
- This suggests that patients with 1p/19q Retained status may have poorer early post-operative outcomes in terms of residual tumor and inflammation (edema).

Non-Significant but Clinically Relevant Findings

- Tumor progression was observed more frequently in the 1p/19q Retained group (9.1%) at 6 months compared to the 1p/19q Co-deleted group (4.5%), but this did not reach statistical significance (p = 0.52).
- By 12 months, the 1p/19q Retained group had a higher proportion of tumor change (18.2%) compared to the 1p/19q Co-deleted group (4.5%), but the difference was not statistically significant (p = 0.085).

Long-Term Stability

Tumor status was stable in most patients (93.6%), and while the 1p/19q Retained group had a higher proportion of tumor change, this was not statistically significant.

Clinical Implications

- The 1p/19q Retained group may have a higher risk of early postoperative residual tumor and edema, indicating a potentially more aggressive or treatment-resistant disease course.
- However, by 12 months, all patients showed radiological stability, regardless of genetic status.
- The lack of significant tumor progression or new enhancement at 12 months suggests that surgical and adjuvant treatments were effective in preventing further tumor growth.
- Future studies could explore longer follow-ups beyond 1 year to assess whether the 1p/19q Retained group has a higher risk of delayed progression.

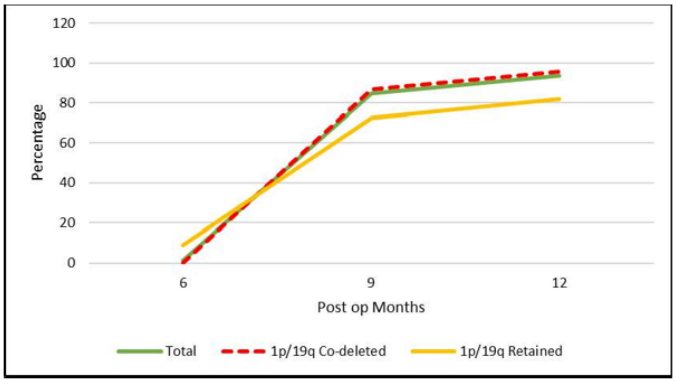

Figure 8: Residual Lesion Progression Over Time in 1p/19q Co-deleted and Retained Glioma Patients

The line chart illustrates the percentage of patients with residual lesions at 6, 9, and 12 months postoperatively, comparing 1p/19q co-deleted, 1p/19q retained, and total patient groups. A steady increase in residual lesion presence is observed across all groups over time.

Patients with 1p/19q co-deletion exhibit the highest percentage of residual lesions at 12 months (~95.5%), suggesting a persistent postoperative tumor presence despite treatment. Conversely, the 1p/19q retained group shows a relatively lower residual lesion percentage, though it also increases over time. The total group trend follows an intermediate pattern.

These findings highlight a potential genetic influence on postoperative tumor behavior, with 1p/19q co-deletion associated with a higher residual lesion burden. This could have implications for long- term treatment planning and monitoring in glioma patients.

Discussion

IDH Mutation and Prognosis

The IDH mutation is a crucial prognostic factor for LGG patients, with a prevalence of approximately 80% in our cohort. IDH-mutant patients tend to have a better prognosis, with longer progression-free survival (PFS) compared to IDH-wildtype patients [23]. Numerous studies have demonstrated that IDH mutations are independent prognostic markers for improved overall survival (OS) and PFS in glioma patients. Li G Zang conducted a meta-analysis encompassing 55 observational studies involving 9,487 patients revealed that IDH1/2 mutations were associated with a 58% reduction in the risk of progression (HR = 0.42) and a 61% reduction in the risk of death (HR = 0.39). Specifically, in low-grade gliomas (WHO grade II and III), IDH mutations correlate with improved survival outcomes [30]. For instance, a study found that the mean 3-year PFS was 73.9 months for patients with IDH-mutant tumors compared to 61.4 months for those with wild-type IDH. In high-grade gliomas, including glioblastomas, IDH mutations also confer a survival advantage. A cohort study reported that IDH-mutant primary glioblastomas had a median OS of 39.4 months and median PFS of 25.9 months, significantly longer than the 13.6 months OS and 8.7 months PFS observed in IDH-wildtype glioblastomas [31]. Parson et al in 2008 conducted a comprehensive genomic analysis provided insights into the molecular underpinnings of glioblastoma, including the identification of IDH mutations as significant genetic alterations [35].

