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Maximizing outcomes in diffusely infiltrative gliomas: A systematic review of surgical innovations and molecular predictors

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Resumen

Introduction: Diffuse gliomas are highly infiltrative brain tumors associated with poor prognosis and limited therapeutic response. Surgical resection remains a cornerstone of treatment, yet the balance between maximizing extent of resection (EOR) and preserving neurological function remains challenging. Advances in intraoperative technologies and molecular profiling have opened new possibilities for individualized treatment.

Materials and methods: A systematic review was conducted in accordance with PRISMA guidelines. Studies evaluating surgical strategies—subtotal resection (STR), gross total resection (GTR), and supramaximal resection (SMR)—were included. Additionally, we assessed the prognostic and therapeutic implications of molecular biomarkers such as IDH mutations, MGMT promoter methylation, and 1p/19q codeletions.

Results: IDH-mutant gliomas were consistently associated with longer overall survival and better responses to adjuvant therapies. MGMT promoter methylation correlated with improved overall survival in patients receiving temozolomide. Supramaximal resection outperformed gross total resection and subtotal resection in terms of progression-free and overall survival. Fluorescence-guided surgery and intraoperative imaging modalities reduced residual tumor volume, enhanced resection accuracy, and lowered complication rates. However, aggressive resections were linked to increased risk of postoperative neurological deficits.

Discussion: Integrating surgical innovation with molecular characterization enables more precise and effective glioma management. While maximizing the extent of resection is beneficial oncologically, it must be weighed against potential functional impairment. Technological adjuncts can help mitigate this trade-off, especially in eloquent regions.

Conclusions: Advanced surgical techniques combined with biomarker-driven strategies improve survival outcomes in diffuse gliomas. Personalized approaches are essential to tailor both surgical and adjuvant treatments, ultimately enhancing quality of life and extending survival.

Palabras clave: Glioma, biomarkers, neurosurgery, margins of excision, bank filtration, minimally invasive surgical procedures.

Maximización de los resultados en gliomas difusamente infiltrativos: una revisión sistemática de innovaciones quirúrgicas y predictores moleculares

Abstract

Introducción: los gliomas difusos son tumores cerebrales altamente infiltrativos, con mal pronóstico y limitada respuesta terapéutica. La resección quirúrgica es fundamental, pero lograr un equilibrio entre la extensión de la resección (EOR) y la preservación de la función neurológica representa un desafío. Los avances en tecnologías intraoperatorias y perfil molecular han abierto nuevas posibilidades para un tratamiento individualizado.

Materiales y métodos: se realizó una revisión sistemática siguiendo las guías PRISMA. Se incluyeron estudios que evaluaban estrategias quirúrgicas como la resección subtotal (STR), la resección total macroscópica (GTR) y la resección supramáxima (SMR). También se analizaron biomarcadores moleculares como las mutaciones en IDH, la metilación del promotor de MGMT y las codeleciones 1p/19q.

Resultados: los gliomas con mutaciones en IDH mostraron una mayor supervivencia global y mejor respuesta a terapias adyuvantes. La metilación del promotor de MGMT se asoció con mayor supervivencia global en pacientes tratados con temozolomida. La resección supramáxima fue superior a la resección total macroscópica y a la resección subtotal en mejorar la supervivencia libre de progresión y la supervivencia global. Las cirugías guiadas por fluorescencia e imagen intraoperatoria redujeron el volumen tumoral residual, mejoraron la precisión de la resección y disminuyeron las complicaciones. No obstante, las resecciones agresivas se asociaron a un mayor riesgo de déficits neurológicos postoperatorios.

Discusión: la integración de innovaciones quirúrgicas con la caracterización molecular permite un manejo más preciso y eficaz de los gliomas. Aunque maximizar la extensión de la resección mejora el pronóstico oncológico, debe ponderarse con el riesgo funcional. Las herramientas tecnológicas pueden reducir esta tensión, especialmente en áreas elocuentes.

Conclusiones: las técnicas quirúrgicas avanzadas combinadas con estrategias guiadas por biomarcadores mejoran los desenlaces en pacientes con gliomas difusos. Los enfoques personalizados son esenciales para adaptar los tratamientos quirúrgicos y adyuvantes, mejorando la calidad de vida y prolongando la supervivencia.

Palabras clave: glioma, biomarcadores, neurocirugía, márgenes de escisión, filtración en margen, procedimientos quirúrgicos mínimamente invasivos

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Introduction

Diffuse gliomas are characterized by their invasive growth and resistance to treatment and remain among the most challenging neuro-oncological diseases to manage (1-4). These tumors infiltrate normal brain tissue, making complete surgical removal difficult without risking significant neurological deficits (5,6). Over the last two decades, advances in surgical techniques and molecular profiling have created new opportunities to improve outcomes for patients with these aggressive tumors (1,5,7). However, the optimal balance between maximizing the extent of resection (EOR) and preserving neurological function continues to be debated, particularly as the definition of "maximal safe resection" continues to evolve (8-10). Surgical resection is central to the management of diffuse gliomas, as it provides both a cytoreductive benefit and critical material for molecular characterization (1,7,9,11,12). Figure 1 illustrates the primary approaches to resection: Subtotal Resection (STR), Gross Total Resection (GTR), and Supramaximal Resection (SMR).

In addition to surgical advancements, molecular markers have revolutionized the understanding and management of diffuse gliomas. IDH mutations, MGMT promoter methylation, and ATRX loss have proven to be powerful prognostic tools, influencing both survival outcomes and therapeutic decisions (11-14). IDH-mutant gliomas, for instance, are associated with slower progression and better responses to both surgery and adjuvant therapies compared to their wild-type counterparts (4,8,9,15). Similarly, MGMT promoter methylation has emerged as a predictor of sensitivity to temozolomide chemotherapy, guiding postoperative treatment strategies (16-18).

The integration of molecular profiling into surgical decision-making has enabled a more personalized approach to treatment. By correlating molecular characteristics with imaging and intraoperative findings, clinicians can tailor the extent of resection and postoperative management to individual patients (7,9,19,20). However, challenges remain in determining how best to combine these insights with advanced surgical techniques, such as fluorescence-guided resection and intraoperative imaging, to achieve the optimal balance between maximal resection and functional preservation (5-7,21).

This study aims to explore the interplay between surgical strategies and molecular predictors in the management of diffuse gliomas. By evaluating the role of advanced resection techniques and biomarker-driven approaches, this work seeks to provide a framework for optimizing both oncological outcomes and quality of life for patients with this devastating disease.

Methods

This review was prospectively registered in the PROSPERO database (CRD42024623052), and its reporting adhered to the standards outlined in the PRISMA 2020 guidelines (22).

Literature search strategy

An extensive literature search was performed across PubMed, Scopus, and Web of Science, aiming to identify studies addressing the surgical treatment of diffusely infiltrative gliomas. The search emphasized the role of advanced surgical techniques and molecular biomarkers in influencing key outcomes, including progression-free survival (PFS), overall survival (OS), extent of resection (EOR), and postoperative complications.

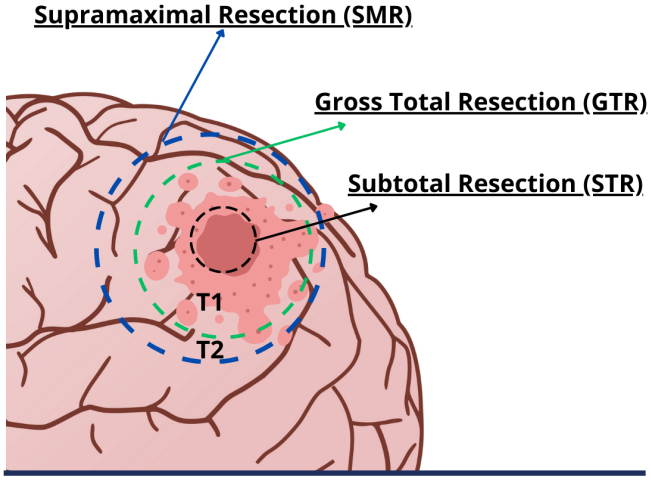

Figure 1. Resection techniques for diffusely infiltrative gliomas

Note. STR: Represented by the green dashed line, involves partial removal of the tumor, often limited by its location in eloquent brain areas; GTR: Shown by the solid green line, aims to remove all visible tumor margins identified on imaging; SMR: Represented by the blue dashed line, extends beyond the tumor's visible borders on T1-weighted; MRI: Targeting regions of potential infiltration identified on T2-weighted or FLAIR imaging.

Source: Own elaboration.

Search terms and inclusion criteria

The search terms employed included: (("Glioma"[Mesh] OR "Diffuse Glioma"[tiab] OR "Infiltrative Glioma"[tiab] OR "glioblastoma"[tiab] OR "astrocytoma"[tiab] OR "oligodendroglioma"[tiab]) AND ("Surgical Procedures, Operative"[Mesh] OR "Neurosurgery"[Mesh] OR "surgical resection"[tiab] OR "maximal safe resection"[tiab] OR "fluorescence-guided surgery"[tiab] OR "5-ALA"[tiab] OR "DTI"[tiab] OR "functional mapping"[tiab]) AND ("Biomarkers"[Mesh] OR "Isocitrate Dehydrogenase"[Mesh] OR "IDH Mutation"[tiab] OR "EGFR amplification"[tiab] OR "TERT mutation"[tiab] OR "1p/19q codeletion"[tiab])).

