

REVIEW OPEN ACCESS

Efficacy Assessment of Supramarginal Resection Versus Gross Total Resection in Glioblastoma: A Systematic Literature Review and Meta-Analysis

Dipak Chaulagain¹  | Volodymyr Smolanka¹  | Andriy Smolanka¹  | Kashif Qureshi²  | Kivanc Yangi³  | Oleg Devinyak⁴  | Bipin Chaurasia⁵ 

¹Neurosurgery Department, Regional Clinical Center of Neurosurgery and Neurology, Uzhhorod National University, Uzhhorod, Ukraine | ²Department of Neurosurgery, Yale School of Medicine, New Haven, Connecticut, USA | ³Department of Neurosurgery, Barrow Neurological Institute, Phoenix, Arizona, USA | ⁴Department of Pharmaceutical Sciences, Uzhhorod National University, Uzhhorod, Ukraine | ⁵Neurosurgery Department, Neurosurgery Clinic, Birgunj, Nepal

Correspondence: Bipin Chaurasia (trozexa@gmail.com)

Received: 10 February 2025 | **Revised:** 1 April 2026 | **Accepted:** 2 April 2026

Keywords: glioblastoma multiforme | supramarginal resection | gross total resection

ABSTRACT

Background: The standard treatment for glioblastoma multiforme (GBM) typically involves a surgical resection followed by radiation therapy and chemotherapy. The extent of resection (EOR) plays a significant role in predicting the prognosis of GBM. The literature showed improved survival outcomes with greater removal of contrast-enhancing tumor mass. We aim to compare the effects of supramarginal resection and gross total resection for the management of GBM.

Methods: A systematic search was conducted from electronic databases (PubMed/Medline, Cochrane Library, and Google Scholar) from inception to February 10, 2024. All statistical analyses were conducted in Review Manager 5.4.1. Twelve studies meeting the inclusion criteria were selected. A random-effects model was used when heterogeneity was observed to pool the studies, and the results were reported as hazard ratio (HR), odds ratio (OR), and standard mean difference (SMD), along with their respective 95% confidence intervals (CI). Primary outcomes were overall survival, Karnofsky Performance Status, and age; secondary outcomes included median progression-free survival, mortality, and tumor recurrence.

Results: Supramarginal resection was associated with improved overall survival compared with gross total resection (HR = 0.90, 95% CI 0.84–0.97; $p = 0.005$; $I^2 = 96\%$), and increasing age was associated with decreased survival (HR = 1.03, 95% CI 1.00–1.05; $p = 0.02$; $I^2 = 0\%$). No statistically significant association was observed between lower Karnofsky Performance Status and survival (HR = 0.77, 95% CI 0.53–1.12; $p = 0.18$; $I^2 = 74\%$).

Conclusion: Supramarginal resection of GBM yielded more favorable results than gross total resection, with minimal difference between adverse effects.

1 | Introduction

Glioblastoma multiforme (GBM) is the most prevalent and aggressive form of glioma. Statistical evidence suggests a median

survival time of 15–18 months, and the 5-year survival remains below 10% (Wen et al. 2020). The standard treatment for GBM typically involves surgical resection followed by radiation therapy and chemotherapy (Wen et al. 2020; Marko et al. 2014). The

[Correction added on 4 June 2026, after first online publication: The author's name "Oleg Devnyak" was misspelled. The correct author's name is "Oleg Devinyak". In addition, their affiliation should be corrected from "Pharmacology Department, Uzhhorod National University, Uzhhorod, Ukraine" to "Department of Pharmaceutical Sciences, Uzhhorod National University, Uzhhorod, Ukraine."]

This is an open access article under the terms of the [Creative Commons Attribution](https://creativecommons.org/licenses/by/4.0/) License, which permits use, distribution and reproduction in any medium, provided the original work is properly cited.

© 2026 The Author(s). *Brain and Behavior* published by Wiley Periodicals LLC.

extent of resection (EOR) plays a significant role in predicting the prognosis of GBM (Marko et al. 2014). The literature has shown improved survival outcomes with greater removal of contrast-enhancing tumor mass (Marko et al. 2014).

GBM has characteristic radiological features: a nodule with contrast enhancement on T1-weighted magnetic resonance imaging (MRI), surrounded by an irregularly shaped, widespread T2 hyperintense signal. This T2 signal is commonly believed to indicate infiltrated brain tissue (Stummer et al. 2008). Recent data suggest that complete resection provides greater benefits than partial removal or biopsy (Stummer et al. 2008; Chaichana et al. 2013). However, achieving complete resection is often challenging because gliomas infiltrate the surrounding brain tissue. Furthermore, the areas with lower cancer cell densities may not be visible on MRI scans, making it challenging for surgeons to accurately identify and remove all affected tissue during surgery (Baldock et al. 2013). Therefore, eliminating the tumor-invaded brain tissue may not always be the optimal approach. As a result, the surgical strategy for brain gliomas is known as “maximal safe resection.” This approach aims to remove the tumor as much as possible without worsening the patient’s condition. However, the precise extent of maximal safe resection lacks a standardized objective criterion, leading to different interpretations based on the surgeon’s judgment (Marko et al. 2014; Karschnia et al. 2023).

Building on the concept of maximal safe resection, Duffau described and implemented supratotal resection (SpTR) in the setting of awake mapping, extending resection beyond the tumor margins to include adjacent infiltrated tissue, with favorable functional and oncologic outcomes reported in low-grade gliomas (Duffau 2016). In subsequent literature, Yordanova et al. (2011) described this approach as supratotal resection (SpTR), which has also been referred to as supra-complete, supramaximal, and supramarginal resection (SMR). In GBM, where true microscopic margins are not well defined, “supramaximal” may better capture the intent of safely maximizing tissue removal to improve overall survival without introducing new neurological deficits (Karschnia et al. 2023). The standards used to assess whether complete removal of all tumor tissue, known as gross-total resection (GTR), has been achieved have historically relied on T1-enhanced MRI following surgery. However, a recent investigation suggests that further extraction of areas displaying high signal intensity on T2-FLAIR MRI can significantly enhance survival rates (Li et al. 2016).

In this meta-analysis, we aim to compare functional outcomes in patients with GBM undergoing SpTR versus GTR.

2 | Methods

2.1 | Search Strategy and Databases

The systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (Hutton et al. 2015). An electronic search was performed using PubMed/Medline, Cochrane Trial Register, and Google Scholar from inception through February 10, 2024. The following search string was used: (glioblastoma OR GBM OR high-grade

glioma OR glioma) AND (supramarginal resection OR supra total resection) AND (gross total resection OR complete resection). We additionally searched the referenced articles of previously published meta-analyses, cohort studies, and review articles to identify any relevant studies.

2.2 | Study Selection Criteria

Studies were selected if they followed our PICOS: P (Patients): Patients with Glioblastoma multiforme, glioma, or high-grade glioma; I (Intervention): supratotal/supramarginal resection of the tumor; C (Control): gross total resection of the tumor; O (Outcomes): primary outcomes are overall survival, Karnofsky Performance status (KPS) score (for functional outcomes), and effect of increasing age while secondary were miscellaneous outcomes (e.g., death, tumor recurrence); S (Studies): Observational studies and Randomized Controlled Trials.