Data on PFS: In our cohort, 59 out of 60 IDH-mutant patients had 12 months of progression-free survival, while only 18 IDH-wildtype patients experienced progression or recurrence, typically at 3, 6, and 9 months. These findings align well with earlier studies, including those by Ma et al. (2013) study conducted in 40 patients showed 35 IDH mutant patient have better progression free survival then 5 IDH wild type patients who experience progression within 1 year. [32] Brandner and von Deimling (2015) in study conducted in 75 LGG patients showed 60 IDH mutant has better progression free survival then 15 IDH wild type, showing IDH-mutant gliomas have a better prognosis in terms of PFS. [33]

Age and IDH Status

Median Age: The median age for diagnosis in our cohort is 41.5 years, with those harboring IDH- wildtype tumors being significantly older (median age 51 years) compared to those with IDH- mutant tumors (median age 37.6 years).This is consistent with studies suggesting that older age at diagnosis correlates with IDH-wildtype tumors and poorer prognosis, as noted by several researchers Hartmann et al., 2010 conducted a study in 285 LGG patients showing age >40, partial tumor resection, IDH wild type have poor clinical outcome [24]. Olar et al., 2015 in a study conducted in 558 LGG patient showed age >45-50 in 48 IDH wild type showed poor clinical outcome [25].

Age as a Prognostic Factor

The study confirms that patients aged 40 years and older have a significantly shorter PFS, as demonstrated by a highly significant P-value (<0.0001). This is consistent with findings by Soffietti et al. (2010), who observed that older patients with LGGs tend to have a more aggressive disease course [26]. In line with earlier work. Baumert et al., 2016 study conducted in 477 LGG patients and; Buckner et al., 2016 in a study conducted in 217 patients showed older patients, particularly those with lower-grade gliomas, are often considered high-risk and included in treatment trials involving upfront chemotherapy and radiation therapy [27].

IDH Status and Age Interaction

The study also highlights an important finding: while older age generally predicts worse outcomes, this relationship is more pronounced in patients with IDH-wildtype tumors. In fact, in IDH-mutant gliomas, age did not significantly affect the prognosis, as demonstrated by the lack of a statistically significant difference when comparing IDH-mutant astrocytomas of grade III across different age groups. This supports findings from other studies, Hartmann et al., 2010 in 285 LGG patients; Reuss et al., 2015 in 75 LGG patients suggest the prognostic impact of age is less pronounced in IDH-mutant gliomas [28,29] The results align well with a growing body of evidence that IDH mutation status plays a pivotal role in determining the prognosis of glioma patients, and specifically, that IDH-mutant lower-grade gliomas have a more favorable progression-free survival compared to IDH-wildtype gliomas.

Clinical Implications

These findings support the use of IDH mutation status as a key factor in determining the treatment approach for LGG patients. The IDH-wildtype status might justify more aggressive treatment regimens, particularly in older patients, who tend to have a poorer prognosis. In contrast, IDH- mutant patients, even older ones, could potentially benefit from more conservative treatment strategies, or at least close monitoring before escalating therapy.

1p19q Codeletion

The discovery of 1p/19q codeletion as a prognostic biomarker for better outcomes in oligodendrogliomas (Cairncross et al., 1994) laid the groundwork for molecular-based classifications of gliomas [34]. The identification of IDH mutations in 2008, study conducted by Brandner and von Deimling, 2015 in 210 LGG patients IDH mutant status play important role in deciding further line of management, 175 IDH mutant patient showed

better outcome and increase sensitivity to chemotherapy/ radiotherapy treatment as compared to 35 IDH wild type patients which represented another pivotal moment in glioma research [33]. This was a turning point in how gliomas are classified and prognosticated, especially given that IDH-mutant gliomas are associated with better survival outcomes.

Integrated Diagnostic Approach

The goal of an integrated diagnostic approach that incorporates molecular markers (rather than relying on histologic classification and grade alone) has been progressively realized through studies like The Cancer Genome Atlas (TCGA) and subsequent publications which include study conducted by Cancer Genome Atlas Research et al., 2015; This landmark study integrated genomic, transcriptomic, and epigenomic data to redefine the classification of lower-grade gliomas, emphasizing the importance of molecular markers such as IDH mutations and 1p/19q codeletion in determining prognosis and guiding treatment strategies [35]. Eckel-Passow et al., 2015. This integrated approach has helped redefine glioma subtypes based on a combination of genetic, molecular, and histological data, making it more reflective of the underlying biology of the disease. IDH-mutant, 1p/19q codeleted patients show significantly better progression-free survival (PFS) compared to IDH-wildtype tumors ($P < 0.0001$). This is in line with what has been observed in many studies, confirming that these molecular markers are crucial for prognosis. Specifically, your data corroborate previous findings showing that IDH-mutant, 1p/19q-codeleted gliomas have a substantially progression free survival compared to IDH-mutant, 1p/19q-retained gliomas [36]. This is consistent with other research done by Wang et al. in 2014 that has established the 1p/19q codeletion as both a prognostic and predictive biomarker for treatment response and survival outcomes [37].