Inclusion criteria

Adult patients diagnosed with diffusely infiltrative gliomas, including glioblastomas, astrocytomas, and oligodendrogliomas, were included in this review. Eligible interventions involved surgical resection, with or without advanced techniques such as 5-ALA fluorescence, neuronavigation, or functional mapping. The primary outcomes considered were overall survival (OS), progression-free survival (PFS), extent of resection (EOR), and postoperative complications. The review focused on studies employing randomized controlled trials, prospective or retrospective cohort designs, and case series with at least 10 patients. Only studies published in English from the year 2000 onward were included.

Exclusion criteria

Studies were excluded if they involved case series with fewer than 10 patients, focused on non-diffuse gliomas, or lacked surgical intervention or biomarker data.

Additionally, the reference lists of all included studies were manually reviewed to identify any other relevant manuscripts.

Data extraction and management

The study systematically recorded key characteristics, including general information such as author names, year of publication, study design, and sample size; patient demographics, including age, sex, and glioma subtype (e.g., IDH-mutant or IDH-wildtype); and details of the surgical interventions, such as the use of 5-ALA guidance, neuronavigation, or intraoperative brain mapping. Outcomes were classified into primary outcomes—overall survival (OS) and progression-free survival (PFS)—and secondary outcomes, including extent of resection (EOR), postoperative complications, and patient-reported quality of life. Data extraction was independently performed by two reviewers (JR and CC) to ensure accuracy and minimize bias. Discrepancies were resolved through discussion or by consulting a third reviewer (JA). All collected data were recorded and managed using a standardized Excel spreadsheet.

Quantitative data analysis was performed using Python software. Descriptive statistics were used to summarize patient demographics, surgical techniques, and outcomes.

Quality assessment

We assessed the methodological quality of studies using the Newcastle-Ottawa Scale (23). This tool allowed us to evaluate bias, validity, and reliability.

Data synthesis

A narrative synthesis was conducted to summarize the findings of the included studies. The synthesis focused on describing:

- The efficacy of different surgical techniques for achieving maximal safe resection.
- The impact of molecular biomarkers on surgical outcomes.
- The safety profile and complication rates associated with surgical interventions.

Where applicable, a meta-analysis was performed to pool results and provide a quantitative summary of outcomes such as OS, PFS, and EOR. Random-effects models were used to account for heterogeneity, and I^2 statistics were calculated to measure the degree of heterogeneity.

Subgroup analyses

Subgroup analyses were planned based on:

- Molecular Subtypes: IDH-mutant vs. IDH-wildtype.
- Surgical techniques: Advanced techniques (e.g., 5-ALA, neuronavigation) vs. conventional surgery.

- Glioma grade: Low-grade gliomas (LGGs) vs. high-grade gliomas (HGGs).

This approach allows for a detailed exploration of how specific factors influence surgical outcomes in diffusely infiltrative gliomas.

Results

A total of 1,113 studies were initially identified through the PubMed, Scopus, and Web of Science searches. After applying the inclusion and exclusion criteria, 345 studies were selected for full-text review. Of these, 70 studies met the inclusion criteria for the final analysis (Figure 2). These studies collectively included 12,288 patients. Table 1 details the quality assessment of the included studies, evaluated according to the Newcastle-Ottawa Scale (23).

The characteristics of the included studies are summarized in Table 2. Most studies were retrospective case series, with a mean sample size of 175 patients (ranging from 10 to 2,514). The mean age of patients was 55.32 years (36.5 - 65.8), with a mean Karnofsky Performance Status (KPS) of 78.78 (ranging from 30 to 100). The most common disease site was supratentorial (92.7%), followed by deep-seated lesions (5.7%) and infratentorial (1.4%). The follow-up duration across studies ranged from 5.2 to 113.9 months.

Oncological outcomes

A total of 70 studies were included in this analysis, evaluating the impact of various surgical strategies and molecular predictors on PFS, OS, and postoperative complication rates (Table 3). The median PFS

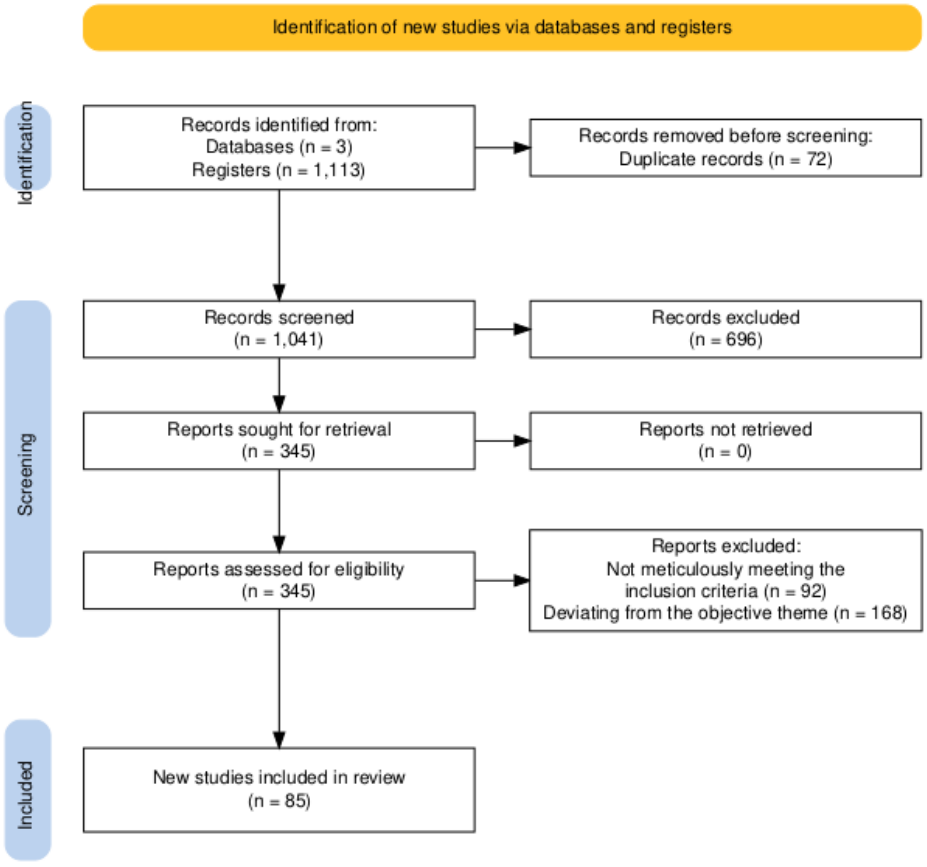

Figure 2. PRISMA Flow chart (22)

Source: Own elaboration.

Table 1. Newcastle-Ottawa scale (23)

		Selection			Comparability			Exposure			
Author	**Year**	**The case definition is adequate with independent validation**	**Consecutive or obviously representative series of cases**	**Community controls**	**Controls with no history of disease (end point)**	**Cases and controls with comparable ages**	**Cases and controls with comparability on any other factors**	**Ascertainment of exposure using secure records (e.g. surgical records) or structured interviews with blinding to case/ control statuses**	**Ascertainment of exposure using the same method for cases and controls**	**Ascertainment of exposure with non-response rate for both groups**	**Total Quality Score**
Beiko et al.	2014	*	*		*	*	*	*	*	*	8
Valdés et al.	2015	*	*		*	*	*	*	*	*	8
Cordier et al.	2015	*	*		*	*	*	*	*	*	8
Tully et al.	2016	*	*	*	*	*	*	*	*	*	9
Wefel et al.	2016	*	*		*	*	*	*	*	*	8
Kawaguchi et al.	2016	*	*		*	*			*	*	6
Behling et al.	2017	*	*		*	*	*	*	*	*	8
Eseonu et al.	2017	*	*	*	*	*	*	*	*	*	9
Eseonu et al.	2017	*	*		*	*	*	*	*	*	8
Saito et al.	2017	*	*	*	*	*	*	*	*	*	9
Grau et al.	2017	*	*	*	*	*	*	*	*	*	9
Fujii et al.	2018	*	*	*	*	*	*	*	*	*	9
Beaumont et al.	2018	*	*	*	*	*	*	*	*	*	9
Opoku-Darko et al.	2018	*	*		*	*	*	*	*	*	8
Sharma et al.	2018	*	*		*	*			*	*	6
Zhang et al.	2018	*	*		*	*	*	*	*	*	8
Muto et al.	2018	*	*	*	*	*	*	*	*	*	9
Im et al.	2018	*	*		*	*	*	*	*	*	8
Kim et al.	2019	*	*	*	*	*	*	*	*	*	9
Hou et al.	2019	*	*		*	*	*		*	*	7
Mistry et al.	2019	*	*		*	*	*	*	*	*	8
Mandonnet et al.	2019	*	*		*	*		*	*	*	7
Picart et al.	2019	*	*		*	*	*	*	*	*	8

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Dupont et al.	2019	*	*	*	*	*	*		*	*	8
Still et al.	2019	*	*	*	*	*	*	*	*	*	9
Della Puppa et al.	2019	*	*	*	*	*	*	*	*	*	9
Delev et al.	2019	*	*	*	*	*	*	*	*	*	9
Hong et al.	2020	*	*	*	*	*	*	*	*	*	9
Antoine et al.	2020	*	*		*	*	*	*	*	*	8
Charalampaki et al.	2020	*	*		*	*			*	*	6
Hallaert et al.	2020	*	*		*	*	*	*	*	*	8
Schwartz et al.	2020	*	*	*	*	*	*	*	*	*	9
Roh et al.	2020	*	*		*	*	*	*	*	*	8
Molinaro et al.	2020	*	*	*	*	*	*	*	*	*	9
Scherer et al.	2020	*	*	*	*	*	*	*	*	*	9
Bo et al.	2020	*	*	*	*	*	*	*	*	*	9
Hirono et al.	2021	*	*	*	*	*	*	*	*	*	9
Lietke et al.	2021	*	*	*	*	*	*	*	*	*	9
Motomura et al.	2021	*	*	*	*	*	*	*	*	*	9
Garton et al.	2021	*	*	*	*	*	*	*	*	*	9
Hosmann et al.	2021	*	*	*	*	*	*	*	*	*	9
Boaro et al.	2021	*	*		*	*	*	*	*	*	8
Pallud et al.	2021	*	*		*	*			*	*	6
Wang et al.	2021	*	*		*	*	*	*	*	*	8
Ort et al.	2021	*	*	*	*	*	*	*	*	*	9
Lasica et al.	2021	*	*		*	*	*	*	*	*	8