2.3 | Data Extraction and Quality Assessment

Two reviewers screened the electronic databases. The EndNote Reference Library version 20.0.1 (Clarivate Analytics, London, UK) was used to extract data, and duplicate articles were removed. Two investigators entered the data extracted from the selected studies into an Excel spreadsheet (Microsoft Corporation, Redmond, WA, USA). The KPS is a simple and quick way to evaluate patients’ performance in daily activities, commonly applied in medical oncology; this score not only helps track the illness’s progression but also provides valuable prognostic insights. Variables extracted included KPS, overall survival (OS), patient age, progression-free survival (PFS), and adverse effects.

Quality assessment was performed using the Newcastle-Ottawa Scale (NOS) for observational studies and the Cochrane Collaboration Tool for clinical trials. NOS scores of 1–5 were considered high risk for bias, 6–7 were moderate, and scores >7 were considered low risk of bias.

2.4 | Statistical Analysis

Review Manager (version 5.4.1; Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2020) was used for the statistical analyses. The data from studies were pooled using a random-effects model when heterogeneity was seen. Analysis of results was performed by calculating hazard ratios (HR), odds ratios (ORs), and standard mean differences (SMD), along with their respective 95% confidence intervals (CIs). The chi-square test assesses any differences between the subgroups. Sensitivity analysis was conducted to assess whether any individual study was driving the results and to explore the reasons for high heterogeneity. As per the *Cochrane Handbook*, the scale for heterogeneity was considered as follows: $I^2 = 25\%$ – 60% —moderate, 50% – 90% —substantial, 75% – 100% —considerable heterogeneity, and $p < 0.1$ indicated significant heterogeneity (Cumpston et al. 2019). A p -value < 0.05 was considered significant.

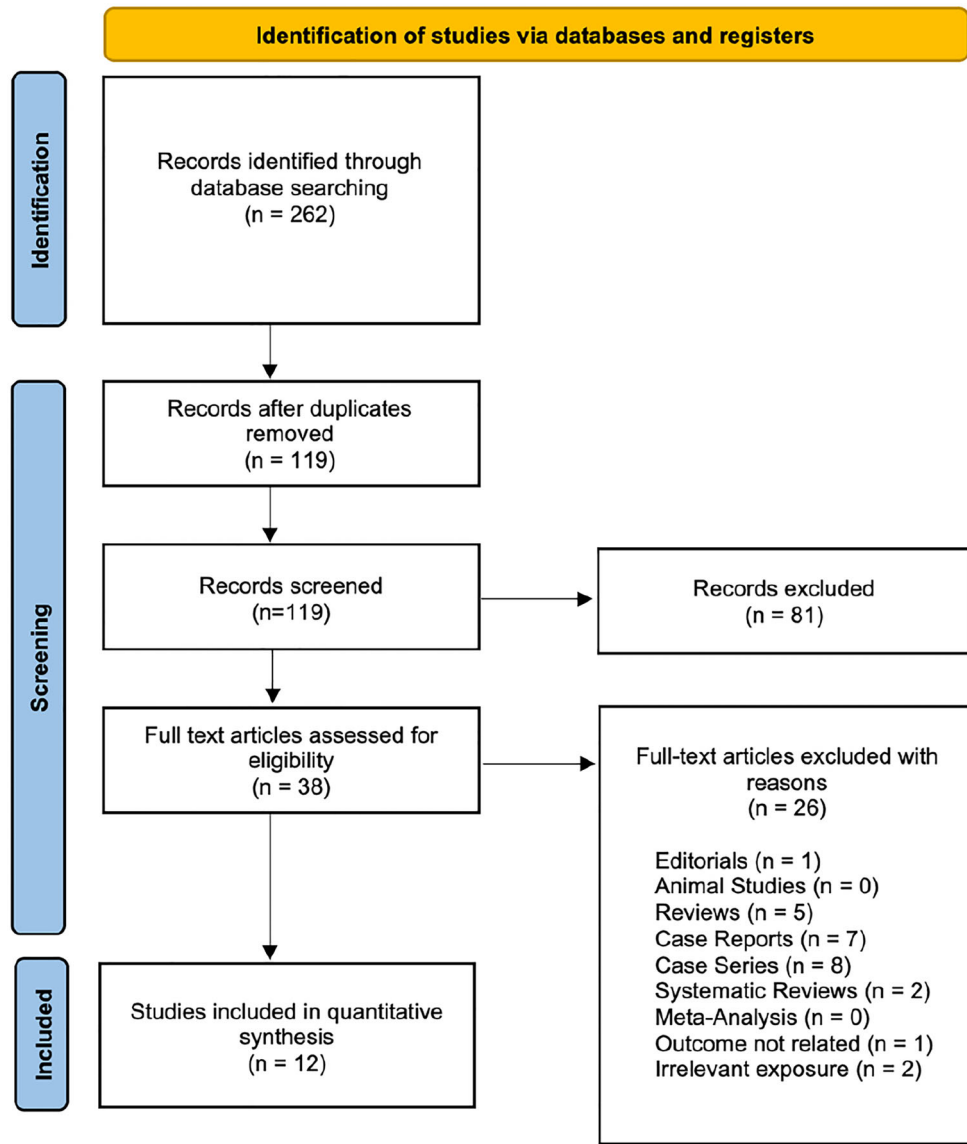


FIGURE 1 | PRISMA flow diagram illustrating the summary of the literature search.

3 | Results

3.1 | Literature Search Results

The initial literature review using three electronic databases revealed 262 potential studies. After reviewing the title and abstract, 81 studies were excluded. After duplicate removal, 119 records were screened; 38 full-text articles were assessed for eligibility, and 26 were excluded. Full-text exclusions were primarily due to ineligible publication type (e.g., reviews, editorials, case reports/series), non-clinical studies, or lack of relevant exposure/outcome data. Twelve studies were selected for quantitative analysis. Figure 1 summarizes the results of our literature search.

3.2 | Study Characteristics

The clinical and demographic details of the selected studies are provided in Table 1 (Di et al. 2022; Roh et al. 2019; Vivas-Buitrago et al. 2021; Glenn et al. 2018; Lopez-Rivera et al. 2021; Mampre

et al. 2018; Ahmadipour et al. 2019; Pessina et al. 2017; Hirono et al. 2021; Yoo et al. 2021; Shah et al. 2020; Schneider et al. 2019). The total patient population of the 12 cohort studies was 6524. The SMR group included 3317 patients, and the GTR group included 3045 patients. The mean age of the included subjects was 61.2 years.

3.3 | Publication Bias and Quality Assessment

All studies had a low risk of bias, except for one which had a moderate risk of bias. Publication bias could not be assessed, as the number of articles in each forest plot was less than 10 (Table 2).