1p/19q Codeletion: Chemo Sensitivity and Prognosis

The 1p/19q codeletion not only predicts better overall survival but also chemosensitivity, meaning tumors with this codeletion tend to respond better to chemotherapy, leading to longer PFS. Zao J et al conducted meta-analysis, encompassing 28 studies with 3,408 glioma cases, revealed that the codeletion of 1p and 19q is associated with improved progression-free survival (HR = 0.63) and overall survival (HR = 0.43), indicating a significant survival advantage for patients with this genetic alteration. This finding further emphasizes the role of molecular profiling in stratifying glioma patients [38]. 55 1p/19q codeleted tumors showed better responses to chemotherapy in terms of stable residual lesion/ no recurrent lesion, which is crucial for tailoring treatment strategies and improving patient outcomes as compared to 23, 1p 19q retained patients in which despite early initiation of CT/RT there was progression/recurrent lesion.

Implications for Future Research and Treatment

The integration of molecular biomarkers like IDH mutations and 1p/19q codeletion into routine diagnostic practice represents a significant step forward. This integrated approach is essential not only for prognosis but also for personalized treatment strategies. For instance, identifying tumors with 1p/19q codeletion could lead to more aggressive chemotherapy, whereas IDH-mutant, 1p/19q- retained tumors might require a different treatment approach. Our findings reinforce the growing importance of incorporating molecular biomarkers into glioma diagnostics and treatment planning. This integrated, molecular-based approach provides a more accurate understanding of the disease and helps deliver more personalized treatment options. Additionally, our study highlights the need for ongoing research into the molecular characteristics of gliomas, as advances in molecular genetics will continue to refine how we classify and treat these tumors. Lin et al conducted a study in year 2021 that analyzed the tumor immune microenvironment in lower-grade gliomas, finding that IDH mutations and 1p/19q codeletions were associated with distinct immunological profiles, which could inform immunotherapy strategies [39].

IDH-Wildtype Grade III Gliomas

IDH-wildtype Grade III tumours have a significantly worse prognosis aligns with studies indicating that these tumours share molecular features with glioblastomas (GBM), specifically IDH-wildtype GBMs. Grade III IDH-wildtype gliomas exhibit similar molecular characteristics to IDH-wildtype glioblastomas, and thus might be considered biologically akin to WHO grade IV tumours (GBMs). This is particularly important as GBMs, even when classified as Grade IV, are associated with a poor prognosis, with rapid progression and limited treatment options. The similarity between Grade III IDH-wildtype gliomas and glioblastomas suggests that the former may follow a similarly aggressive clinical course. Brat et al conducted study of IDH-wildtype Grade III gliomas is crucial due to their molecular and clinical characteristics that significantly impact patient prognosis and treatment strategies. Clinically, IDH-wildtype Grade III gliomas exhibiting these molecular features demonstrate a median overall survival (OS) of approximately 17 months, comparable to that of GBMs, whereas those lacking such alterations have a median OS of around 23 months. This underscores the necessity of incorporating molecular profiling into the diagnostic process to accurately stratify patients and tailor appropriate therapeutic interventions [40].

Comparison with IDH-Mutant Gliomas

Interestingly, IDH-mutant gliomas, including Grade III tumors, have a better prognosis than IDH- wildtype tumors. This distinction in prognosis between IDH-mutant Grade III gliomas and IDH- wildtype Grade III gliomas further emphasize the critical role of IDH mutation status in glioma prognosis. While Grade III IDH-mutant gliomas are associated with longer progression-free survival and better overall survival outcomes, Grade III IDH-wildtype gliomas share characteristics with glioblastomas, which are notoriously aggressive. The finding that IDH-wildtype Grade III gliomas may actually be more dangerous than IDH-mutant glioblastomas challenge traditional assumptions about glioma grading, as the molecular status appears to be more important than the histologic grade in these cases.

Proposed Reclassification of IDH-Wildtype Grade III Gliomas

Based on the molecular characteristics of Grade III IDH-wildtype gliomas and their resemblance to glioblastomas, it is conceivable that IDH-wildtype Grade III tumors could be reclassified in the future as part of the GBM spectrum. This would reflect their

similar prognosis and molecular behavior, even if histologically they are classified as lower-grade tumors (Grade III). Such a reclassification would also impact clinical treatment decisions. Given their similar aggressive nature to glioblastomas, IDH-wildtype Grade III gliomas might require treatment regimens that are typically reserved for GBMs, such as more intensive chemotherapy and radiation protocols. The studies, Hartmann et al., 2010 in 285 LGG patients also provide evidence that IDH-wildtype gliomas, particularly Grade III tumors, exhibit molecular features of glioblastomas, which supports the idea that these tumors should be treated with the same urgency and aggression as glioblastomas. This concept of glioblastoma-like behavior in Grade III tumors can be transformative in how clinicians approach treatment [28]. In our study 21 Grade III patients despite safe maximal resection early initiation of CT/RT, 5 patients experienced progression of residual lesion at interval of 9 months and 6 patients experienced recurrent lesion at interval of 12 months.

Surgical Resection in LGGs

Infiltrative Nature of LGGs: It's well-established that LGGs are infiltrative tumors that typically cannot be cured by surgery alone. Complete resection is often challenging due to the tumor's tendency to infiltrate healthy brain tissue, making it difficult to remove all affected areas without causing significant neurological deficits.