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Hou et al.	2021	*	*	*	*	*	*	*	*	*	9
Zhou et al.	2021	*	*		*	*	*		*	*	7
Yahanda et al.	2021	*	*	*	*	*	*	*	*	*	9
Certo et al.	2021	*	*	*	*	*	*	*	*	*	9
Chi et al.	2022	*	*	*	*	*	*	*	*	*	9
Weiss Lucas et al.	2022	*	*	*	*	*	*	*	*	*	9
Sweeney et al.	2022	*	*		*	*	*	*	*	*	8
Szylberg	2022	*	*		*	*			*	*	6
Zhang et al.	2022	*	*		*	*	*	*	*	*	8
Hennessy et al.	2022	*	*	*	*	*	*	*	*	*	9
Vivas-Buitrago et al.	2022	*	*		*	*	*	*	*	*	8
Zeppa et al.	2022	*	*	*	*	*	*	*	*	*	9
Aabedi et al.	2022	*	*		*	*	*		*	*	7
Gupta et al.	2023	*	*	*	*	*	*	*	*	*	9
Watts et al.	2023	*	*	*	*	*	*	*	*	*	9
Que et al.	2023	*	*	*	*	*	*	*	*	*	9
Birladeanu et al.	2023	*	*	*	*	*	*	*	*	*	9
Quach et al.	2023	*	*	*	*	*	*	*	*	*	9
Elia et al.	2023	*	*	*	*	*	*	*	*	*	9
Honeyman et al.	2024	*	*	*	*	*	*	*	*	*	9
Black et al.	2024	*	*		*	*	*	*	*	*	8
da Silva et al.	2024	*	*		*	*			*	*	6
Aydin et al.	2024	*	*		*	*	*	*	*	*	8

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Zhang et al.	2024	*	*	*	*	*	*	*	*	*	9
Ghimire et al.	2024	*	*	*	*	*	*	*	*	*	9
Baran et al.	2024	*	*	*	*	*	*	*	*	*	9
Johnstad et al.	2024	*	*	*	*	*	*	*	*	*	9
Yamamura et al.	2024	*	*	*	*	*	*	*	*	*	9
Byeon et al.	2024	*	*	*	*	*	*	*	*	*	9
Dono et al.	2024	*	*	*	*	*	*	*	*	*	9
Staub-Bartelt et al.	2024	*	*	*	*	*	*	*	*	*	9
Massaad et al.	2024	*	*		*	*	*	*	*	*	8
Toyoda et al.	2024	*	*		*	*			*	*	6
Que et al.	2024	*	*		*	*	*	*	*	*	8
Ahmeti et al.	2024	*	*	*	*	*	*	*	*	*	9
Li et al.	2024	*	*		*	*	*	*	*	*	8
Tropeano et al.	2024	*	*	*	*	*	*	*	*	*	9
Ryba et al.	2024	*	*		*	*	*		*	*	7
Hekimoglu et al.	2024	*	*		*	*	*		*	*	7

Source: Own elaboration.

Table 2. Characteristics of the reviewed studies

Author	Year	Type of study	Main Topic	Number of cases	Sex	Median KPS (range)	Mean age (SD)/ Median Age (range)	Location(s) Supratentorial Infratentorial Deep-seated	Tumor type	WHO grade	Mutation(s)	Type of resection
Beiko et al.	2014	Prospective cohort study	Surgical management	335	F138 M187	≥80 (89%); <80 (11%)	50.3 (18.3 - 79.0)	S319, I20	Anaplastic AST (38%), GBM (62%)	III, IV	IDH (mutant= 42; WT=130)	Maximal surgical resection
Valdés et al.	2015	Retrospective cohort study	5-ALA	12	NA	NA	NA	NA	LGG	II	NA	GTR
Cordier et al.	2015	Retrospective cohort study	Molecular Markers	200	F91, M109	NA	38.9 (17 - 66)	S187, I13	LGG	II	1p19q (no deletion (118), codeletion (57), single deletion (1p (4) 19q (16), IDH1 (155))	Maximal surgical resection
Tully et al.	2016	Retrospective cohort study	Reoperations	204	F79, M125	NA	66 (26 - 90)	S209	GBM	IV	IDH-1	Maximal surgical resection
Wefel et al.	2016	Clinical Study	Prognostic factors	119	F81, M38	90	54.4 (13.8)	S66	Anaplastic AST (35%), GBM (65%)	II, IV	IDH-WT	GTR
Eseonu et al.	2017	Retrospective cohort study	Molecular Markers	109	F46, M63	90 (80 - 100)	37 (19 - 74)	S109	AST (73), OLA (36)	II	1p/19q co-del	Volumetric Maximal surgical resection
Eseonu et al.	2017	Retrospective cohort study	Molecular Markers	25	F32, M42	80 (50 - 100)	54 (18 - 80)	NA	Insular GA	II, IV	NA	Volumetric Maximal surgical resection
Fujii et al.	2018	Retrospective cohort study	Surgical management	81	F34, M47	100 (40 - 100)	40 (17-78)	S77, I4	Anaplastic AST (81), Anaplastic OLA (41)	III	IDH-1 mutated	Maximal surgical resection
Opoku-Darko et al.	2018	Retrospective cohort study	Surgical management	501	F17, M17	95 (90 - 100)	40.8 (20 - 63)	S33, D1	LGG	II	IDH-1	Maximal surgical resection
Zhang et al.	2018	Retrospective cohort study	Fluorescein sodium-guiding	18	NA	NA	NA	NA	GA	III	NA	Fluorescence-guided surgery

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Author	Year	Type of study	Main Topic	Number of cases	Sex	Median KPS (range)	Mean age (SD)/ Median Age (range)	Location(s) Supratentorial Infratentorial Deep-seated	Tumor type	WHO grade	Mutation(s)	Type of resection
Muto et al.	2018	Prospective cohort study	Surgical management	39	F21, M18	100 (60 - 100)	36.5	S39	LGG	II	NA	Functional-based maximal surgical resection
Kim et al.	2019	Retrospective cohort study	5-ALA	31	F12, M19	NA	60.6 (±11.2)	S24, I2, D5	HGG	III	NA	Fluorescence-guided surgery
Hou et al.	2019	Clinical Study	5-ALA	50	NA	NA	NA	NA	GA	II, III	NA	Fluorescence-guided surgery
Mistry et al.	2019	Retrospective cohort study	Outcomes	232	NA	80 (70 - 80)	60.8 (51.3 - 69.2)	NA	GBM	IV	IDH-1/2, MGMT	Ventricular Entry
Mandonnet et al.	2019	Case series	Surgical management	12	F6, M6	NA	40 (21 - 72)	NA	Insular GA	II	IDH-mutated	Transopercular resection
Picart et al.	2019	Retrospective cohort study	Surgical management	23	F10, M13	NA	32.2 (7.8)	S18, I/D5	GA	II	NA	Iterative tailored surgical resections
Dupont et al.	2019	Clinical trial	PDT	10	NA	NA	NA	NA	GBM	IV	NA	GTR + PDT
Still et al.	2019	Retrospective cohort study	Surgical management	346	F150, M196	90 (60 - 100)	35.0 (17 - 69)	S260, I/D86	LGG	II	NA	Maximal surgical resection
Della Puppa et al.	2019	Prospective cohort study sodium-guiding	5-ALA + Fluorescein	18	F2, M1	NA	NA	S18	GBM	IV	IDH-WT	Maximal surgical resection
Delev et al.	2019	Bi-centric retrospective analysis	Surgical management codeletion	299	NA	NA	37.8 (6 - 64)	S120, D5	LGG	II	IDH-1, 1p/19q	GTR
Hong et al.	2020	Retrospective cohort study	Surgical management	113	F27, M35	80 (40 - 90)	48 (18 - 82)	S32, D24	Anaplastic GA	III	IDH-1, 1p/19q codeletion	Volumetric Maximal surgical resection
Hallaert et al.	2020	Retrospective cohort study	Surgical management	159	F59, M100	70 (40 - 100)	61.5 (31 - 80)	NA	GBM	IV	MGMT-unmethylated, IDH-WT	Partial resection
Schwartz et al.	2020	Retrospective multicenter Study	Surgical management	160	F62, M59	80	73.1 ± 5.1	S155, I5	GBM	IV	MGMT-unmethylated, IDH-WT	Maximal surgical resection
Roh et al.	2020	Prospective observational study	Surgical management	40	F13, M27	75 (40 - 100)	62 (34 - 73)	S44	GBM	IV	IDH-WT	Supratotal resection, GTR
Molinaro et al.	2020	Retrospective multicenter Study	Surgical management	704	F499, M468	60	60 (51.7 - 67.7)	S688, I2, D14	GBM	IV	IDH-WT	GTR