3.4 | Results

Twelve studies were used in this analysis to evaluate the clinical outcomes of GBM patients undergoing surgical resection (Di et al. 2022; Roh et al. 2019; Vivas-Buitrago et al. 2021; Glenn et al.

TABLE 1 | The baseline table showing the demographic characteristics extracted from the included studies.

Study	Country	Intervention	Total patients (n)	Mean age (years)	Female (%)	Outcomes assessed
Di et al. (2022)	USA	SMR	48	60.8	58.3	KPS, OS, age
		GTR	54	61.6	31.5	
Roh et al. (2019)	Korea	SpTR	20	62	30	KPS, OS, age, median PFS, median OS
		GTR	20	60	35	
Vivas-Buitrago et al. (2021)	USA	SMR	101	59.8	33	KPS, OS
Glenn et al. (2018)	USA	SMR	7	56.3	14.3	OS, median OS, nonspecified complication, mortality
		GTR	9	58.1	22.2	
Lopez-rivera et al. (2021)	USA	SpTR	2907	72	44	OS, age
		GTR	2451	71	43	
Mampre et al. (2018)	USA	GTR	245	59.8	39	OS
Ahmadipour et al. (2019)	Germany	SpTR	21	60.2	46	Age, median OS
		GTR	234	62.9	38	
Pessina et al. (2017)	Italy	SpTR	21	61	37.2	Median OS, nonspecified complication
		GTR	60			
Schneider et al. (2019)	Germany	GTR	24	68	46	Median OS, median PFS
Hirono et al. (2021)	Japan	SpTR	7	56	71.4	Nonspecified complication Local recurrence Distant recurrence
		GTR	23	57	52.1	
Shah et al. (2020)	USA	GTR	37	65	59.5	Nonspecified complication Mortality
Yoo et al. (2021)	Korea	SpTR	41	55.4	34.1	Local recurrence Distant recurrence
		GTR	194	55.8	40.7	

Abbreviations: GTR, gross total resection; KPS, Karnofsky performance status; OS, overall survival; PFS, progression-free survival; SMR, supramarginal resection; SpTR, supratotal resection.

2018; Lopez-Rivera et al. 2021; Mampre et al. 2018; Ahmadipour et al. 2019; Pessina et al. 2017; Hirono et al. 2021; Yoo et al. 2021; Shah et al. 2020; Schneider et al. 2019). Pooled results are given in Figures 2–4. The following three factors were assessed in the forest plot (Figure 2) to see their effects on the survival outcome of GBM patients: KPS, OS, and age. Figure 2 includes separate pooled models for each factor and demonstrates that effect sizes differ across these factor-specific analyses (test for subgroup differences: $\chi^2 = 13.42$, $df = 2$, $p = 0.001$). The forest plot (Figure 3) shows the effect on median OS and median PFS when SMR was compared to GTR in GBM patients. This figure shows that the pooled median OS included five studies (83 SMR/SpTR vs. 347 GTR), while the pooled median PFS included two studies (34 SMR/SpTR vs 44 GTR). Adverse event and recurrence outcomes are summarized in Figure 4 using odds ratios with subgroup and overall pooled estimates (Figure 4).

3.4.1 | Karnofsky Performance Status

Three studies were used to analyze the association between lower KPS scores and postoperative survival in GBM patients (Di et al. 2022; Roh et al. 2019; Vivas-Buitrago et al. 2021). Analysis revealed

an insignificant relationship between survival and lower KPS scores (HR = 0.77 [0.53, 1.12]; $p = 0.18$; $I^2 = 74\%$) (Figure 2). Study weights were 46.5%, 31.2%, and 22.3% (Figure 2). At the study level, the reported HRs ranged from 0.48 (0.27, 0.85) to 0.99 (0.94, 1.03), indicating variability in effect estimates across cohorts.

3.4.2 | Overall Survival

Six studies assessed the effects of the extent of resection (supramarginal resection) on OS (Di et al. 2022; Roh et al. 2019; Vivas-Buitrago et al. 2021; Glenn et al. 2018; Lopez-Rivera et al. 2021; Mampre et al. 2018). Pooled analysis showed a statistically significant association of OS with SMR in GBM patients (HR = 0.90 [0.84, 0.97]; $p = 0.005$; $I^2 = 96\%$) (Figure 2). Study weights were uneven (26.8%, 26.4%, 26.3%, 20.0%, 0.3%, and 0.2%), with three studies contributing ~80% of the pooled estimate (Figure 2). Across individual studies, HRs ranged from 0.08 (0.01, 0.45) to 1.03 (1.01, 1.05), demonstrating wide variation in the magnitude and direction of effects (Figure 2).

The analysis of median OS in GBM patients included five studies (Roh et al. 2019; Ahmadipour et al. 2019; Pessina et al. 2017;

TABLE 2 | The results of the quality assessment of the included studies.

Study	Selection				Comparability			Outcome			Total Score
	Representation of exposed cohort	Selection of nonexposed cohort	Ascertainment of exposure	Outcome not present at the start of this study				Assessment of OUTCOME	Length of follow-up	Adequacy of follow-up	
Pessina et al. (2017)	1	1	1	0	2	1	1	1	1	1	8
Glenn et al. (2018)	1	1	1	0	2	1	1	1	1	1	8
Mampre et al. (2018)	1	1	1	0	2	1	1	1	1	1	8
Ahmadipour et al. (2019)	1	1	1	0	2	1	1	1	1	1	8
Roh et al. (2019)	1	1	1	0	2	1	1	1	1	1	8
Schneider et al. (2019)	1	1	1	0	2	1	1	1	1	1	8
Shah et al. (2020)	1	1	1	0	2	1	1	1	1	1	8
Hirono et al. (2021)	1	1	1	0	2	1	1	1	1	1	8
Lopez-Rivera et al. (2021)	1	1	1	0	2	1	1	1	1	1	8
Vivas-Buitrago et al. (2021)	1	1	1	0	2	1	1	1	1	1	8
Yoo et al. (2021)	1	1	1	0	2	1	1	1	1	1	8
Di et al. (2022)	1	1	1	0	2	1	1	1	1	1	8

Note: Risk of bias was assessed using the Newcastle–Ottawa scale (NOS). For selection and outcome items, each criterion is scored 0/1 (criterion not met/met). For the comparability domain, the entry can be 0, 1, or 2 depending on whether the study controlled for none, one, or two prespecified confounders (maximum 2).