Optimal Timing and Extent of Resection

Despite these challenges, the consensus has evolved that early surgical intervention, aiming for as much safe tumor resection as possible, is crucial in improving OS and PFS. Hayhurst, 2017 conducted a study in 240 LGG patients which showed 110 patients with safe maximal resection followed by early initiation of CT/RT showed better clinical outcome [18]. Jakola et al., 2017 in study conducted in 40 LGG patients where complete resection was performed in 5 patients and GTR was performed in 35 patients.[19] Patient with GTR followed by CT/RT despite presence of residual lesion in post op MRI showed better clinical outcome then the patients with complete resection. This aligns with the general approach to maximal safe resection in gliomas, where the goal is to remove as much tumor as possible without compromising function.

Extent of Resection and Prognosis

In more extensive tumors, especially those involving multiple lobes, complete resection is often not feasible. In these cases, large tumor volume and extensive tumor extension are significant predictors of poor outcomes. Mariani et al., 2004 in a study conducted in 80 LGG patients showed 35 large tumor patients (>5cm) with extensive tumor extension despite safe maximal resection, early initiation of chemotherapy and radiotherapy showed poor clinical outcome in terms progression and recurrence [41]. The study by Rosenblum et al. (2009) provides valuable insights into the recurrence patterns of adult supra tentorial low-grade gliomas (LGGs) following neurosurgeon-determined gross-total resection (GTR). This prospective clinical trial, initiated by the Radiation Therapy Oncology Group in 1998, involved 111 patients under 40 years of age who underwent GTR for World Health Organization (WHO) Grade II astrocytomas, oligodendrogliomas, or mixed oligoastrocytomas [17]. Thus, while complete resection is ideal, it is not always achievable in more aggressive or widespread LGGs.

Percentage of Complete Resection

In our cohort, complete resection was achieved in 30 patients (38.4%), which is a relatively low percentage. This finding is consistent with other studies, such as RTOG 9802 This trial supports the use of combined modality treatment (radiation therapy plus chemotherapy) in patients with LGGs, particularly those with high-risk features [42]. Buckner et al conducted a study in 2016, where 40% of patients achieved complete resection [20]. EORTC 22033-26033. Baumert et al., 2016 where 17% of patients had gross total resection (GTR) [21]. This low percentage of complete resections in our cohort mirrors the challenges encountered in clinical practice, where achieving GTR is often difficult due to the infiltrative nature of LGGs.

IDH Status and Resection

IDH-Mutant vs. IDH-Wildtype Tumors: Interestingly, IDH-mutant tumors were more amenable to complete resection (28 IDH-mutant vs. 2 IDH-wildtype), although this difference was not statistically significant in our study. This aligns with findings from other studies Beiko et al, 2014 conducted in 215 LGG patients out of which 175 IDH mutant were completely resected and 40 IDH wild type underwent subtotal resection suggesting that IDH-mutant gliomas may be more likely to be successfully resected. This may be because IDH-wildtype tumors tend to be more diffuse and infiltrative, making them harder to delineate and surgically remove [42]. Hyare et al., 2019 conducted study on 75 LGG patients out of which 25 IDH wildtype tumor 20 underwent subtotal resection and 5 underwent biopsy [43]. This observation raises an important point: IDH-wildtype tumors are often biologically more aggressive and infiltrative, which could explain why they are less amenable to complete surgical resection compared to IDH-mutant gliomas. IDH-mutant tumors are often more well-defined and localized, allowing for better surgical outcomes. Maximal Safe Resection: The key takeaway from your study and the broader literature is that maximal safe resection should still be considered the optimal approach whenever feasible, even in infiltrative LGGs. Surgical resection can substantially improve PFS and potentially OS in these patients, as shown by your findings. IDH Status as a Predictor: IDH-mutant tumors may offer a better surgical prognosis due to their more localized nature, while IDH-wildtype tumors may require different treatment strategies, possibly including more aggressive surgery or adjuvant therapies. Tumor Extent and Resection Strategy: For more extensive tumors (e.g., those involving multiple lobes), achieving complete resection may not be possible. In these cases, it is essential to identify patients who might benefit from stereotactic biopsy or debulking surgery, followed by adjuvant therapies such as radiation or chemotherapy. Additionally, preoperative imaging and molecular profiling can help guide decisions regarding surgical strategies. Even with gross total resection, adjuvant therapies like radiation and chemotherapy often play a critical role in extending survival. Future studies could explore how molecular markers like IDH status or 1p/19q codeletion interact with surgical resection to inform adjuvant treatment choices.

