Beyond the margins: evaluating the necessity and timing of supramarginal resection in glioblastoma management

Abstract. Glioblastoma, classified as a grade IV astrocytoma by the World Health Organization, continues to be a very aggressive cancer that requires a comprehensive strategy comprising surgery, radiation, and chemotherapy. Traditionally, gross total resection has primarily targeted the contrast-enhanced regions shown on T1-weighted magnetic resonance images. However, current studies suggest a more aggressive approach that focuses on removing the areas around the tumor, called supramarginal resection. This innovative strategy seeks to go beyond traditional boundaries, offering possible advantages for survival. However, it also raises worries over the removal of brain tissue that is crucial for important functions. The extremely poor prognosis of glioblastoma, characterized by a median survival of 10 months, highlights the pressing need for novel approaches to treatment. The aim of the study is to evaluate the influence of resection with a margin that extends much beyond the contrast enhancement on the survival of certain glioblastoma patients. The potential advantages documented in previous collections of cases are consistent with the notion of personalized surgical decision-making, which questions the prevailing approach of achieving the greatest possible removal of the tumor that is enhanced by contrast. Nevertheless, the potential neurological risks should be thoroughly evaluated. The objective of this study is to provide significant insights into improving the management of glioblastoma by examining the careful trade-off between aggressive tumor removal and preserving neurological function in specific groups of patients.

Keywords: supramarginal resection; gross total resection; glioblastoma; glioma; high-grade glioma

Introduction

Glioblastoma, categorized as a grade IV astrocytoma by the World Health Organization, continues to pose a significant obstacle in the field of neuro-oncology due to its highly aggressive characteristics and the scarcity of available treatment choices [1].

The conventional treatment strategy entails a synergistic use of surgical excision, radiation, and chemotherapy. Prior studies have found that achieving a minimal extent of resection (EOR) of around 70% based on T1-weighted contrast-enhanced imaging leads to increased survival rates. Due to the positive outcomes observed with increased EOR, there has been a focused endeavor to develop and use cutting-edge technology and surgical instruments with the goal of improving the safety and efficiency of resection treatments. The effectiveness of surgical intervention, specifically, has been a central focus of research, with EOR having a critical influence on patient outcomes [2].

Historically, the objective of glioblastoma surgery has been to remove the visible areas of increased contrast on T1-weighted magnetic resonance imaging (MRI), known as gross total resection (GTR). Nevertheless, improving understanding of the invasive characteristics of glioblastoma has resulted in a fundamental change in perspective. Recent
research suggest implementing a more assertive approach called supramarginal resection, which aims to go beyond traditional boundaries in order to target regions surrounding the tumor that have been invaded. The invasion of diseased cells into the normal white matter around the neoplastic core creates distinct zones that pose a special challenge and potential in the therapy of glioblastoma [3].

The existing literature indicates an increasing amount of data that suggests supramarginal resection may have potential advantages in terms of survival compared to traditional gross total resection. Nevertheless, this method raises worries about the possibility of removing brain tissue that is crucial for normal brain function. Therefore, it is important to carefully balance the goal of removing the tumor as much as possible while still protecting neurological function [4].

This article aims to thoroughly assess the need and optimal time for supramarginal resection in the therapy of glioblastoma by doing a comparative analysis with the conventional approach of gross total resection. Our objective is to analyze and combine the results of relevant research in order to clarify the possible advantages and disadvantages of supramarginal resection. This will provide valuable insights into how this surgical procedure may be used to make personalized decisions for patients with glioblastoma.

Supramarginal resection: advantages and mechanisms

Glioblastoma, a highly malignant form of brain cancer, poses significant challenges due to its infiltrative nature. Surgical resection is a crucial component of the treatment strategy, and recent research have explored the advantages and mechanisms of supramarginal resection in glioblastoma cases [5–12].

Advantages of supramarginal resection

1. Maximizing tumor removal: the supramarginal gyrus, located in the parietal lobe, is often implicated in glioblastoma cases. Resection of this region aims to maximize the removal of tumor tissue, potentially reducing the risk of recurrence and improving overall patient outcomes.

2. Preserving critical functions: advances in neuroimaging and surgical techniques allow for more precise targeting during supramarginal resection. This precision minimizes damage to surrounding healthy brain tissue and preserves critical functions associated with the supramarginal gyrus, such as language processing and spatial awareness.

3. Enhanced patient outcomes: studies suggest a correlation between the extent of tumor resection and improved patient outcomes in glioblastoma. Supramarginal resection, when performed carefully, may contribute to better progression-free survival and quality of life for patients.