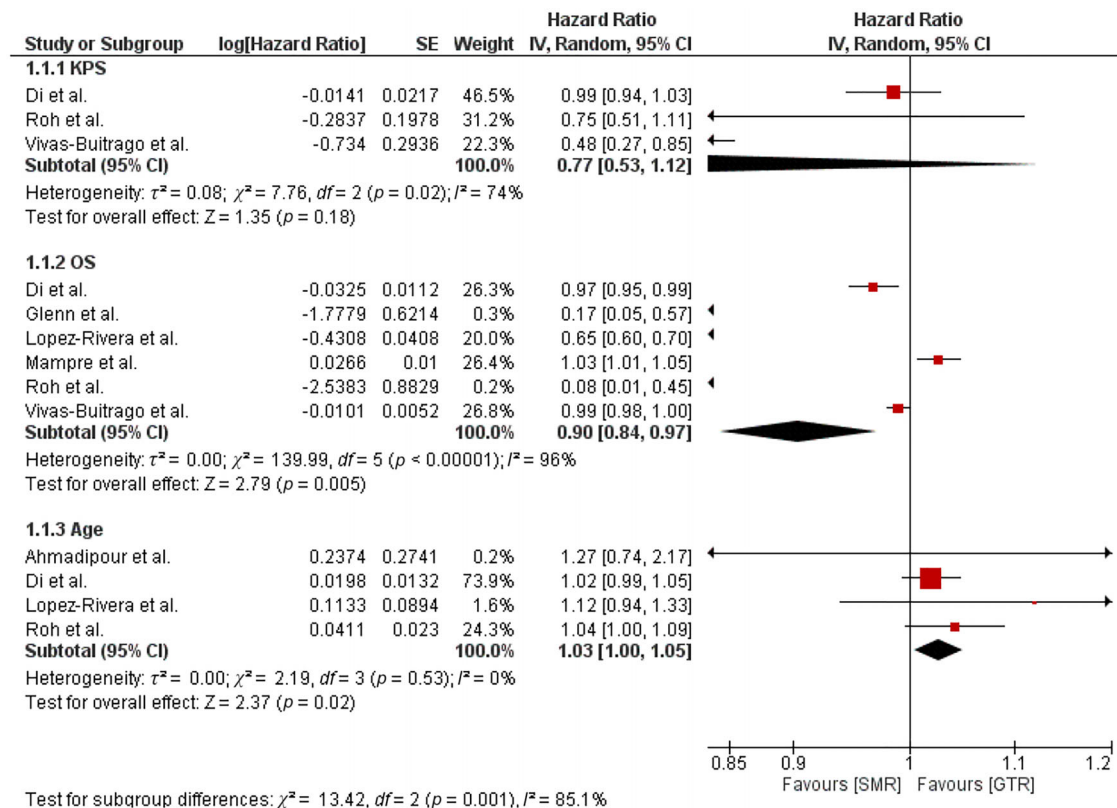


FIGURE 2 | Illustration of the quantitative results of Karnofsky performance status (KPS), overall survival (OS), and age.

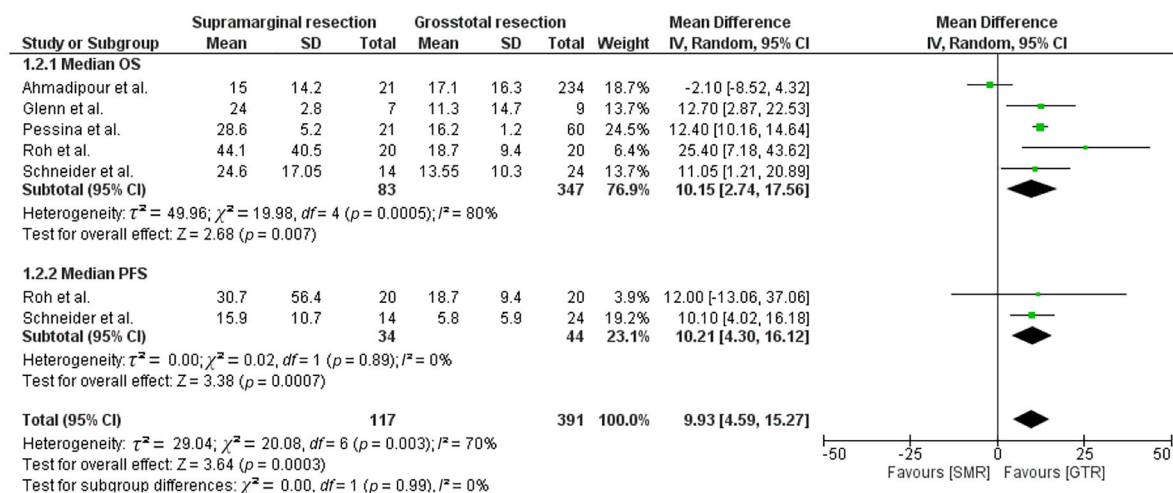


FIGURE 3 | Illustration of the quantitative results for median overall survival (OS) and median progression-free survival (PFS).

Schneider et al. 2019; Al-Mefty et al. 1996). As compared with the experimental group, GTR had a statistically significant effect on median OS (SMD = 10.15 [2.74, 17.56]; $p = 0.007$; $I^2 = 80\%$) (Figure 3).

3.4.3 | Age

The effects of age on survival were assessed by four studies (Di et al. 2022; Roh et al. 2019; Lopez-Rivera et al. 2021; Ahmadipour et al. 2019). A significant association was found between higher

age and decreased survival in GBM patients (HR = 1.03 [1.00, 1.05]; $p = 0.02$; $I^2 = 0\%$).

3.4.4 | Progression Free-Survival

Two studies were used to assess the effects of the experimental and control groups on median PFS (Di et al. 2022; Schneider et al. 2019). Median PFS was significantly improved in the SMR group of GBM patients (SMD = 10.21 [4.30, 16.12]; $p = 0.0007$; $I^2 = 0\%$).

