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ADVANCES IN SURGICAL RESECTION TECHNIQUES FOR GLIOBLASTOMA: IMPLICATIONS FOR SURVIVAL AND PRECISION. A REVIEW OF CURRENT LITERATURE

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ABSTRACT

Introduction: Glioblastoma multiforme is the most common and aggressive type of primary brain tumor, often presenting with a poor prognosis and limited survival, despite available treatment options. The tumor's inherent resistance to treatment and its heterogeneity pose significant challenges for management.
Aim: This article aims to assess the impact of various surgical resection techniques on the survival of patients with glioblastoma, focusing on the importance of maximizing tumor resection while minimizing postoperative complications.
Methods and Materials: A literature review was conducted, focusing on studies published in the past five years. The review examined factors such as the extent of surgical resection, the use of intraoperative guidance, and postoperative care, evaluating their influence on survival rates.
Discussion: Complete tumor resection is positively associated with improved survival, but the extent of resection remains a debated topic. Advanced surgical methods, including fluorescence-guided imaging, are increasingly used to improve resection accuracy and reduce harm to healthy tissue. However, the prognosis for glioblastoma patients remains poor, and new approaches are needed to address the tumor's resistance mechanisms.
Conclusions: Surgical resection is a key component of glioblastoma treatment, with a significant impact on survival. However, there is a need for further clinical studies to refine surgical methods, optimize resection strategies, and develop new therapeutic options to improve long-term survival for patients.

KEYWORDS

Glioblastoma, Surgery, Survival Rate

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Introduction.

Glioblastoma (GBM) is predominantly a primary central nervous system neoplasm and represents the highest-grade malignancy (WHO Grade IV), with a median survival of 12–18 months despite aggressive treatment. It is characterized by marked intratumoral heterogeneity, whereby distinct cellular subpopulations within the same tumor exhibit divergent gene expression profiles and phenotypic behaviors [1].

Gliomas are aggressive primary brain tumors arising from glial or neuronal precursor cells. The WHO classifies them into grades I–IV, with grades III and IV considered high-grade malignancies [2]. Malignant gliomas include glioblastoma (GBM), anaplastic astrocytoma, and anaplastic oligodendroglioma. GBM, a WHO grade IV tumor, is the most common malignant CNS neoplasm, accounting for ~48.3% of cases and associated with poor prognosis [3–5]. Common clinical features include headaches, seizures, and focal neurological deficits [6].

The current standard of care (SOC) consists of maximal safe surgical resection followed by radiotherapy in combination with adjuvant Temozolomide (TMZ) chemotherapy. Despite this multimodal approach, the prognosis remains poor, with a 2-year survival rate of only 26–33% [7]. A five-year survival rate accounts for less than 10%, and a recurrence rate of ~90% [8].

Surgical resection plays a critical role in improving clinical outcomes by achieving tumor debulking, cytoreduction, and alleviation of mass effect, and has been shown to significantly prolong progression-free survival (PFS) [7]. Surgical resection, including gross total resection (GTR), is positively correlated with survival time in patients with GBM [9]. There is no doubt that epidemiological and etiological data are vital for treating this type of disease [10].

Surgical resection has been associated with a higher incidence of postoperative neurological deficits (odds ratio [OR] 2.05; 95% confidence interval [CI], 1.02–4.09). While resection confers a survival advantage

over biopsy alone—demonstrating improved overall survival (OS) up to one year post-intervention—this benefit is offset by an increased risk of neurologic morbidity [11].

Owing to the pronounced intratumoral heterogeneity of glioblastoma, the development and application of selective therapeutic strategies that target distinct tumor cell subpopulations are of paramount importance. Despite the availability of standard interventions—comprising maximal surgical resection, fractionated radiotherapy, and adjuvant chemotherapy with temozolomide—the prognosis remains poor, with limited gains in long-term survival. Combination therapy has become a foundational paradigm in contemporary oncologic treatment, aiming to overcome resistance mechanisms and intratumoral complexity. This approach is continuously evolving, as evidenced by a growing body of preclinical and clinical studies investigating novel therapeutic combinations and targeted agents [12].

This review focuses on the current understanding of GBM pathophysiology and highlights recent advancements in therapeutic surgical strategies targeting tumor heterogeneity considering survival rates in different subject groups.

Materials and methods

A targeted literature search was conducted in the PubMed database on May 2, 2025, using the keywords: glioblastoma, surgery, and survival rate. The search was restricted to articles published in the past five years. A total of 97 records were retrieved. Articles were selected based on relevance to the review topic, with preference given to peer-reviewed primary research, case reports, systematic reviews, and recent high-impact narrative reviews. Non-English publications, and studies not primarily addressing surgical outcomes or survival were excluded. Reference lists of included articles were also screened to identify additional relevant sources.