Table 2. Characteristics of the reviewed studies

Author	Year	Type of study	Main Topic	Number of cases	Sex	Median KPS (range)	Mean age (SD)/ Median Age (range)	Location(s) Supratentorial Infratentorial Deep-seated	Tumor type	WHO grade	Mutation(s)	Type of resection
Scherer et al.	2020	Retrospective cohort study	Surgical management	140	NA	NA	39 (18 - 70)	S140	LGG	II	NA	GTR
Hirono et al.	2021	Retrospective cohort study	Surgical management	30	F17, M13	70 (60 - 100)	57 (19 - 78)	S17, I/D13	GBM	IV	IDH-WT	Supratotal resection, GTR
Lietke et al.	2021	Retrospective cohort study	PDT	47	F20, M27	80 (70 - 100)	49.4 (33.4 - 87.0)	S13, D31	GBM	IV	IDH-WT, MGMT-methylated	Fluorescence-guided surgery
Motomura et al.	2021	Retrospective cohort study	Surgical management	126	F52, M74	100 (60 - 100)	42.8 (17 - 56)	S126	GA	II, III	IDH-WT	Maximal surgical resection
Garton et al.	2021	National cancer center database analysis	Surgical management	2514	F1407, M1107	NA	56	S2373, I46	GA	II, III	1p/19q codeletion	Supratotal resection, GTR
Hosmann et al.	2021	Retrospective multicenter study	5-ALA	59	F26, M33	NA	38.8 (20.4 - 65.5)	S48, D1	LGG	II	NA	Fluorescence-guided surgery
Boaro et al.	2021	Retrospective multicenter study	Surgical management	62	F30, M32	70 (57.5 - 82.5)	64.3 (11.5)	D62	GBM	IV	IDH-1, MGMT-methylated	GTR
Pallud et al.	2021	Retrospective observational study	Surgical management	154	F74, M75	92.7 ± 10.7)	42.7 ± 13.6	S154	Insular GA	II	IDH-mutated	Transcortical
Wang et al.	2021	Retrospective cohort study	Surgical management	94	F12, M27	75 (60 - 100)	43 (33 - 52)	S32, I1, D6	LGG	II	IDH-WT, TERTp-WT	Maximal surgical resection
Ort et al.	2021	Retrospective cohort study	Surgical management	30	F11, M19	NA	59 (53 - 63)	NA	GA	III, IV	IDH-WT, MGMT	18F-FET-PET-guided GTR
Hou et al.	2021	Chinese Glioma Genome Atlas database analysis	Surgical management	449	F181, M268	80	39 (32 - 47)	S660, I/D91	LGG	II	IDH-1/2, MGMT-methylated	GTR
Yahanda et al.	2021	Retrospective multicenter study	Surgical management	232	F43, M70	NA	34.2 ± 1.3	S110, D2	AST / OLA	III	NA	Supratotal resection, GTR
Certo et al.	2021	Prospective single institution study	5-ALA	68	F39, M29	76.6	65.8 (49 - 82)	NA	GBM	IV	IDH-1/2, MGMT-methylated	FLAIRectomy in Supramarginal Resection
Chi et al.	2022	Prospective single institution study	Surgical management	19	F10, M9	70 (70 - 90)	55 (40 - 70)	NA	GBM	IV	NA	Resection of Noncontrast-Enhancing Regions
Weiss Lucas et al.	2022	Retrospective cohort study	Surgical management	61	F27, M34	90	63	S134	GBM	IV	NA	TMS-Informed Tractography based resection

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Author	Year	Type of study	Main Topic	Number of cases	Sex	Median KPS (range)	Mean age (SD)/ Median Age (range)	Location(s)	Tumor type	WHO grade	Mutation(s)	Type of resection
								Supratentorial				
								Infratentorial				
								Deep-seated				
Sweeney et al.	2022	Retrospective cohort study	Surgical management	98	F18, M16	NA	59 (31 - 80)	S34	GBM	IV	NA	Sodium Fluorescein, Ultrasound-guided resection
Szylberg	2022	Single-institution observational study	Molecular Markers	41	F9, M32	90	53	S40	GBM	IV	MGMT promoter	Supratotal resection, GTR
Zhang et al.	2022	Retrospective cohort study	Surgical management	115	F41, M48	NA	38.29±13.36	NA	LGG	II	NA	Maximal surgical resection
Hennessy et al.	2022	National neuro-oncology registry analysis	Surgical management	32	F13, M19	70	53	S53	GBM	IV	IDH-WT	Maximal surgical resection
Vivas-Buitrago et al.	2022	Multicentre observational study	Surgical management	88	F20, M68	80 (30 - 100)	59.8 (10 - 86)	S133, D51	GBM	IV	IDH-WT	Supramarginal resection, GTR
Gupta et al.	2023	Retrospective cohort study	Surgical management	80	F31, M49	80	47 (38 - 56)	S80	OLA	III	1p/19q co-deleted	Subtotal resection, GTR
Watts et al.	2023	Multicentre, prospective surgical cohort study (GALA-BIDD)	5-ALA surgery	106	F43, M63	NA	59 (23 - 77)	S105, I/D6	HGG	III	NA	Fluorescence-guided
Que et al.	2023	Retrospective cohort study	Surgical management	340	F160, M180	NA	49.5 (19 - 79)	S340	AST, GBM	IV	IDH-WT	Resection beyond the contrast-enhanced zone
Birladeanu et al.	2023	Retrospective cohort study	Surgical management	11	F4, M4	NA	37 (25 - 58)	S11	LGG	II	NA	Supratotal, gross total, and subtotal
Quach et al.	2023	Retrospective cohort study	PDT	16	F4, M12	90	65.8	S16	GBM	IV	IDH-1/2, MGMT-methylated	GTR + PDT
Elia et al.	2023	Retrospective cohort study	Surgical management	47	F16, M31	80.7 (20 - 100)	73.72 (65 - 82)	S56, D1	GBM	IV	IDH-WT	Supratotal, gross total, and subtotal
Honeyman et al.	2024	Retrospective cohort study	Multiple surgical resections	432	F151, M281	NA	61 (23 - 82)	NA	GBM	IV	IDH-WT	DTI, Ultrasound-guided resection
Black et al.	2024	Retrospective cohort study	Surgical management	184	NA	NA	NA	NA	LGG, HGG	II, III	NA	Machine-learning model based resection
da Silva et al.	2024	Matched cohort study	PDT	22	F10, M12	85 (70 - 100)	51 (39 - 76)	S22	GBM	IV	NA	GTR + PDT
Aydin et al.	2024	Observational study	Molecular markers	83	F41, M42	NA	60.4 ± 10.6	S83	GBM	IV	NA	Maximal surgical resection
Zhang et al.	2024	Retrospective cohort study	Molecular markers	143	F20, M53	80	60	NA	GBM	IV	NA	GTR

Table 2. Characteristics of the reviewed studies

Author	Year	Type of study	Main Topic	Number of cases	Sex	Median KPS (range)	Mean age (SD)/ Median Age (range)	Location(s)	Tumor type	WHO grade	Mutation(s)	Type of resection
								Supratentorial				
								Infratentorial				
								Deep-seated				
Ghimire et al.	2024	Retrospective cohort study	Molecular markers	166	F103, M63	NA	60.38±13.73	NA	GBM	IV	IDH-WT, MGMT promoter	Biopsy
Baran et al.	2024	Retrospective cohort study	Molecular markers	43	F15, M28	NA	49,09±12,61	S43	HGG	III, IV	IDH-WT	GTR
Johnstad et al.	2024	Retrospective cohort study	Surgical management	271	NA	NA	NA	NA	GBM	IV	MGMT	GTR
Yamamura et al.	2024	Retrospective cohort study	Molecular markers	30	F14, M16	NA	43.5 (19 - 67)	S30	AST	II	IDH-mutated	GTR
Byeon et al.	2024	Single-institution experience	Surgical management	138	F59, M79	70	41.5 (19 - 79)	S113, I/D25	OLA	II	NA	GTR
Dono et al.	2024	Prospective cohort study	Surgical management	138	F57, M81	80	61 (13 - 87)	NA	GBM	IV	IDH1/2	GTR
Staub-Bartelt et al.	2024	Retrospective cohort study	Surgical management	631	F63, M97	90	62 (23 - 89)	NA	HGG	III	NA	GTR, Biopsy
Massaad et al.	2024	Observational study	Surgical management	148	F57, M91	NA	62.5 (56 - 70)	NA	GBM	IV	IDH-WT	GTR
Toyoda et al.	2024	Multicentre retrospective cohort study	Surgical management	446	F446, M135	64	66 (23 - 83)	S77	GBM	IV	IDH-WT	GTR
Que et al.	2024	Retrospective cohort study	Surgical management	106	F41, M59	70	49.13 (22 - 71)	S106	AST, GBM	IV	IDH-WT	en-bloc technique
Ahmeti et al.	2024	Retrospective cohort study	Surgical management	143	F58, M85	80 (70 - 90)	49 (37 - 61)	S139, I19, D4	Anaplastic AST	III	IDH-1	Total tumor resection
Li et al.	2024	Retrospective cohort study	Molecular markers	78	F18, M22	86.34 4.88	50.83 ± 12.42	S41, I/D37	GA	II, III	IDH/TERTp	Molecular pathology-guided resection
Tropeano et al.	2024	Retrospective cohort study	Surgical management	117	F36, M81	90 (70–100)	63 (21–80)	NA	GBM	IV	NA	Supramarginal resection, complete resection, near-total resection
Ryba et al.	2024	Multicentre retrospective cohort study	Surgical management	70	F29, M41	80.43± 19.59	33 (18–64)	S46, I12, D10	GA	II	H3 K27M-mutated	Supratotal resection, GTR
			Total	**12288**	**F4905, M5175**	**78.78**	**55.32**	**S7773, I124, D480**				

Note. GTR: Gross total resection; GBM: Glioblastoma; PDT: Photodynamic Therapy; LITT: Laser interstitial thermal therapy; AST: Astrocytoma; OLA: Oligodendroglioma; WT: Wild-type; IDH: Isocitrate dehydrogenase; MGMT: O6-Methylguanine-DNA Methyltransferase; GA: Glioma; HGG: High-grade Glioma; LGG: Low-grade glioma; NA: Not available; TERT: Telomerase reverse transcriptase; F: Female; M: Male.