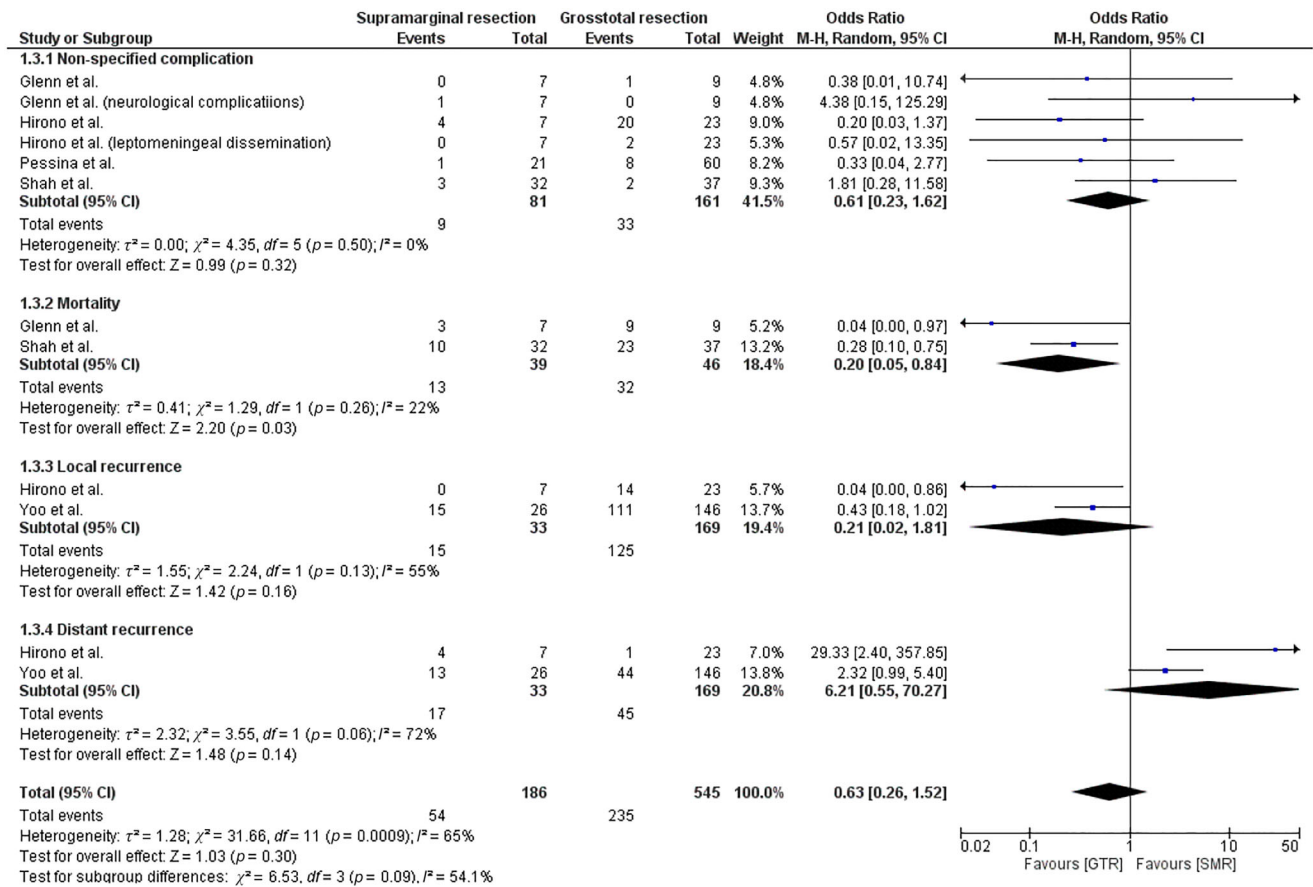


FIGURE 4 | Forest plot illustrating the overall analysis of complications associated with the extent of resection, and subgroup analyses for Non-specific complications, mortality, local recurrence, and distant recurrence.

The overall effect of SMR on median PFS and OS in GBM patients was statistically improved, compared to the GTR group (SMD = 9.93 [4.59, 15.27]; $p = 0.0003$; $I^2 = 70\%$).

3.4.5 | Adverse Effects

The forest plot (Figure 4) shows the analysis of the following adverse effects in the two groups of patients: non-specified complications, mortality, local recurrence, and distant recurrence. Effect estimates are reported as ORs using random-effects models.

Four studies assessed the risk of non-specified complications following surgical resection in patients with GBM (Glenn et al. 2018; Pessina et al. 2017; Hirono et al. 2021; Shah et al. 2020). An insignificant difference was noted in the rate of complications between the two groups of patients (SMD = 0.61 [0.23, 1.62]; $p = 0.32$; $I^2 = 0\%$). This analysis included 81 SMR patients and 161 GTR patients, with 9 versus 33 total events, respectively (Figure 4). No heterogeneity was observed ($\tau^2 = 0.00$; $\chi^2 = 4.35$, $df = 5$, $p = 0.50$; $I^2 = 0\%$).

Two studies reported mortality incidence in GBM (Glenn et al. 2018; Shah et al. 2020). When compared to the GTR, SMR was associated with a significantly lower mortality incidence (SMD = 0.20 [0.05, 0.84]; $p = 0.03$; $I^2 = 22\%$). This pooled analysis included

39 SMR patients and 46 GTR patients, with 13 versus 32 total events, respectively (Figure 4). Heterogeneity was low ($\tau^2 = 0.41$; $\chi^2 = 1.29$, $df = 1$, $p = 0.26$; $I^2 = 22\%$).

The incidence of local and distant recurrence following surgical resection was assessed by two studies (Hirono et al. 2021; Yoo et al. 2021). Pooled analysis revealed an insignificant difference in the rate of local recurrence in GBM patients (SMD = 0.21 [0.02, 1.81]; $p = 0.16$; $I^2 = 55\%$). Local recurrence pooled 33 SMR patients and 169 GTR patients, with 15 versus 125 total events, respectively (Figure 4). Heterogeneity was moderate ($\tau^2 = 1.55$; $\chi^2 = 2.24$, $df = 1$, $p = 0.13$; $I^2 = 55\%$). Similarly, no significant difference was observed in the rate of distant recurrence (SMD = 6.21 [0.55, 70.27]; $p = 0.14$; $I^2 = 72\%$). Distant recurrence pooled 33 SMR patients and 169 GTR patients, with 17 versus 45 total events, respectively (Figure 4). Heterogeneity was substantial ($\tau^2 = 2.32$; $\chi^2 = 3.55$, $df = 1$, $p = 0.06$; $I^2 = 72\%$), and confidence intervals were wide.

The overall incidence of adverse effects was similar in the two patient groups (SMD = 0.63 [0.26, 1.52]; $p = 0.30$; $I^2 = 65\%$). Across all adverse-effect outcomes combined, there were a total of 186 SMR patients and 545 GTR patients, with 54 versus 235 total events, respectively (Figure 4). Overall heterogeneity was moderate ($\tau^2 = 1.28$; $\chi^2 = 31.66$, $df = 11$, $p = 0.0009$; $I^2 = 65\%$). Differences across adverse-effect subgroups were not statistically

significant (test for subgroup differences: $\chi^2 = 6.53$, $df = 3$, $p = 0.09$; $I^2 = 54.1\%$) (Figure 4).

4 | Discussion

The study aimed to assess the impact of factors such as KPS, OS, age, and extent of resection (SMR vs. GTR) on survival outcomes in GBM patients. Specifically, we examined the association between lower KPS scores and postoperative survival, the effect of age on survival, and the impact of SMR versus GTR on median OS and PFS in GBM patients. Additionally, the study explored the adverse effects, including unspecified complications, mortality, local recurrence, and distant recurrence, associated with different surgical resection techniques in GBM patients. The findings aimed to provide comprehensive insights into the factors affecting the prognosis and outcomes of patients with GBM undergoing surgical procedures.

Numerous studies have demonstrated that the extent of removal during surgery is a significant predictor of outcomes in individuals with GBM (D'Amico et al. 2017; Lacroix et al. 2001). It has been consistently observed that patients who undergo more extensive resection experience longer survival times compared to those who receive less aggressive treatment (Sanai et al. 2011). When GTR was achieved, patients experienced a decrease in pseudoprogression and an overall increase in survival time (Park et al. 2016). The median OS doubled compared to when GTR was not achieved (Roh et al. 2017). In our study, analysis of five studies investigating median OS in GBM patients revealed a strong correlation between GTR and improved outcomes compared with the experimental group. There was a statistically significant increase in median OS among GBM patients who underwent GTR (Roh et al. 2019; Glenn et al. 2018; Ahmadipour et al. 2019; Pessina et al. 2017; Schneider et al. 2019).