Conclusion

In this study evaluating the impact of extent of resection, MRI findings, and 1p/19q status on tumor progression in low-grade glioma (LGG) patients over a 12-month follow-up, we observed several key findings:

1. Age

Diffuse low-grade gliomas are more common in young people, and an age over 40 is a risk factor for poor prognosis. In this study, the median age for diagnosis is 41.5 years, with those harboring IDH-wildtype tumors being significantly older (median age 51 years) compared to those with IDH- mutant tumors (median age 37.6 years).

2. Tumor Stability

Regardless of the initial form of therapy LGG progress over period of time. At 12 months, no evidence of tumor progression was noted in any patient. The majority of patients (93.6%) had a stable residual lesion, while 6.4% showed changes on MRI. No cases of enhancement, edema, or progression were observed at 12 months.

3. IDH mutant vs IDH wild type

Glioma with mutant IDH appeared to be more sensitive to treatment standards of care, such as radiotherapy and chemotherapy compared with its wild-type counterpart.

4. 1p/19q Status and MRI Findings

Patients with 1p/19q retention exhibited a significantly higher incidence of residual tumor at 6 months post-operatively ($p = 0.013$) and greater edema ($p = 0.013$) compared to those with 1p/19q co-deletion. In contrast, other MRI parameters, including post-treatment changes, contrast enhancement, and tumor progression, did not differ significantly between the two groups at any assessed time point.

5. Surgical Resection

Due to the infiltrative nature of Low-Grade Gliomas (LGGs) achieving complete resection can be challenging but maximizing safe resection is a key goal, potentially improving survival. In our cohort, complete resection was achieved in 30 patients (38.4%)

6. Short-Term Post-Treatment MRI Changes

Post-treatment changes were common at 6 months (82.1% of patients), but this did not differ between 1p/19q co-deleted and retained groups ($p = 0.983$). A stable residual lesion was the most frequent MRI finding at 12 months (84.6%), with no significant difference between 1p/19q groups ($p = 0.097$).

Implications & Limitations

- The absence of tumor progression at 12 months suggests effective disease control following surgical resection and post-operative treatment.
- The association of 1p/19q retention with early post-op residual tumor and edema may indicate a less favorable short-term response compared to the co-deleted group.
- Survival analysis could not be performed as no deaths occurred, and limited data restricted further statistical modeling.
- Longer follow-up is needed to assess long-term progression, recurrence patterns, and treatment response beyond 12 months.

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References

1. Nakasu S, Notsu A, Nakasu Y (2021) Prevalence of incidental meningiomas and gliomas on MRI: a meta-analysis and meta-regression analysis. Acta Neurochir (Wien) 163: 3401-3415.
2. Louis DN, Perry A, Wesseling P, Brat DJ, Cree IA, et al. (2021) The 2021 WHO Classification of Tumors of the Central Nervous System: a summary. Neuro Oncol 23: 1231 1251.
3. Duffau H, Taillandier L (2015) New concepts in the management of diffuse low-grade glioma: proposal of a multistage and individualized therapeutic approach. Neuro Oncol 17: 332 342.
4. Gupta T, Achari R, Chatterjee A, Chen ZP, Mehta M, et al. (2019) Comparison of epidemiology and outcomes in neuro-oncology between the East and the West: challenges and opportunities. Clin Oncol (R Coll Radiol) 31: 539 548.
5. Yeole BB (2008) Trends in the brain cancer incidence in India. Asian Pac J Cancer Prev 9: 267 270.
6. Ostrom QT, Cioffi G, Gittleman H, Patil N, Waite K, et al. (2019) CBTRUS Statistical Report: primary brain and other central nervous system tumors diagnosed in the United States in 2012 2016. Neuro Oncol 21: v1 100.
7. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, et al. (2018) Global cancer statistics 2018: GLOBOCAN

estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin 68: 394 424.
8. Klein M, Duffau H, De Witt Hamer PC (2012) Cognition and resective surgery for diffuse infiltrative glioma: an overview. J Neurooncol 108: 309 318.
9. Alderton G (2011) The origins of glioma. Nat Rev Cancer 11: 627.
10. Alcantara LS, Parada L (2016) Cell of origin of glioma: biological and clinical implications. Br J Cancer 115: 1445 1450.
11. Zong H, Verhaak RG, Canoll P (2012) The cellular origin for malignant glioma and prospects for clinical advancements. Expert Rev Mol Diagn 12: 383 394.
12. Doetsch F, Caille I, Lim DA, Garcia-Verdugo JM, Alvarez-Buylla A (1999) Subventricular zone astrocytes are neural stem cells in the adult mammalian brain. Cell 97: 703 716.
13. Ohgaki H, Kleihues P (2005) Epidemiology and etiology of gliomas. Acta Neuropathol 109: 93 108.
14. Mandonnet E (2011) Mathematical modelling of glioma on MRI. Neurosurg Rev 167: 715 720.
15. Pallud J, Audureau E, Blonski M, Sanai N, Bauchet L, et al. (2014) Epileptic seizures in diffuse low-grade gliomas in adults. Brain 137: 449 462.
16. Gogos AJ, Young JS, Pereira MP, Morshed RA, Potts MB, et al. (2021) Surgical management of incidentally discovered low-grade gliomas. J Neurosurg 135: 480-487.
17. Edward G Shaw, Brian Berkey, Stephen W Coons, Dennis Bullard, David Brachman, et al. (2008) Recurrence following neurosurgeon-determined gross-total resection of adult supratentorial low-grade glioma: results of a prospective clinical trial. J Neurosurg 109: 735 744.
18. Hayhurst C (2017) Low-grade gliomas: The role of extent of resection and early adjuvant therapy. J Neurooncol 135: 345 352.
19. Jakola AS, Skjulsvik AJ, Myrmel KS, Sjåvik K, Unsgård G, et al. (2017) Surgical resection versus watchful waiting in low-grade gliomas. Ann Oncol 28: 1942 1948.
20. Buckner JC, Shaw EG, Pugh SL, Chakravarti A, Gilbert MR, et al. (2016) Radiotherapy plus procarbazine, lomustine, and vincristine in low-grade glioma. N Engl J Med 374: 1344 1355.
21. Bale TA, Rosenblum MK (2022) The 2021 WHO Classification of Tumors of the Central Nervous System: An update on pediatric low-grade gliomas and glioneuronal tumors. Brain Pathol 32: e13060.
22. Xia L, Wu B, Fu Z, Feng F, Qiao E, et al. (2015) Prognostic role of IDH mutations in gliomas: A meta-analysis of 55 observational studies. Oncotarget 6: 17354 17365.
23. Hartmann C, Hentschel B, Wick W, Capper D, Felsberg J, et al. (2010) Patients with IDH1 wild-type anaplastic astrocytomas exhibit worse prognosis than IDH1-mutated glioblastomas. Acta Neuropathol 120: 707 718.
24. Olar A, Wani KM, Alfaro K, Aldape KD, Brat DJ (2015) IDH mutation status and role of WHO grade and mitotic index in overall survival in grade II III diffuse gliomas. J Clin Oncol 33: 5270.
25. Soffietti R, Baumert BG, Bello L, van den Bent MJ, Delattre JY (2010) Management of adult diffuse gliomas: Report of the EANO ESMO consensus conference. Ann Oncol 21: 1038 1054.
26. Baumert BG, Hegi ME, van den Bent MJ, von Deimling A, Gorlia T, et al. (2016) Temozolomide chemotherapy vs radiotherapy in high-risk low-grade glioma (EORTC 22033-26033): A phase 3 study. Lancet Oncol 17: 1521 1532.
27. Hartmann C, Hentschel B, Wick W, Capper D, Felsberg J, et al. (2010) Patients with IDH1 wild-type anaplastic astrocytomas exhibit worse prognosis than IDH1-mutated glioblastomas. Acta Neuropathol 120: 707 718.
28. Reuss DE, Mamatjan Y, Schrimpf D, Capper D, Hovestadt V, et al. (2015) IDH mutant diffuse and anaplastic astrocytomas have similar age at presentation and little difference in survival. Acta Neuropathol 129: 867 873.
29. Li G, Zhang J, Zhang Y, Zhang Z (2015) Prognostic role of IDH mutations in gliomas: A meta-analysis of 55 observational studies. Sci Rep 5: 14410.
30. Reuss DE, Mamatjan Y, Schrimpf D, Capper D, Hovestadt V, et al. (2015) IDH mutant diffuse and anaplastic astrocytomas have similar age at presentation and little difference in survival. Acta Neuropathol 129: 867 873.
31. Ma J, Zhang J, Wang Y, Zhang Z (2013) Prognostic significance of IDH1/2 mutations in low-grade gliomas: A retrospective study. J Clin Neurosci 20: 688 692.
32. Brandner S, von Deimling A (2015) The role of IDH mutations in gliomas. Acta Neuropathol 129: 867 873.
33. Cairncross JG, Ueki K, Zlatescu MC, Lisle DK, Finkelstein DM, et al. (1998) Specific genetic predictors of chemotherapeutic response and survival in anaplastic oligodendrogliomas. J Natl Cancer Inst 90: 1473 1479.
34. Cancer Genome Atlas Research Network (2015) Comprehensive, integrative genomic analysis of diffuse lower-grade gliomas. N Engl J Med 372: 2481 2491.
35. Eckel-Passow JE, Lachance DH, Molinaro AM, Walsh KM, Decker PA, et al. (2015) Glioma groups based on 1p/19q, IDH, and TERT promoter mutations in tumors. N Engl J Med 372: 2499 2508.
36. Ovesen C, Christensen A, Nielsen JK, Christensen H (2013) External validation of the ability of the DRAGON score to predict outcome after thrombolysis treatment. J Clin Neurosci 20: 1635 1636.
37. Zhao J, Wenjie Ma, Hong Zhao (2014) Loss of heterozygosity 1p/19q and survival in glioma: A meta-analysis. Neuro Oncol 16: 103 112.
38. Lin W, Qiu X, Sun P, Ye Y, Huang Q, et al. (2021) Association of IDH mutation and 1p19q co-deletion with tumor immune microenvironment in lower-grade glioma. Mol Ther Oncolytics 21: 288 302.
39. Brat DJ, Aldape K, Colman H, Holland EC, Louis DN, et al. (2018) cIMPACT-NOW update 3: recommended diagnostic criteria for "Diffuse astrocytic glioma, IDH-wildtype, with molecular features of glioblastoma, WHO grade IV". Acta Neuropathol 136: 05 10.
40. Mariani L (2004) Management of adult low-grade gliomas: A prospective study of 80 patients. J Clin Oncol 22: 1483 1489.
41. Beiko J, Suki D, Hess KR, Fox BD, Cheung V, et al. (2014) IDH1 mutant malignant astrocytomas are more amenable to resection and show survival benefit with maximal resection. Neuro Oncol 16: 81 91.
42. Lasocki A, Xenos C, Chandra RV (2019) Cystic lesion in the posterior fossa. J Clin Neurosci 67: 294.