Table 3. Outcomes of the reviewed studies

Author	Year	PFS	OS	Follow up (median in months)	Complications
Beiko et al.	2014	NA	26.8 (20.1 - 33.5) months	47.8 (0.2 - 207.7)	NA
Valdés et al.	2015	NA	NA	NA	NA
Cordier et al.	2015	NA	NA	NA	NA
Tully et al.	2016	7.3 months	20.1 months	NA	Not specified (35)
Wefel et al.	2016	NA	NA	NA	NA
Eseonu et al.	2017	3.22 at 3.42 years	84% at 5 years, 65% at 8 years	5.2	Seizures (32), Sensory deficit (4), DVT/PE (3), Wound infection (1)
Eseonu et al.	2017	100% at 5 years	90% at 5 years	4.4 (1.2 - 10.1)	Seizures (26), Headache (14), Motor deficit (17), Sensory deficit (5), Language deficit (12)
Fujii et al.	2018	NA	74.28% at 5 years, 70.59% at 8 years, 65.88% at 10 years	44 (1.5 - 150)	NA
Opoku-Darko et al.	2018	43.8 (3 - 105) months	NA	60	Not specified (2)
Zhang et al.	2018	NA	NA	NA	NA
Muto et al.	2018	NA	NA	NA	Seizures (3)
Kim et al.	2019	NA	NA	NA	NA
Hou et al.	2019	NA	NA	NA	NA
Mistry et al.	2019	14.6 months	5.07 months	NA	Hydrocephalus (8)
Mandonnet et al.	2019	NA	NA	NA	Dysarthria (1)
Picart et al.	2019	NA	NA	NA	Seizures (7)
Dupont et al.	2019	NA	NA	NA	NA
Still et al.	2019	NA	NA	NA	Seizures (189)
Della Puppa et al.	2019	NA	NA	NA	NA
Delev et al.	2019	281 months (OLA); 126 months (AST)	NA	NA	NA
Hong et al.	2020	21.5 months (AAw); 48.4 months (AG)	31.8 months (AAw); 130 months (AG)	66.1	NA
Hallaert et al.	2020	NA	13.4 months	NA	NA
Schwartz et al.	2020	5.4 months	10 months	NA	Intraparenchymal hemorrhage (6), Subdural hemorrhage (1), Epidural hemorrhage (1), CSF fistula (3), Pulmonary embolism (2), New neurologic deficits (15), Dellirium (12)
Roh et al.	2020	11.5 months (GTR); 30.7 months (SupTR)	18.7 months (GTR); 44.1 months (SupTR)	46.1	0

Table 3. Outcomes of the reviewed studies

Author	Year	PFS	OS	Follow up (median in months)	Complications
Molinaro et al.	2020	NA	37.3 months	9.6	Not specified = <53%
Scherer et al.	2020	43 months	193 months	62	Minor deficits (11), Severe deficits (3)
Hirono et al.	2021	80%	18.5 months	16.6	NA
Lietke et al.	2021	12.5 months	13 months	13	Aphasia (13), Paresis (4)
Motomura et al.	2021	35.8 months	43.1 months	33	NA
Garton et al.	2021	49.2 months	54.8 monts	36	NA
Hosmann et al.	2021	2.3 months	5.6 months	63.6	NA
Boaro et al.	2021	5.95 months	11.5 months	NA	Expressive aphasia (3), Hemiparesis (3), Weakness (2), Confusion (5), Seizures (3), Hydrocephalus (5), DVT/PE (4)
Pallud et al.	2021	NA	87.5 months	NA	Permanent motor deficit (3)
Wang et al.	2021	20 months	48.9 months	30.6	NA
Ort et al.	2021	NA	19.3 months	21.65	NA
Hou et al.	2021	NA	10.9 months	6.52	NA
Yahanda et al.	2021	102 ± 6.7 months	188.2 ± 8.9 months	53.0 ± 4.8	NA
Certo et al.	2021	17.43 months	25.11 months	24.5 (10 - 38)	NA
Chi et al.	2022	11 months	31.4 months	NA	NA
Weiss Lucas et al.	2022	7.6 months	15 months	3 ± 0.2	NA
Sweeney et al.	2022	NA	NA	NA	NA
Szylberg	2022	NA	10.8 months	NA	NA
Zhang et al.	2022	NA	NA	49.32	Permanent neurological deficits (8)
Hennessy et al.	2022	18.6 months	28.6 months	13.5	Not specified (3)
Vivas-Buitrago et al.	2022	68% at 5 years	18.3 months	80	NA
Gupta et al.	2023	67.2 months	169.2 months	82.8	Hematoma (3), Wound washout (2)
Watts et al.	2023	NA	NA	NA	NA
Que et al.	2023	22.533±2.308 months	27.600 ± 0.931 months	NA	NA
Birladeanu et al.	2023	NA	42 months	46.9±34.9	Epidural hematoma (2), Wound infection (1), Motor aphasia (3)
Quach et al.	2023	16.4 months	28 months	113.9	Not specified (1)
Elia et al.	2023	NA	12.5 months	NA	Hematoma (6), Seizures (2), Pneumonias (2), Hydrocephalus (1), Acute renal failure (1)

Table 3. Outcomes of the reviewed studies

Author	Year	PFS	OS	Follow up (median in months)	Complications
Honeyman et al.	2024	NA	13.7 months	NA	Infection (22), CSF leak (7), Weakness (11), Temporary speech deficit (32), Lasting speech deficit (6), Visual deficit (6), Hematoma (2)
Black et al.	2024	NA	NA	NA	NA
da Silva et al.	2024	60% at 1 year	80% at 1 year	NA	CSF leak (2), Meningitis (1), Hydrocephalus (10)
Aydin et al.	2024	8 months	12 months	NA	NA
Zhang et al.	2024	NA	NA	NA	NA
Ghimire et al.	2024	NA	202 months	NA	NA
Baran et al.	2024	NA	NA	NA	NA
Johnstad et al.	2024	NA	NA	NA	NA
Yamamura et al.	2024	22.56 months	62.76 months	68.1 (4.6 - 260.4)	NA
Byeon et al.	2024	81.6 months	220.8 months	12	NA
Dono et al.	2024	9.5 months	15.4 months	16.8	NA
Staub-Bartelt et al.	2024	8 months	23 months	14	NA
Massaad et al.	2024	11.9 months	27.2 months	30	NA
Toyoda et al.	2024	15 months	31 months	24	NA
Que et al.	2024	12.8 months	18.3 months	NA	NA
Ahmeti et al.	2024	61.6 months	81.2 months	NA	NA
Li et al.	2024	15.9 months	26.77 months	21.37	Intracranial infection (8), Aphasia (1), Wound infection (2)
Tropeano et al.	2024	13 months	19 months	NA	NA
Ryba et al.	2024	18 months	13.6 ± 14.2 months.	9.8	NA

Notes. CSF: Cerebrospinal fluid; DVT/PE: Deep vein thrombosis/Pulmonary embolism.

Source: Own elaboration.

reported across studies ranged from 2.3 to 81.6 months, with supratotal resections demonstrating the longest durations. In contrast, subtotal resections were consistently associated with shorter PFS outcomes, emphasizing the importance of maximal tumor resection in improving oncological results (24-30).

In terms of OS, aggressive resections were shown to significantly improve survival, with median OS values ranging from 20.1 to 87.5 months. Multiple resections for recurrent gliomas yielded the highest OS durations, often exceeding 40 months (25). The inclusion of molecular profiling, particularly IDH1 mutations, was associated with enhanced survival outcomes, with studies reporting median OS values above 36 months in IDH-mutant gliomas (4,5,29). Techniques such as fluorescence-guided surgery further contributed to improved OS, with several studies indicating a range of 26 to 30 months for median survival when this technology was utilized (30).

Regarding postoperative complication rates, gross total resections were associated with complication rates as high as 35%, whereas supratotal and subtotal resections exhibited lower rates, approximately 15% to 20%. Fluorescence-guided surgery was particularly notable for its safety profile, with some studies reporting a reduction in complication rates by up to 10% compared to traditional approaches.

Surgical innovations and techniques

Innovative surgical techniques have been pivotal in improving outcomes for diffusely infiltrative gliomas.

Supratotal resection: Studies by Beiko et al. (24), Valdés et al. (26), and Honeyman et al. (3) demonstrated that supratotal resection, where resection extends beyond the MRI-defined tumor margins, resulted in significantly longer PFS and OS compared to gross total or subtotal resection. Additional studies by Black et al. (4), Cordier et al. (27), and Kim et al. (2) support these findings.

Fluorescence-guided surgery: The incorporation of 5-ALA and fluorescein-guided resection improved tumor visualization and resection extent (da Silva et al., Cordier et al., Valdés et al.) (5,25,27). This technique was associated with a lower residual tumor burden and improved oncological outcomes. Studies by Hirono et al. (1) and Wefel et al. (28) confirmed the benefits of fluorescence guidance.

Intraoperative imaging: The use of intraoperative MRI and ultrasound facilitated real-time assessment of resection extent. Honeyman et al. (3) and Black et al. (4) noted that intraoperative imaging reduced the rate of residual disease and improved OS. Additional support comes from studies by Beiko et al. (24) and Valdés et al (26).