The literature presented a wide range of evidence supporting the benefits of higher EOR for GBM patients, underscoring its effectiveness in treating this type of cancer (Roh et al. 2019; Vivas-Buitrago et al. 2021; Glenn et al. 2018; Molinaro et al. 2020; Michaelsen et al. 2013). In patients with GBM undergoing SMR, a critical reference point was identified. A study by Di et al. analyzed 48 SMR patients, with temporal lesions being the most common (39.6%). In contrast, GTR had higher frequencies in temporal (33.3%), frontal (31.5%), and parietal (13%) regions. SMR procedures predominantly utilized awake craniotomy with intraoperative mapping (72.9%) and other mapping techniques. The mean EOR for TIC+ tumor volume was notably high at 97.4%, demonstrating the effectiveness of the SMR approach in achieving thorough tumor removal (Di et al. 2022). Similarly, our analysis of six studies (Di et al. 2022; Roh et al. 2019; Vivas-Buitrago et al. 2021; Glenn et al. 2018; Lopez-Rivera et al. 2021; Mampre et al. 2018) examining the influence of SMR on overall survival in patients with GBM revealed a notable, statistically significant correlation, as evidenced by an HR. This discovery implies that individuals who undergo SMR experience a 10% reduction in mortality risk compared to those who do not receive the EOR technique. Shah et al. conducted a substantial comparative study on lobectomy versus oncologic resection (lesionectomy) for newly diagnosed GBM. The study revealed that patients who underwent

lobectomy showed significantly better OS and PFS (symptomatic progression) than those who received GTR alone, after adjusting for age, location, and size (Shah et al. 2020). Additionally, SMR is beneficial as it reduces any remaining microscopic disease, thus maximizing the effectiveness of adjuvant treatments (Shah et al. 2020).

In our study, the comparison of mortality incidence between SMR and GTR in GBM, as reported in two studies, showed a significant association (Glenn et al. 2018; Shah et al. 2020). This suggests that patients who underwent SMR had a lower risk of mortality compared to those who received GTR for their GBM treatment, supported by other studies (Di et al. 2022; Michaelsen et al. 2013; Zhao et al. 2019).

Patients with top-tier Karnofsky scores at the time of tumor diagnosis tend to have better survival rates and quality of life throughout their illness journey (Ferrucci et al. 2007). A study by Chaichana et al. included 80 matched patients who were similar in terms of KPS, age, eloquent involvement, radiation treatment, and temozolomide use. The results showed that surgical resection significantly improved OS compared to needle biopsy without increasing perioperative complications. This finding was consistent even when analyzing a subgroup of 26 patients separately (Chaichana et al. 2011). However, a study by Di et al. included 102 patients, of whom 48 underwent SMR and 54 GTR. The results showed no significant difference in postoperative complication rates or KPS scores between the SMR and GTR groups (Di et al. 2022). Similarly, in our study, we found that the analysis of three studies (Di et al. 2022; Roh et al. 2019; Vivas-Buitrago et al. 2021), evaluating the effect of lower KPS scores on postoperative survival in GBM patients resulted in a non-significant relationship. This suggests that lower KPS scores may not significantly affect the postoperative survival of GBM patients. However, previous research has established a clear, strong correlation between higher KPS scores and improved outcomes in this patient population (Liu et al. 2022; Marina et al. 2011).

5 | Limitations

Our study has some limitations. First, the evidence base included only observational studies, so residual confounding and selection bias may influence the observed associations. Second, relatively few studies contributed to some pooled outcomes, which limits precision and the strength of inference for those factors. Third, several analyses demonstrated substantial heterogeneity across studies, which may limit generalizability. Several included studies predate WHO CNS5, and diagnostic terminology varies across publications (Louis et al. 2021). Finally, postoperative functional measures were not uniformly reported across studies, and the association between KPS and outcomes should be interpreted cautiously; additional prospective work is needed to better define the relationship between KPS and post-surgical outcomes in GBM (Farooq et al. 2023; Encarnacion-Santos et al. 2024; Ahmed et al. 2024; Okon et al. 2024; Rybaczek and Chaurasia 2024; Ferini et al. 2024; Gorlia et al. 2008; Lamborn et al. 2004; Curran et al. 1993).

In this systematic review and meta-analysis of observational studies, supramarginal resection was associated with improved overall survival compared with gross total resection in patients with glioblastoma. Increasing age was associated with lower survival rates, whereas KPS was not significantly associated with survival. Some of the analyses showed significant heterogeneity, while there was variability in the reporting of adverse events. Hence, this information should be interpreted as associations rather than causal relationships. Further prospective studies with consistent reporting of outcomes and extent of resection, particularly functional outcomes, would help to determine the degree of benefit and which patients would derive the greatest benefit from supramarginal resection.

Author Contributions

Dipak Chaulagain: concept and design, statistical analysis, first draft of manuscript; Volodymyr Smolanka: study supervision; Andriy Smolanka and Bipin Chaurasia: study supervision, critical revision of the first draft; Oleg Devinyak: study supervision. Kashif Qureshi: manuscript revision in response to first-round peer-review comments. Kivanc Yangi: study supervision, critical revision of the first draft. All authors have revised and approved the submitted version.

Funding

The authors have nothing to report.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

Data sharing not applicable to this article as no datasets were generated or analyzed during the current study.

References

- Ahmadipour, Y., M. Kaur, D. Pierscianek, et al. 2019. "Association of Surgical Resection, Disability, and Survival in Patients With Glioblastoma." *Journal of Neurological Surgery Part A: Central European Neurosurgery* 80, no. 4: 262–268.
- Ahmed, N., M. D. N. Hossain, R. Ahmed, et al. 2024. "Safety, Efficacy, and Side Effects of Sodium Fluorescein-Aided Resection of Glioblastoma: A Quasi-Experimental Study." *Annals of Medicine and Surgery* 86, no. 11: 6521–6530. <https://doi.org/10.1097/MS9.0000000000002633>.
- Al-Mefty, O., L. A. B. Borba, N. Aoki, E. Angtuaco, and T. G. Pait. 1996. "The Transcondylar Approach to Extradural Nonneoplastic Lesions of the Craniovertebral Junction." *Journal of Neurosurgery* 84, no. 1: 1–6.
- Baldock, A. L., R. C. Rockne, A. D. Boone, et al. 2013. "From Patient-Specific Mathematical Neuro-Oncology to Precision Medicine." *Frontiers in Oncology* 3: 62. <https://doi.org/10.3389/fonc.2013.00062>.
- Chaichana, K. L., T. Garzon-Muvdi, S. Parker, et al. 2011. "Supratentorial Glioblastoma Multiforme: The Role of Surgical Resection Versus Biopsy Among Older Patients." *Annals of Surgical Oncology* 18, no. 1: 239–245. <https://doi.org/10.1245/s10434-010-1242-6>.
- Chaichana, K. L., I. Jusue-Torres, R. Navarro-Ramirez, et al. 2013. "Establishing Percent Resection and Residual Volume Thresholds Affecting Survival and Recurrence for Patients With Newly Diagnosed Intracranial

Glioblastoma." *Neuro-Oncology* 16, no. 1: 113–122. <https://doi.org/10.1093/neuonc/not137>.