Annexure A: Case Record Form

Patient's Coad No:	Age:	Gender:	Date of enrolment:

1. Clinical Information:

- Date of Diagnosis:

2. Clinical Presentation:
- Symptoms at presentation:
- Neurological deficits:

3. Tumor Information:
Tumor Type (per WHO CNS Classification 2021):

- **Tumor Location:**
- **Tumor Grade:**
- **Histopathological Diagnosis**
- **Biomarkers:**

4. Radiological Findings:

MRI/CT Findings:

- Tumor size and location
- Enhancement pattern
- Peritumoral edema
- Other relevant radiological features

5. Treatment Information:

Surgery:

- Date of surgery
- Extent of resection
- Surgical complications
- Post operative chemo/radiotherapy

6. Post operative radiological findings

MRI/CT Findings:

	1 week	3 months	6 months	1 year
Tumor location (in case of recurrence)				
Tumor size				
Enhancement pattern				
Peritumoral edema				

7. Neurological status in follow up

	1 week	3 months	6 months	1 year
Higher motor function				
Cranial nerves				
Motor				
Sensory				
Speech				
Memory				

8. Evaluation at the end of 1 year:
- Progression-free survival
- Adverse events

Additional Notes/Comments:

Conclusion of patient participation: Completed/Withdrawn/ Loss to Follow up

Student's Signature Guide's Signature
Date: Date:

Annexure - A
Part II: Participant Information Sheet

Principal Investigator: Dr. Harsh R Patel Department of Neurosurgery
Kokilaben Dhirubhai Ambani Hospital and Medical Research Institute

Thesis/Study Title: Exploring the Impact of Extent of Resection, MRI Findings and Genetic markers on Overall Survival in Low Grade Glioma Patients: Evaluation at the end of 1 year.

1. Introduction
You are invited to participate in a Thesis/Study Project titled Exploring the Impact of Extent of Resection, MRI Findings and Genetic markers on Overall Survival in Low Grade Glioma Patients : Evaluation at the end of 1 year.

I am, diplomat of national board student in neurosurgery department in Kokilaben Dhirubhai Ambani Hospital and Medical Research Institute under guidance of Dr.Abhaya Kumar, Consultant Neurosurgery. We are doing Thesis/Study on Exploring the Impact of Extent of Resection, MRI Findings and Genetic markers on Overall Survival in Low Grade Glioma Patients: Evaluation at the end of 1 year.

Before you agree to participate in this Thesis/Study, you need to know the Thesis/Study details including risks and benfits so you can make an informed decision. This process is known as "informed consent".

This consent form tells you about the Thesis/Study that you may wish to join. Please read the information carefully and discuss it with anyone you want. If you have questions, please ask the Study Doctor or Study staff to answer them.

Your participation in this research study is voluntary. You may decide not to participate or you may withdraw from the Study at any time without any penalty or loss of benefits to which you are entitled at this site. In case you decide to participate in the Study and then choose to step out at a later time, no new information will be collected post your withdrawal decision; however, any previously collected information will be utilized in the Study.

Your Study Doctor may withdraw you from the study at any time should he/she feel it is in your best interest.

2. Purpose of the Study

The purpose of this Study is to to evaluate the effect of surgical excision, MRI findings and genetic markers on survival in patients with low-grade glioma (LGG)

3. Participant Selection

You have been asked to participate as you meet the eligibility criteria for the Study.

- Patients who agree to give informed consent form to undergo surgical resection and or biopsy would be part of the study.
- Only Primary CNS Gliomas which are biopsy proven would be part of the study.
- Those who are willing to undergo surgery/biopsy and NGS testing.