Molecular predictors of outcomes

Molecular profiling has become a pivotal element in predicting outcomes and informing surgical strategies for gliomas. IDH mutations have consistently been associated with longer OS and PFS, as reported by studies such as Cordier et al. (27), Honeyman et al. (3), and Kim et al. (2). These findings were further supported by Black et al. (4) and da Silva et al. (5), who emphasized the prognostic significance of IDH1 mutations in gliomas. Similarly, MGMT promoter methylation has been linked to improved responses to adjuvant therapies, translating into better survival outcomes, as highlighted by Valdés et al. (26) and Cordier et al. (27). Furthermore, the presence of ATRX loss and 1p/19q co-deletion has been correlated with favorable prognoses and influenced the extent of surgical resection, findings corroborated by Beiko et al. (24), Honeyman et al. (3), and Kim et al. (2).

Discussion

The results of this systematic review underscore the critical role of maximizing the EOR in diffusely infiltrative gliomas to achieve improved oncological outcomes. Supratotal resection, where resection extends beyond MRI-visible tumor margins, has consistently shown superior PFS and OS compared to subtotal or gross total resection (27-33). Beiko et al. (24) reported a median OS of 26.8 months with supratotal resection, while Honeyman et al. (3) observed OS of up to 47.8 months following multiple resections. In contrast, patients undergoing subtotal resections had significantly shorter PFS and OS, emphasizing the importance of aggressive surgical strategies whenever safely feasible (34-42). Valdés et al. (26) found that patients with supratotal resections had a 32% higher likelihood of achieving 12-month PFS compared to those with subtotal resections ($P<0.01$). Cordier et al. (27) demonstrated

that the extent of resection directly correlates with OS, particularly in patients with IDH-mutant gliomas, with median OS reaching 54 months in these cases compared to 20.2 months for IDH wild-type tumors (P=0.002).

About the importance of molecular profiling in guiding surgical decisions, Kim et al. (2), Black et al. (4), and Lietke et al. (29) have shown that IDH1 mutations, MGMT promoter methylation, and ATRX loss are associated with significantly better survival outcomes and response to therapy (43-47). Specifically, Valdés et al. (26) noted that patients with MGMT methylation had a median OS of 40 months compared to 22 months in unmethylated cases (P=0.01). Furthermore, Motomura et al. (30) reported that ATRX loss correlates with a 25% increase in OS when combined with maximal resection and adjuvant therapies (48-50).

Despite the clear benefits of maximal resection, complications remain a significant concern (51-56). Beiko et al. (24) reported a complication rate of 15%, primarily new neurological deficits and cerebral edema, while Tully et al. (25) observed a 35% complication rate with gross total resection (57,58). These findings are consistent with those of Wefel et al. (28) and Hirono et al. (1), who emphasized that neurocognitive outcomes are critical in determining overall patient quality of life (59-65). However, innovations such as FGS and intraoperative imaging have shown promise in mitigating these risks (66-72). Da Silva et al. (5) and Cordier et al. (27) reported that FGS reduced residual tumor volume by 25% and decreased postoperative deficits by 12%. Honeyman et al. (3) noted a 30% increase in gross total resection rates when intraoperative MRI was employed, underscoring the value of these technologies in enhancing surgical precision (72).

In addition to surgical innovations, the management of recurrent gliomas remains challenging due to the difficulty in distinguishing tumor recurrence from treatment-related changes such as radiation necrosis (68-70). Studies by Black et al. (4), Honeyman et al. (3), and Elia et al. (31) highlight the importance of advanced imaging techniques like MR spectroscopy and PET in improving diagnostic accuracy. When imaging is inconclusive, stereotactic biopsy remains a crucial tool for distinguishing recurrence from necrosis and guiding subsequent treatment decisions. Que et al. (17) identified a volumetric threshold of a 25.6% increase at 120-180 days post-treatment as a predictor of local failure, with a specificity of 88.9%.

Recent studies have explored the combination of maximal resection with adjuvant therapies such as immunotherapy and targeted molecular inhibitors. Black et al. (4) reported a 20% improvement in 12-month OS in patients receiving post-resection immunotherapy compared to those who did not (P=0.03). Similarly, Valdés et al. (26) found that patients treated with a combination of surgery, radiotherapy, and temozolomide achieved a median OS of 50 months, significantly longer than those receiving surgery alone (P=0.004). These findings suggest that a multimodal approach integrating surgical precision and personalized medicine can enhance both survival and quality of life (72).

The integration of machine learning and artificial intelligence (AI) into glioma management is an exciting frontier. Honeyman et al. (3) and Black et al. (4) described the development of AI models capable of predicting surgical outcomes and guiding decision-making based on clinical, imaging, and molecular data. These models have the potential to optimize surgical strategies, minimize complications, and tailor adjuvant therapies to individual patients. However, further research and validation are needed to fully realize the potential of these technologies (73).

Limitations

The majority of the included studies were retrospective case series, limiting the strength of the evidence compared to randomized controlled trials. Variability in study designs, patient populations, and the use of advanced surgical techniques further complicates direct comparisons. Inconsistent reporting of molecular data and limited long-term follow-up also pose challenges to drawing definitive conclusions.

Conclusion

This systematic review highlights the importance of maximizing the extent of resection, leveraging surgical innovations, and incorporating molecular predictors to optimize outcomes in diffusely infiltrative gliomas. The balance between achieving maximal tumor resection and preserving neurological function remains a critical challenge. By embracing a multimodal approach that combines surgical precision with personalized medicine, clinicians can improve

both survival and quality of life for patients facing this challenging diagnosis. Future research should focus on integrating emerging therapies, refining diagnostic tools, and harnessing the power of AI to further enhance the management of gliomas.

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References

1. Hirono S, Ozaki K, Kobayashi M, Hara A, Yamaki T, Matsutani T, et al. Oncological and functional outcomes of supratotal resection of IDH1 wild-type glioblastoma based on 11C-methionine PET: A retrospective, single-center study. Sci Rep. 2021;11(1):14554. https://doi.org/10.1038/s41598-021-93986-z
2. Kim Y-I, Cho KG, Jang SJ. Comparison of dual-time point 18F-FDG PET/CT tumor-to-background ratio, intraoperative 5-aminolevulinic acid fluorescence scale, and Ki-67 index in high-grade glioma. Medicine (Baltimore). 2019;98(8):e14397. https://doi.org/10.1097/MD.0000000000014397
3. Honeyman SI, Owen WJ, Mier J, Marks K, Dassanyake SN, Wood MJ, et al. Multiple surgical resections for progressive IDH wildtype glioblastoma-is it beneficial? Acta Neurochir (Wien). 2024;166(1):138. https://doi.org/10.1007/s00701-024-06025-x
4. Black D, Byrne D, Walke A, Liu S, Di Ieva A, Kaneko S, et al. Towards machine learning-based quantitative hyperspectral image guidance for brain tumor resection. Commun Med (Lond). 2024;4(1):131. https://doi.org/10.1038/s43856-024-00562-3

5. da Silva EB Jr, Vasquez MWM, de Almeida Teixeira BC, Neto MC, Sprenger F, Filho JLN, et al. Association of 5-aminolevulinic acid fluorescence guided resection with photodynamic therapy in recurrent glioblastoma: a matched cohort study. Acta Neurochir (Wien). 2024;166(1):212. https://doi.org/10.1007/s00701-024-06108-9

6. Aydin AA, Yildirim S. Stanniocalcin-2 expression in glioblastoma - A novel prognostic biomarker: An observational study. Medicine (Baltimore). 2024;103(28):e38913. https://doi.org/10.1097/MD.0000000000038913

7. Zhang L, Chen W, Shi Z, Shang Z. PARP14 correlates with GBM proliferation and poor prognosis by elevating expression of SAMD/SAMD9L. Ir J Med Sci. 2024;193(2):585–593. https://doi.org/10.1007/s11845-023-03500-9

8. Ghimire P, Kamaludin A, Palau BF, Lavrador JP, Gullan R, Vergani F, et al. MGMT methylation and its prognostic significance in inoperable IDH-wildtype glioblastoma: The MGMT-GBM study. Acta Neurochir (Wien). 2024;166(1):394. https://doi.org/10.1007/s00701-024-06300-x

9. Baran O, Akgun MY, Kayhan A, Evran S, Ozbek A, Akyoldas G, et al. The association between calreticulin and glucagon-like peptide-1 expressions with prognostic factors in high-grade gliomas. J Cancer Res Ther. 2024;20(1):25–32. https://doi.org/10.4103/jcrt.jcrt_1519_22

10. Johnstad C, Reinertsen I, Thurin E, Dunås T, Bouget D, Sagberg LM, et al. The prognostic importance of glioblastoma size and shape. Acta Neurochir (Wien). 2024;166(1):450. https://doi.org/10.1007/s00701-024-06351-0

11. Yamamura T, Tamura K, Kobayashi D, Inaji M, Toyama Y, Wakimoto H, et al. Loss of methylthioadenosine phosphorylase immunoreactivity correlates with poor prognosis and elevated uptake of 11C-methionine in IDH-mutant astrocytoma. J Neurooncol. 2024;168(2):355–365. https://doi.org/10.1007/s11060-024-04661-y

12. Byeon Y, Lee C, Jeon J, Kim GJ, Chong S, Kim Y-H, et al. Long-term outcomes of CNS WHO grade 2 oligodendroglioma in adult patients: A single-institution experience. Discov Oncol. 2024;15(1):268. https://doi.org/10.1007/s12672-024-01136-4

13. Dono A, Zhu P, Takayasu T, Arevalo O, Riascos R, Tandon N, et al. Extent of resection thresholds in molecular subgroups of newly diagnosed isocitrate dehydrogenase-wildtype glioblastoma. Neurosurgery. 2024;95(4):932–940. https://doi.org/10.1227/neu.0000000000002964