Cumpston, M., T. Li, M. J. Page, et al. 2019. "Updated Guidance for Trusted Systematic Reviews: A New Edition of the Cochrane Handbook for Systematic Reviews of Interventions." *Cochrane Database of Systematic Reviews* 10, no. 10: Ed000142.

Curran, W. J., C. B. Scott, J. Horton, et al. 1993. "Recursive Partitioning Analysis of Prognostic Factors in Three Radiation Therapy Oncology Group Malignant Glioma Trials." *Journal of the National Cancer Institute* 85, no. 9: 704–710. <https://doi.org/10.1093/jnci/85.9.704>.

D'Amico, R. S., Z. K. Englander, P. Canoll, and J. N. Bruce. 2017. "Extent of Resection in Glioma—A Review of the Cutting Edge." *World Neurosurgery* 103: 538–549.

Di, L., A. H. Shah, A. Mahavadi, et al. 2022. "Radical Supramaximal Resection for Newly Diagnosed Left-Sided Eloquent Glioblastoma: Safety and Improved Survival Over Gross-total Resection." *Journal of Neurosurgery* 138, no. 1: 62–69. <https://doi.org/10.3171/2022.3.JNS212399>.

Duffau, H. 2016. "Long-Term Outcomes After Supratotal Resection of Diffuse Low-Grade Gliomas: A Consecutive Series With 11-Year Follow-up." *Acta Neurochirurgica* 158, no. 1: 51–58. <https://doi.org/10.1007/s00701-015-2621-3>.

Encarnacion-Santos, D., G. Chmutin, I. Bozkurt, J. Wellington, and B. Chaurasia. 2024. "Optimizing the Management of Glioblastoma per Neurosurgical Approach and Therapeutic Interventions on Patient Outcomes: A Systematic Review and Meta-Analysis." *Annals of Oncology Research and Therapy* 4, no. 1: 7–14. https://doi.org/10.4103/aort.aort_5_24.

Farooq, M., G. Scalia, G. Umana, et al. 2023. "A Systematic Review of Nanomedicine in Glioblastoma Treatment: Clinical Efficacy, Safety, and Future Directions." *Brain Sciences* 13, no. 12: 1727. <https://doi.org/10.3390/brainsci13121727>.

Ferini, G., G. Scalia, M. Harikar, et al. 2024. "Comparative Analysis of Recurrent Glioblastoma Target Contours via (11)C-Methionine, (68)Ga-Prostate-Specific Membrane Antigen Positron Emission Tomography, and Magnetic Resonance Imaging: Implications for Precision Radiotherapy Planning." *Advances in Radiation Oncology* 9, no. 9: 101548. <https://doi.org/10.1016/j.adro.2024.101548>.

Ferrucci, L., C. Koh, S. Bandinelli, and J. M. Guralnik. 2007. "Disability, Functional Status, and Activities of Daily Living." In *Encyclopedia of Gerontology*, edited by J. E. Birren, 427–436, 2nd ed. Elsevier.

Glenn, C. A., C. M. Baker, A. K. Conner, et al. 2018. "An Examination of the Role of Supramaximal Resection of Temporal Lobe Glioblastoma Multiforme." *World Neurosurgery* 114: e747–e755. <https://doi.org/10.1016/j.wneu.2018.03.072>.

Gorlia, T., M. J. Van Den Bent, M. E. Hegi, et al. 2008. "Nomograms for Predicting Survival of Patients With Newly Diagnosed Glioblastoma: Prognostic Factor Analysis of EORTC and NCIC Trial 26981-22981/CE.3." *The Lancet Oncology* 9, no. 1: 29–38. [https://doi.org/10.1016/S1470-2045\(07\)70384-4](https://doi.org/10.1016/S1470-2045(07)70384-4).

Hirono, S., K. Ozaki, M. Kobayashi, et al. 2021. "Oncological and Functional Outcomes of Supratotal Resection of IDH1 Wild-Type Glioblastoma Based on (11)C-methionine PET: A Retrospective, Single-Center Study." *Scientific Reports* 11, no. 1: 14554. <https://doi.org/10.1038/s41598-021-93986-z>.

Hutton, B., G. Salanti, D. M. Caldwell, et al. 2015. "The PRISMA Extension Statement for Reporting of Systematic Reviews Incorporating Network Meta-Analyses of Health Care Interventions: Checklist and Explanations." *Annals of Internal Medicine* 162, no. 11: 777–784. <https://doi.org/10.7326/M14-2385>.

Karschnia, P., J. S. Young, A. Dono, et al. 2023. "Prognostic Validation of a New Classification System for Extent of Resection in Glioblastoma: A Report of the RANO Resect Group." *Neuro-Oncology* 25, no. 5: 940–954. <https://doi.org/10.1093/neuonc/noac193>.

Lacroix, M., D. Abi-Said, D. R. Fourney, et al. 2001. "A Multivariate Analysis of 416 Patients With Glioblastoma Multiforme: Prognosis, Extent