Discussion

Glioblastoma multiforme (GBM) is the most common and aggressive primary malignant brain tumor in adults, accounting for approximately 47.7% of all malignant central nervous system (CNS) tumors and 57% of all gliomas. Worldwide, about 300, 000 new cases are diagnosed each year. Despite aggressive treatment, the median survival for GBM patients is around 15 to 18 months, with a five-year survival rate of approximately 6.9%. Prognostic factors influencing survival outcomes include age, performance status, the extent of surgical resection, and molecular markers such as MGMT promoter methylation [14].

The median age at diagnosis is 65 years, with rates highest in the group aged 75 to 84 years. Glioblastoma is 1.58 times more common in males compared with females, with an annual age-adjusted incidence of 4.00 compared with 2.53 per 100, 000 population, respectively. Globally, glioblastoma incidence is highest in North America, Australia, and Northern and Western Europe [14].

The clinical presentation of the disease may vary widely and is dependent on numerous variables, such as tumor location and size at the time of diagnosis. The most common presenting symptoms at the time of diagnosis are typically headache and nausea, secondary to a large tumor size or a significant amount of edema [15].

The decision regarding the initial surgical approach—whether radical tumor resection or biopsy—should be based on three key factors: the patient's overall health status (e.g., ASA score, WHO performance status), the tumor's location and resectability, and the patient's preferences regarding treatment options [16].

Despite advances in current surgical techniques, there remains a critical need for enhanced intraoperative guidance to maximize the extent of resection and, ultimately, improve patient prognosis. One promising approach to address this challenge is the use of fluorescence-guided probes, which can effectively illuminate tumor margins that are otherwise indistinguishable from normal brain tissue under traditional white light imaging [7].

The treatment for newly diagnosed glioblastoma is multifaceted and complex. [figure 1]Initial treatment typically consists of maximal-safe surgical resection of the tumor, followed by RT and concurrent chemotherapy. This course is then followed by further maintenance chemotherapy. The chemotherapy agent of choice for GBM is temozolomide, which is an alkylating agent. The addition of temozolomide is associated with both increased overall survival and progression-free survival [8].

While surgical resection plays a critical role in the multimodal treatment schema of GBM, there has historically been variability in the extent of resection (EOR) goals of surgery—ranging from minimally invasive biopsies to gross total resections (GTR) [figure 2]. In 2020, a study expanded upon the current literature by examining the most recent studies on the impact of SpTR—defined in our review as resection beyond contrast-enhancing regions of tumor on MRI including any amount of T2 FLAIR signal and any anatomical resection beyond the region of contrast-enhancing tumor—upon OS and PFS in GBM specifically. The review suggests that supratotal resection (SpTR) may be associated with improved overall survival (OS)

compared to gross total resection (GTR) in glioblastoma (GBM), particularly when anatomical SpTR is performed. However, this finding is limited by variability in study designs and significant clinical and methodological heterogeneity across studies. Prospective clinical data are needed to better define the parameters for the use of SpTR in the management of GBM. [table 1]

A postoperative contrast-enhanced MRI should be performed within 48 hours to assess the extent of resection and establish a baseline for future therapeutic interventions. In cases where surgery or microsurgical resection is not feasible—due to medical contraindications or patient refusal—stereotactic or open biopsy remains a viable alternative. This step is crucial not only for obtaining a histological diagnosis but also for enabling molecular testing, which can guide subsequent therapy [14].

Treatment options in the relapsed or recurrent setting are less well defined, with no established standard of care and little evidence for any interventions that prolong OS. Indeed, a significant proportion of patients may not even be eligible for second-line therapy. It is estimated that only about 25% of patients with a recurrence are considered for repeat debulking surgery [8].