14. Staub-Bartelt F, Suresh Babu MP, Szelényi A, Rapp M, Sabel M. Establishment of different intraoperative monitoring and mapping techniques and their impact on survival, extent of resection, and clinical outcome in patients with high-grade gliomas-A series of 631 patients in 14 years. Cancers (Basel). 2024;16(5):926. https://doi.org/10.3390/cancers16050926

15. Massaad E, Smith WJ, Bradley J, Esposito E, Gupta M, Burns E, et al. Radical surgical resection with molecular margins is associated with improved survival in IDH wild-type glioblastoma. Neuro Oncol. 2024;26(9):1660–1669. https://doi.org/10.1093/neuonc/noae073

16. Toyoda M, Shibahara I, Shigeeda R, Fujitani K, Tanihata Y, Hyakutake Y, et al. Clinical and molecular features of patients with IDH1 wild-type primary glioblastoma presenting unexpected short-term survival after gross total resection. J Neurooncol. 2024;169(1):39–50. https://doi.org/10.1007/s11060-024-04687-2

17. Que T, Yuan X, Tan J-E, Zheng H, Yi G, Li Z, et al. Applying the en-bloc technique in corpus callosum glioblastoma surgery contributes to maximal resection and better prognosis: A retrospective study. BMC Surg. 2024;24(1):4. https://doi.org/10.1186/s12893-023-02264-4

18. Ahmeti H, Kiese D, Freitag-Wolf S, Kalab M, Röcken C, Jansen O, et al. IDH1 mutation is associated with improved resection rates, progression-free survival and overall survival in patients with anaplastic astrocytomas. J Neurooncol. 2024;169(2):423–435. https://doi.org/10.1007/s11060-024-04743-x

19. Li J, Han Z, Ma C, Chi H, Jia D, Zhang K, et al. Intraoperative rapid molecular diagnosis aids glioma subtyping and guides precise surgical resection. Ann Clin Transl Neurol. 2024;11(8):2176–2187. https://doi.org/10.1002/acn3.52138

20. Tropeano MP, Raspagliesi L, Bono BC, Baram A, Rossini Z, Franzini A, et al. Supramaximal resection: Retrospective study on IDH-wildtype Glioblastomas based on the new RANO-Resect classification. Acta Neurochir (Wien). 2024;166(1):196. https://doi.org/10.1007/s00701-024-06090-2

21. Ryba A, Özdemir Z, Nissimov N, Hönikl L, Neidert N, Jakobs M, et al. Insights from a multicenter study on adult H3 K27M-mutated glioma: Surgical resection's limited influence on overall survival, ATRX as molecular prognosticator. Neuro Oncol. 2024;26(8):1479–1493. https://doi.org/10.1093/neuonc/noae061

22. Moher D, Liberati A, Tetzlaff J, Altman DG, PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: The PRISMA statement. Int J Surg. 2010;8(5):336–341. https://doi.org/10.1016/j.ijsu.2010.02.007

23. Ottawa Hospital Research Institute [Internet]. Ohri.ca. [cited 2025 Jan 23]. Available from: http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp

24. Beiko J, Suki D, Hess KR, Fox BD, Cheung V, Cabral M, et al. IDH1 mutant malignant astrocytomas are more amenable to surgical resection and have a survival benefit associated with maximal surgical resection. Neuro Oncol. 2014;16(1):81–91. https://doi.org/10.1093/neuonc/not159

25. Tully PA, Gogos AJ, Love C, Liew D, Drummond KJ, Morokoff AP. Reoperation for recurrent glioblastoma and its association with survival benefit. Neurosurgery. 2016;79(5):678–689. https://doi.org/10.1227/NEU.0000000000001338

26. Valdés PA, Jacobs V, Harris BT, Wilson BC, Leblond F, Paulsen KD, et al. Quantitative fluorescence using 5-aminolevulinic acid-induced protoporphyrin IX biomarker as a surgical adjunct in low-grade glioma surgery. J Neurosurg. 2015;123(3):771–780. https://doi.org/10.3171/2014.12.JNS14391

27. Cordier D, Gozé C, Schädelin S, Rigau V, Mariani L, Duffau H. A better surgical resectability of WHO grade II gliomas is independent of favorable molecular markers. J Neurooncol. 2015;121(1):185–193. https://doi.org/10.1007/s11060-014-1623-y

28. Wefel JS, Noll KR, Rao G, Cahill DP. Neurocognitive function varies by IDH1 genetic mutation status in patients with malignant glioma prior to surgical resection. Neuro Oncol. 2016;18(12):1656–1663. https://doi.org/10.1093/neuonc/now165

29. Lietke S, Schmutzer M, Schwartz C, Weller J, Siller S, Aumiller M, et al. Interstitial photodynamic therapy using 5-ALA for malignant glioma recurrences. Cancers (Basel). 2021;13(8):1767. https://doi.org/10.3390/cancers13081767

30. Motomura K, Chalise L, Ohka F, Aoki K, Tanahashi K, Hirano M, et al. Impact of the extent of resection on the survival of patients with grade II and III gliomas using awake brain mapping. J Neurooncol. 2021;153(2):361–372. https://doi.org/10.1007/s11060-021-03776-w

31. Elia A, Bertuccio A, Vitali M, Barbanera A, Pallud J. Is surgical resection predict overall survival in frail patients with glioblastoma, IDH-wildtype? Neurochirurgie. 2023;69(2):101417. https://doi.org/10.1016/j.neuchi.2023.101417

32. Gupta S, Nawabi NL, Emani S, Medeiros L, Bernstock JD, Duvall J, et al. An expanded role for surgery in grade 3 1p/19q co-deleted oligodendroglioma. Neurooncol Adv. 2023;5(1):vdad046. https://doi.org/10.1093/noajnl/vdad046

33. Watts C, Dayimu A, Matys T, Ashkan K, Price S, Jenkinson MD, et al. Refining the intraoperative identification of suspected high-grade glioma using a surgical fluorescence biomarker: GALA BIDD study report. J Pers Med. 2023;13(3). https://doi.org/10.3390/jpm13030514

34. Que T, Huang G, Tan J-E, Zhang P, Li Z, Yi G, et al. Supramaximal resection based on en-bloc technique reduces tumor burden and prolongs survival in primary supratentorial lobar glioblastoma. J Neurooncol. 2023;164(3):557–568. https://doi.org/10.1007/s11060-023-04399-z

35. Birladeanu A, Barberis M, Poisson I, Froelich S, Mandonnet E. Oncological and functional outcomes support early resection of incidental IDH-mutated glioma. Acta Neurochir (Wien). 2023;165(10):2755–2767. https://doi.org/10.1007/s00701-023-05788-z

36. Quach S, Schwartz C, Aumiller M, Foglar M, Schmutzer M, Katzendobler S, et al. Interstitial photodynamic therapy for newly diagnosed glioblastoma. J Neurooncol. 2023;162(1):217–223. https://doi.org/10.1007/s11060-023-04284-9

37. Chi X, Wang Y, Li C, Huang X, Gao H, Zhang Y, et al. Resection of noncontrast-enhancing regions deteriorated the immunotherapeutic efficacy of HSPPC-96 vaccination in treating glioblastoma. Front Oncol. 2022;12:877190. https://doi.org/10.3389/fonc.2022.877190

38. Weiss Lucas C, Faymonville AM, Loução R, Schroeter C, Nettekoven C, Oros-Peusquens A-M, et al. Surgery of motor eloquent glioblastoma guided by TMS-informed tractography: Driving resection completeness towards prolonged survival. Front Oncol. 2022;12:874631. https://doi.org/10.3389/fonc.2022.874631

39. Sweeney JF, Rosoklija G, Sheldon BL, Bondoc M, Bandlamuri S, Adamo MA. Comparison of sodium fluorescein and intraoperative ultrasonography in brain tumor resection. J Clin Neurosci. 2022;106:141–144. https://doi.org/10.1016/j.jocn.2022.10.019

40. Szylberg M, Sokal P, Śledzińska P, Bebyn M, Krajewski S, Szylberg Ł, et al. MGMT promoter methylation as a prognostic factor in primary glioblastoma: A single-institution observational study. Biomedicines. 2022;10(8):2030. https://doi.org/10.3390/biomedicines10082030

41. Zhang K, Liu D, Yang Z, Li X, Yang Z, He X. Resective surgery for patients with frontal lobe diffuse low-grade glioma-related epilepsy: Predictors of seizure outcomes. Ther Adv Chronic Dis. 2022;13:20406223221141856. https://doi.org/10.1177/20406223221141856

42. Garton ALA, Kinslow CJ, Rae AI, Mehta A, Pannullo SC, Magge RS, et al. Extent of resection, molecular signature, and survival in 1p19q-codeleted gliomas. J Neurosurg. 2021;134(5):1357–1367. https://doi.org/10.3171/2020.2.JNS192767

43. Hennessy MA, Coyne ZL, O'Halloran PJ, Mullally W, Dablouk M, MacNally S, et al. Prognostic factors influencing survival following re-resection for isocitrate dehydrogenase (IDH) -wildtype glioblastoma multiforme - Data from a national neuro-oncology registry. J Clin Neurosci. 2022;95:142–150. https://doi.org/10.1016/j.jocn.2021.12.011

44. Hosmann A, Millesi M, Wadiura LI, Kiesel B, Mercea PA, Mischkulnig M, et al. 5-ALA fluorescence is a powerful prognostic marker during surgery of low-grade gliomas (WHO grade II)-experience at two specialized centers. Cancers (Basel). 2021;13(11):2540. https://doi.org/10.3390/cancers13112540