4. Procedures & Type of Study Intervention

The Study will involve your answering a few questions about yourself, and going through your clinical, radiological and laboratory findings to ascertain residual lesion, neurological deficit, molecular and genetic marker analysis in patients with LGG. I will provide you information and invite you to be part of the Study. There won't be any additional Study producers apart from routinely required.

Describe or explain the exact procedures that will be followed on a step-by-step basis, the tests that will be done, and any drugs that will be given. Explain from the outset what some of the more unfamiliar procedures involve (randomization, biopsy, etc.) Indicate which procedure is routine and which is experimental. Participants should know what to expect and what is expected of them.

Explain in brief about follow up visits (If Any)

Post-surgery /biopsy in total, you will be asked to come at 1week, 3months, 6months and 1 year. .At the end of 1 year, the Study will be completed.

5. Duration of Participation

It should include time period from first visit (consenting visit) to last follow up visit of the patient which would be at 1 year.

6. Your Responsibilities

If you decide to participate in the Study, you are required to follow up regularly post discharge at 3 months and 6 months.

You need to answer few questions regarding your symptoms and allow us for clinical examination and to go through all the investigations done in the past or at the time of the current visit.

7. Side Effects

There are no side effects related to your participation in the Study.

8. Risks

There will not be any additional risk other than those observed in routine care and procedure.

9. Benefits

There may not be any direct benefit for you but your participation is likely to help us find the answer to the Study question. There may not be any benefit to the society at this stage of the Study, but future generations are likely to benefit because the information provided will help us get insight into molecular and genetic markers in gliomas and for targeted therapeutic strategies as per WHO CNS tumor classification 2021

10. Reimbursements

As all visits are as per routine care, no travel reimbursement will be given. There won't be any kind reimbursement as Study participant does not incur any additional cost by participating in the Study.

11. Confidentiality and who will review data and have access to data

All the information obtained in this Study will be kept strictly confidential and used for scientific purposes only. Data taken from this Study may be published or presented in scientific meetings. However your name and other identifying information will be kept confidential and will not be made publicly available. Investigators and Ethics committee members & regulatory authorities (if required by law) may review your personal and medical records.

12. Sharing the Information and Results

The knowledge that we get from doing this Study may be published so other interested people may learn from our Study.

13. Who to Contact

If you have any questions, you may ask them now or later, even after the Study has started. If you wish to ask questions later, you may contact any of the following:

Investigator: Dr Harsh R Patel
Contact: +919408485687
Guide: Dr Abhaya Kumar

This proposal has been reviewed and approved by Institutional Ethics Committee-Academics (IEC-A) which is a committee whose task is to make sure that Study participants are protected from harm. If you wish to find about more about the IEC-A, following are communication details.
Mailing Address IEC-A:

Institutional Ethics Committee Academics (IEC-A) 2nd Floor, Kokilaben Dhirubhai Ambani Hospital & Medical Research Institute, Raosaheb Achutrao Patwardhan Marg, Four Bunglows, Andheri West, Mumbai 400053.

Member Secretary IEC-A:
Dr. Rajesh B. Sawant
MD Pathology

Mailing Address Member Secretary:
7th Floor, Department of Transfusion Medicine Kokilaben Dhirubhai Ambani Hospital & Medical Research Institute,
Rao Saheb Achutrao Patwardhan Marg, Four Bunglows, Andheri

(West), Mumbai 400 053, Mobile: 9223448570
E -mail:rajesh.b.sawant@kokilabenhospitals.com

Chairperson of IEC-A:
Dr Renuka Munshi
Contact No. : 022-30970213
Email : iseb@kokilabenhospitals.com

You will be given a copy of the Participant Information Sheet & signed Informed Consent Document.

Annexure - B: Informed Consent Form

Participant's Initials: ---------- Participant's Name: -------

Date of Birth / Age: ----------

Please Initial Box

(i) I confirm that I have read and understood the information sheet dated [ ]
for the study titled "Exploring the Impact of Extent of Resection, MRI Findings and Genetic markers on Overall Survival in Low Grade Glioma Patients: Evaluation at the end of 1 year" and have had the opportunity to ask questions.

(ii) I understand that my participation in the Study is voluntary and that I am free [ ]
to withdraw at any time, without giving any reason, without my medical
care or legal rights being affected.

(iii) I understand that the Study investigator and Study team, the Ethics Committee and [ ]
the regulatory authorities will not need my permission to look at my health records both in respect of the current Study and any further research that may be conducted in relation to it, even if I withdraw from the Study. I agree to this access. However, I understand my identity will not be revealed in any information which may get published.

(iv) I agree not to restrict the use of any data or results that arise from this Study provide [ ]
such a use is only for scientific purpose(s).

(v) I agree to take part in the above Study. [ ]

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Name of the Participant Sign/Thumb Impression Date

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Name of LAR Sign/Thumb Impression Date
(Legally Acceptable Representative)

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Name of the Investigator Sign Date

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Name of Impartial Witness Sign Date

Contact Details of Impartial Witness: ----------

Address of the Impartial Witness