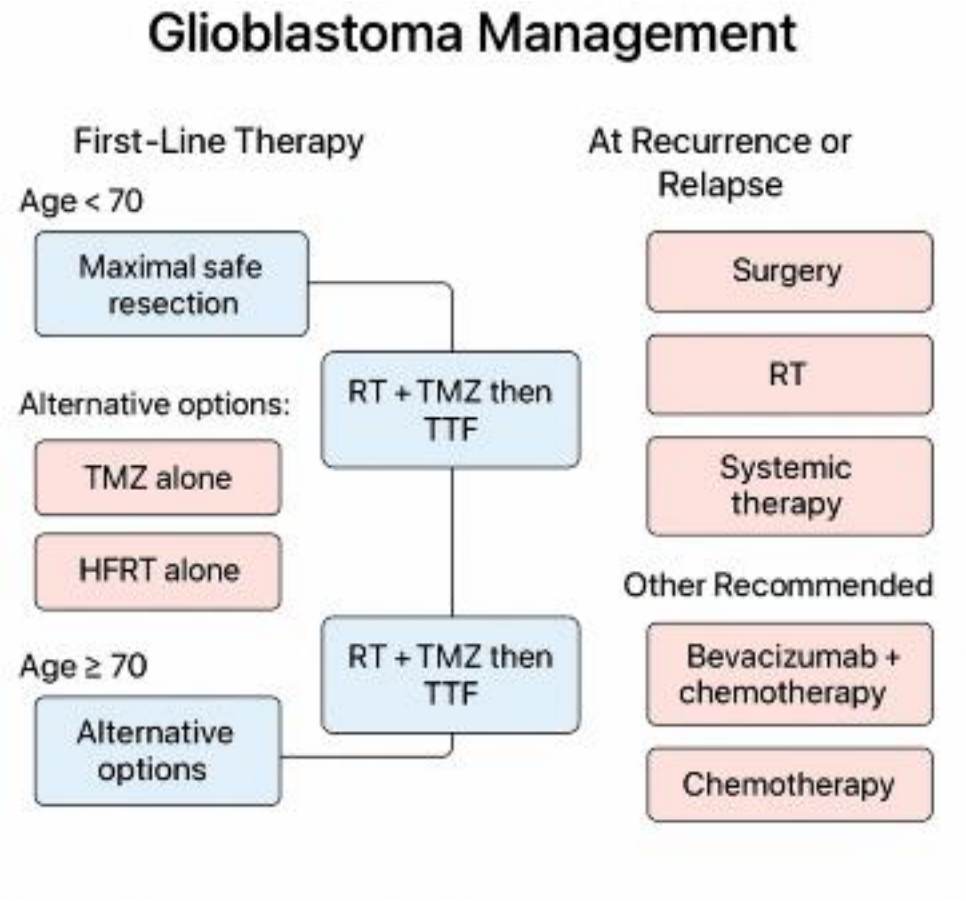

Fig. 1. *Simplified management algorithm for glioblastoma multiforme (GBM). This flowchart outlines the standard treatment pathway including maximal safe resection, radiotherapy, and chemotherapy, with options for recurrence. Adapted from Siegel RL, et al.*

Table 1. Stupp R, Weller M, Aldape K, et al. RANO classification of extent of resection in glioblastoma: Proposal and validation. *Lancet Oncol.* 2024. https://doi.org/10.1016/S1470-2045(24)00130-X [13]

Class	Category	Definition
1	Supramaximal CE Resection	0 cm^3 CE + ≤5 cm^3 non-CE tissue remaining
2	Maximal CE Resection	≤1 cm^3 CE and/or >5 cm^3 non-CE tissue remaining
3	Submaximal CE Resection	>1 cm^3 CE tissue remaining
4	Biopsy Only	No reduction in tumor volume

Fig. 2.

1. Necrosis
2. Contrast enhancing tumor
3. Non contrast enhancing tumor

Conclusions

Glioblastoma multiforme (GBM) remains the most common and aggressive primary malignant brain tumor in adults, with a dismal prognosis despite current multimodal treatment approaches. Key prognostic indicators include age, functional status, molecular markers, and the extent of surgical resection. Emerging evidence suggests that supratotal resection (SpTR) may confer a survival advantage over gross total resection (GTR), particularly when anatomical SpTR is achieved, although current findings are limited by heterogeneity across studies. The integration of advanced intraoperative techniques, such as fluorescence-guided imaging, is essential for optimizing resection while preserving neurological function. Given the absence of standardized treatment protocols for recurrent GBM and the variability in patient outcomes, further prospective studies are warranted to refine surgical strategies and improve overall survival [7, 8].

Disclosure

Author's contribution:

Conceptualization: Wiktoria Suchcicka, Aleksandra Borowy

Methodology: Julia Guzowska, Barbara Wołoszyn, Patrycja Rzeźnik Software: Maciej Sobczyk, Weronika Stachera

Check: Maciej Sobczyk, Weronika Stachera

Formal analysis: Julia Stepień, Małgorzata Zach, Aleksandra Chajnowska Investigation: Julia Guzowska, Barbara Wołoszyn, Patrycja Rzeźnik Resources: Julia Stepień, Małgorzata Zach, Aleksandra Chajnowska Data curation: Maciej Sobczyk, Weronika Stachera

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