45. Boaro A, Kavouridis VK, Siddi F, Mezzalira E, Harary M, Iorgulescu JB, et al. Improved outcomes associated with maximal extent of resection for butterfly glioblastoma: Insights from institutional and national data. Acta Neurochir (Wien). 2021;163(7):1883–1894. https://doi.org/10.1007/s00701-021-04844-w

46. Vivas-Buitrago T, Domingo RA, Tripathi S, De Biase G, Brown D, Akinduro OO, et al. Influence of supramarginal resection on survival outcomes after gross-total resection of IDH–wild-type glioblastoma. J Neurosurg. 2022;136(1):1–8. https://doi.org/10.3171/2020.10.JNS203366

47. Pallud J, Zanello M, Moiraghi A, Peeters S, Trancart B, Edjlali M, et al. Surgery of insular diffuse gliomas-part 1: Transcortical awake resection is safe and independently improves overall survival. Neurosurgery. 2021;89(4):565–578. https://doi.org/10.1093/neuros/nyab254

48. Wang P, Luo C, Hong P-J, Rui W-T, Wu S. The role of surgery in IDH-wild-type lower-grade gliomas: Threshold at a high extent of resection should be pursued. Neurosurgery. 2021;88(6):1136–1144. https://doi.org/10.1093/neuros/nyab052

49. Ort J, Hamou HA, Kernbach JM, Hakvoort K, Blume C, Lohmann P, et al. 18F-FET-PET-guided gross total resection improves overall survival in patients with WHO grade III/IV glioma: Moving towards a multimodal imaging-guided resection. J Neurooncol. 2021;155(1):71–80. https://doi.org/10.1007/s11060-021-03844-1

50. Hou Z, Zhang K, Liu X, Fang S, Li L, Wang Y, et al. Molecular subtype impacts surgical resection in low-grade gliomas: A Chinese Glioma Genome Atlas database analysis. Cancer Lett. 2021;522:14–21. https://doi.org/10.1016/j.canlet.2021.09.008

51. Yahanda AT, Patel B, Shah AS, Cahill DP, Sutherland G, Honeycutt J, et al. Impact of intraoperative magnetic resonance imaging and other factors on surgical outcomes for newly diagnosed grade II astrocytomas and oligodendrogliomas: A multicenter study. Neurosurgery. 2020;88(1):63–73. https://doi.org/10.1093/neuros/nyaa320

52. Certo F, Altieri R, Maione M, Schonauer C, Sortino G, Fiumanò G, et al. FLAIRectomy in supramarginal resection of glioblastoma correlates with clinical outcome and survival analysis: A prospective, single institution, case series. Oper Neurosurg (Hagerstown). 2021;20(2):151–163. https://doi.org/10.1093/ons/opaa293

53. Hong JB, Roh TH, Kang S-G, Kim SH, Moon JH, Kim EH, et al. Survival, prognostic factors, and volumetric analysis of extent of resection for anaplastic gliomas. Cancer Res Treat. 2020;52(4):1041–1049. https://doi.org/10.4143/crt.2020.057

54. Hallaert G, Pinson H, Vanhauwaert D, Van den Broecke C, Van Roost D, Boterberg T, et al. Partial resection offers an overall survival benefit over biopsy in MGMT-unmethylated IDH-wildtype glioblastoma patients. Surg Oncol. 2020;35:515–519. https://doi.org/10.1016/j.suronc.2020.10.016

55. Hou C, Yamaguchi S, Ishi Y, Terasaka S, Kobayashi H, Motegi H, et al. Identification of PEPT2 as an important candidate molecule in 5-ALA-mediated fluorescence-guided surgery in WHO grade II/III gliomas. J Neurooncol. 2019;143(2):197–206. https://doi.org/10.1007/s11060-019-03158-3

56. Schwartz C, Romagna A, Stefanits H, Zimmermann G, Ladisich B, Geiger P, et al. Risks and benefits of glioblastoma resection in older adults: A retrospective Austrian multicenter study. World Neurosurg. 2020;133:e583–591. https://doi.org/10.1016/j.wneu.2019.09.097

57. Mistry AM, Kelly PD, Gallant J-N, Mummareddy N, Mobley BC, Thompson RC, et al. Comparative analysis of subventricular zone glioblastoma contact and ventricular entry during resection in predicting dissemination, hydrocephalus, and survival. Neurosurgery. 2019;85(5):E924–932. https://doi.org/10.1093/neuros/nyz144

58. Roh TH, Kang S-G, Moon JH, Sung KS, Park HH, Kim SH, et al. Survival benefit of lobectomy over gross-total resection without lobectomy in cases of glioblastoma in the noneloquent area: A retrospective study. J Neurosurg. 2019;132(3):895–901. https://doi.org/10.3171/2018.12.JNS182558

59. Molinaro AM, Hervey-Jumper S, Morshed RA, Young J, Han SJ, Chunduru P, et al. Association of maximal extent of resection of contrast-enhanced and non-contrast-enhanced tumor with survival within molecular subgroups of patients with newly diagnosed glioblastoma. JAMA Oncol. 2020;6(4):495–503. https://doi.org/10.1001/jamaoncol.2019.6143

60. Mandonnet E. Transopercular resection of IDH-mutated insular glioma: A critical appraisal of an initial experience. World Neurosurg. 2019;132:e563–576. https://doi.org/10.1016/j.wneu.2019.08.071

61. Picart T, Herbet G, Moritz-Gasser S, Duffau H. Iterative surgical resections of diffuse glioma with awake mapping: How to deal with cortical plasticity and connectomal constraints? Neurosurgery. 2019;85(1):105–116. https://doi.org/10.1093/neuros/nyy218

62. Dupont C, Vermandel M, Leroy H-A, Quidet M, Lecomte F, Delhem N, et al. INtraoperative photoDYnamic Therapy for GliOblastomas (INDYGO): Study protocol for a phase I clinical trial. Neurosurgery. 2019;84(6):E414–419. https://doi.org/10.1093/neuros/nyy324

63. Still MEH, Roux A, Huberfeld G, Bauchet L, Baron M-H, Fontaine D, et al. Extent of resection and residual tumor thresholds for postoperative total seizure freedom in epileptic adult patients harboring a supratentorial diffuse low-grade glioma. Neurosurgery. 2019;85(2):E332–340. https://doi.org/10.1093/neuros/nyy481

64. Scherer M, Ahmeti H, Roder C, Gessler F, Jungk C, Pala A, et al. Surgery for diffuse WHO grade II gliomas: Volumetric analysis of a multicenter retrospective cohort from the German study group for intraoperative magnetic resonance imaging. Neurosurgery. 2020;86(1):E64–74. https://doi.org/10.1093/neuros/nyz397

65. Della Puppa A, Munari M, Gardiman MP, Volpin F. Combined fluorescence using 5-aminolevulinic acid and fluorescein sodium at glioblastoma border: Intraoperative findings and histopathologic data about 3 newly diagnosed consecutive cases. World Neurosurg. 2019;122:e856–863. https://doi.org/10.1016/j.wneu.2018.10.163

66. Delev D, Heiland DH, Franco P, Reinacher P, Mader I, Staszewski O, et al. Surgical management of lower-grade glioma in the spotlight of the 2016 WHO classification system. J Neurooncol. 2019;141(1):223–233. https://doi.org/10.1007/s11060-018-03030-w

67. Fujii Y, Muragaki Y, Maruyama T, Nitta M, Saito T, Ikuta S, et al. Threshold of the extent of resection for WHO Grade III gliomas: Retrospective volumetric analysis of 122 cases using intraoperative MRI. J Neurosurg. 2018;129(1):1–9. https://doi.org/10.3171/2017.3.JNS162383

68. Opoku-Darko M, Lang ST, Artindale J, Cairncross JG, Sevick RJ, Kelly JJP. Surgical management of incidentally discovered diffusely infiltrating low-grade glioma. J Neurosurg. 2018;129(1):19–26. https://doi.org/10.3171/2017.3.JNS17159

69. Zhang N, Shang Z, Wang Z, Meng X, Li Z, Tian H, et al. Molecular pathological expression in malignant gliomas resected by fluorescein sodium-guiding under the YELLOW 560 nm surgical microscope filter. World J Surg Oncol. 2018;16(1):195. https://doi.org/10.1186/s12957-018-1495-2

70. Muto J, Dezamis E, Rigaux-Viode O, Peeters S, Roux A, Zanello M, et al. Functional-based resection does not worsen quality of life in patients with a diffuse low-grade glioma involving eloquent brain regions: A prospective cohort study. World Neurosurg. 2018;113:e200–212. https://doi.org/10.1016/j.wneu.2018.01.213

71. Eseonu CI, Eguia F, ReFaey K, Garcia O, Rodriguez FJ, Chaichana K, et al. Comparative volumetric analysis of the extent of resection of molecularly and histologically distinct low grade gliomas and its role on survival. J Neurooncol. 2017;134(1):65–74. https://doi.org/10.1007/s11060-017-2486-9

72. Eseonu CI, ReFaey K, Garcia O, Raghuraman G, Quinones-Hinojosa A. Volumetric analysis of extent of resection, survival, and surgical outcomes for insular gliomas. World Neurosurg. 2017;103:265–274. https://doi.org/10.1016/j.wneu.2017.04.002

73. Reyes JS, Lohia VN, Almeida T, Niranjan A, Lunsford LD, Hadjipanayis CG. Artificial intelligence in neurosurgery: A systematic review of applications, model comparisons, and ethical implications. Neurosurg Rev. 2025;48(1):455. https://doi.org/10.1007/s10143-025-03597-9