- of Resection, and Survival.” *Journal of Neurosurgery* 95, no. 2: 190–198. <https://doi.org/10.3171/jns.2001.95.2.0190>.
- Lamborn, K. R., S. M. Chang, and M. D. Prados. 2004. “Prognostic Factors for Survival of Patients With Glioblastoma: Recursive Partitioning Analysis.” *Neuro-Oncology* 6, no. 3: 227–235. <https://doi.org/10.1215/S1152851703000620>.
- Li, Y. M., D. Suki, K. Hess, and R. Sawaya. 2016. “The Influence of Maximum Safe Resection of Glioblastoma on Survival in 1229 Patients: Can We Do Better Than Gross-Total Resection?” *Journal of Neurosurgery* 124, no. 4: 977–988. <https://doi.org/10.3171/2015.5.JNS142087>.
- Liu, J., C. Li, Y. Wang, et al. 2022. “Prognostic and Predictive Factors in Elderly Patients with Glioblastoma: A Single-Center Retrospective Study.” *Frontiers in Aging Neuroscience* 13: 777962.
- Lopez-Rivera, V., A. Dono, C. T. Lewis, et al. 2021. “Extent of Resection and Survival Outcomes of Geriatric Patients With Glioblastoma: Is There Benefit From Aggressive Surgery?” *Clinical Neurology and Neurosurgery* 202: 106474. <https://doi.org/10.1016/j.clineuro.2021.106474>.
- Louis, D. N., A. Perry, P. Wesseling, et al. 2021. “The 2021 WHO Classification of Tumors of the Central Nervous System: A Summary.” *Neuro-Oncology* 23, no. 8: 1231–1251. <https://doi.org/10.1093/neuonc/noab106>.
- Mampré, D., J. Ehresman, G. Pinilla-Monsalve, et al. 2018. “Extending the Resection Beyond the Contrast-Enhancement for Glioblastoma: Feasibility, Efficacy, and Outcomes.” *British Journal of Neurosurgery* 32, no. 5: 528–535. <https://doi.org/10.1080/02688697.2018.1498450>.
- Marina, O., J. H. Suh, C. A. Reddy, et al. 2011. “Treatment Outcomes for Patients With Glioblastoma Multiforme and a Low Karnofsky Performance Scale Score on Presentation to a Tertiary Care Institution: Clinical Article.” *Journal of Neurosurgery* 115, no. 2: 220–229. <https://doi.org/10.3171/2011.3.JNS10495>.
- Marko, N. F., R. J. Weil, J. L. Schroeder, F. F. Lang, D. Suki, and R. E. Sawaya. 2014. “Extent of Resection of Glioblastoma Revisited: Personalized Survival Modeling Facilitates More Accurate Survival Prediction and Supports a Maximum-Safe-Resection Approach to Surgery.” *Journal of Clinical Oncology* 32, no. 8: 774–782. <https://doi.org/10.1200/JCO.2013.51.8886>.
- Michaelsen, S. R., I. b J. Christensen, K. Grunnet, et al. 2013. “Clinical Variables Serve as Prognostic Factors in a Model for Survival From Glioblastoma Multiforme: An Observational Study of a Cohort of Consecutive Non-Selected Patients From a Single Institution.” *BMC Cancer* 13: 402. <https://doi.org/10.1186/1471-2407-13-402>.
- Molinaro, A. M., S. Hervey-Jumper, R. A. Morshed, et al. 2020. “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 Oncology* 6, no. 4: 495. <https://doi.org/10.1001/jamaoncol.2019.6143>.
- Okon, I. I., M. Osama, A. Akpan, et al. 2024. “The Evolving Role of Palliative Care in Older People With Glioblastoma.” *World Neurosurgery* 192: 140–149. <https://doi.org/10.1016/j.wneu.2024.09.125>.
- Park, H. H., T. H. Roh, S. G. Kang, et al. 2016. “Pseudoprogression in Glioblastoma Patients: The Impact of Extent of Resection.” *Journal of Neuro-Oncology* 126, no. 3: 559–566. <https://doi.org/10.1007/s11060-015-2001-0>.
- Pessina, F., P. Navarria, L. Cozzi, et al. 2017. “Maximize Surgical Resection Beyond Contrast-Enhancing Boundaries in Newly Diagnosed Glioblastoma Multiforme: Is It Useful and Safe? A Single Institution Retrospective Experience.” *Journal of Neuro-Oncology* 135, no. 1: 129–139. <https://doi.org/10.1007/s11060-017-2559-9>.
- Roh, T. H., S.-G. Kang, J. u H. Moon, et al. 2019. “Survival Benefit of Lobectomy Over Gross-Total Resection Without Lobectomy in Cases of Glioblastoma in the Noneloquent Area: A Retrospective Study.” *Journal of Neurosurgery* 132, no. 3: 895–901. <https://doi.org/10.3171/2018.12.JNS182558>.
- Roh, T. H., H. H. Park, S.-G. Kang, et al. 2017. “Long-Term Outcomes of Concomitant Chemoradiotherapy With Temozolomide for Newly Diagnosed Glioblastoma Patients: A Single-Center Analysis.” *Medicine* 96, no. 27: e7422. <https://doi.org/10.1097/MD.0000000000007422>.
- Rybaczek, M., and B. Chaurasia. 2024. “Advantage and Challenges in the Use of 5-Aminolevulinic Acid (5-ALA) in Neurosurgery.” *Neurosurgical Review* 47, no. 1: 712. <https://doi.org/10.1007/s10143-024-02974-0>.
- Sanai, N., M.-Y. Polley, M. W. McDermott, A. T. Parsa, and M. S. Berger. 2011. “An Extent of Resection Threshold for Newly Diagnosed Glioblastomas: Clinical Article.” *Journal of Neurosurgery* 115, no. 1: 3–8. <https://doi.org/10.3171/2011.2.JNS10998>.
- Schneider, M., A.-L. Potthoff, V. C. Keil, et al. 2019. “Surgery for Temporal Glioblastoma: Lobectomy Outranks Oncosurgical-Based Gross-Total Resection.” *Journal of Neuro-Oncology* 145, no. 1: 143–150. <https://doi.org/10.1007/s11060-019-03281-1>.
- Shah, A. H., A. Mahavadi, L. Di, et al. 2020. “Survival Benefit of Lobectomy for Glioblastoma: Moving Towards Radical Supramaximal Resection.” *Journal of Neuro-Oncology* 148, no. 3: 501–508. <https://doi.org/10.1007/s11060-020-03541-5>.
- Stummer, W., H.-J. Reulen, T. Meinel, et al. 2008. “Extent of Resection and Survival in Glioblastoma Multiforme: Identification of and Adjustment for Bias.” *Neurosurgery* 62, no. 3: 564–576. <https://doi.org/10.1227/01.neu.0000317304.31579.17>.
- Vivas-Buitrago, T., R. A. Domingo, S. Tripathi, et al. 2021. “Influence of Supramarginal Resection on Survival Outcomes After Gross-Total Resection of IDH-Wild-Type Glioblastoma.” *Journal of Neurosurgery* 36, no. 1: 1–8. <https://doi.org/10.3171/2020.10.JNS203366>.
- Wen, P. Y., M. Weller, E. Q. Lee, et al. 2020. “Glioblastoma in Adults: A Society for Neuro-Oncology (SNO) and European Society of Neuro-Oncology (EANO) Consensus Review on Current Management and Future Directions.” *Neuro-Oncology* 22, no. 8: 1073–1113. <https://doi.org/10.1093/neuonc/noaa106>.
- Yoo, J., S.-J. Yoon, K. H. Kim, et al. 2021. “Patterns of Recurrence According to the Extent of Resection in Patients With IDH-Wild-Type Glioblastoma: A Retrospective Study.” *Journal of Neurosurgery* 137, no. 2: 533–543. <https://doi.org/10.3171/2021.10.JNS211491>.
- Yordanova, Y. N., S. Moritz-Gasser, and H. Duffau. 2011. “Awake Surgery for WHO Grade II Gliomas Within “Noneloquent” Areas in the Left Dominant Hemisphere: Toward a “Supratotal” Resection: Clinical Article.” *Journal of Neurosurgery* 115, no. 2: 232–239. <https://doi.org/10.3171/2011.3.JNS101333>.
- Zhao, Y.-H., Z.-F. Wang, Z.-Y. Pan, et al. 2019. “A Meta-Analysis of Survival Outcomes Following Reoperation in Recurrent Glioblastoma: Time to Consider the Timing of Reoperation.” *Frontiers in Neurology* 10: 286. <https://doi.org/10.3389/fneur.2019.00286>.