Mechanisms of supramarginal resection

1. Functional mapping: preoperative functional mapping is a key mechanism in supramarginal resection. Techniques like functional magnetic resonance imaging help identify eloquent areas of the brain, including those associated with the supramarginal gyrus. This mapping guides surgeons in planning the surgery to avoid critical functional regions.

2. Intraoperative monitoring: real-time neurophysiological monitoring during surgery plays a crucial role in the success of supramarginal resection. Monitoring helps assess the functionality of the brain in real time, allowing surgeons to make informed decisions and ensure that vital areas, including those related to the supramarginal gyrus, are spared.

3. Neuronavigation systems: the integration of neuronavigation systems is another mechanism that enhances the precision of supramarginal resection. These systems provide three-dimensional visualization of the brain, aiding surgeons in navigating through complex structures and ensuring accurate targeting during the procedure.

4. Advanced imaging modalities: the use of advanced imaging modalities, such as diffusion tensor imaging, helps surgeons visualize white matter tracts and assess their proximity to the tumor. This information is invaluable in planning supramarginal resection, as it allows for a more comprehensive understanding of the tumor’s relationship with surrounding brain structures.

Gross total resection: limitations and considerations

GTR is a surgical approach aimed at removing the entire visible tumor mass in patients diagnosed with glioblastoma, a highly aggressive and infiltrative form of brain cancer. GTR is a critical component of the multimodal treatment strategy that typically includes surgery, radiation therapy, and chemotherapy. The primary goal of GTR is to maximize the extent of tumor removal, which can potentially improve patient outcomes and prolong survival [13–19].

Advantages of gross total resection

1. Improved survival rates: studies have suggested a positive correlation between the extent of tumor resection and overall survival in glioblastoma patients. GTR aims to remove as much tumor tissue as possible, reducing the risk of recurrence and improving prognosis.

2. Enhanced response to adjuvant therapies: following GTR, adjuvant therapies such as radiation and chemotherapy may be more effective, as there is less tumor burden for these treatments to target. This synergy between surgery and adjuvant therapies is crucial in the comprehensive management of glioblastoma.

3. Quality of life: GTR not only addresses the biological aspects of tumor removal but can also contribute to improved quality of life for patients by alleviating symptoms associated with increased intracranial pressure and mass effect.

Limitations and considerations

1. Tumor infiltration beyond visible margins: glioblastoma is known for its diffuse infiltration into surrounding brain tissue, making it challenging to define clear boundaries between tumor and normal brain. Despite advances in imaging and surgical techniques, some tumor cells may remain beyond the visible margins, limiting the efficacy of GTR alone.

2. Risk of neurological deficits: achieving GTR may involve navigating through eloquent areas of the brain responsible for crucial functions such as motor skills, language, and sensory perception. Aggressive resection in these regions...
The findings indicated that GTR tended to achieve higher outcomes associated with GTR and supramarginal resection on patients’ quality of life. This nuanced exploration encompassed postoperative neurocognitive function, language skills, and motor abilities. The outcomes of this study underscored the potential for supramarginal resection, when individualized to patient characteristics, to yield improved functional outcomes compared to more extensive resection approaches [6]. Building on these insights, Bonosi L. et al. (2023) contributed a prospective study utilizing advanced imaging techniques to assess the efficacy of GTR and supramarginal resection. Their results suggested that while GTR achieved higher rates of macroscopic tumor removal, supramarginal resection presented a more nuanced approach, particularly in cases where preserving critical brain functions took precedence [22]. Collectively, these studies contribute to a growing body of evidence highlighting the multifaceted considerations in selecting between GTR and supramarginal resection strategies for glioblastoma management. GTR is characterized by its overarching goal to eliminate the entire visible tumor mass, providing potential relief from intracranial pressure, and ameliorating symptoms associated with mass effect. Particularly, in cases where the tumor is situated distantly from critical brain regions, GTR has the potential to minimize immediate neurological deficits. Furthermore, GTR is associated with a likelihood of improved overall survival and delayed recurrence, contributing to an extended period of enhanced functional status for select patients. But pursuit of GTR is not without limitations. Notably, GTR poses an elevated risk of neurological deficits, particularly when the tumor is located proximate to or within functionally eloquent brain areas. Surgical interventions in these regions may result in deficits involving motor skills, sensory perception, or language functions. The potential for postoperative neurological deficits consequently has implications for functional outcomes, necessitating comprehensive rehabilitation and supportive care strategies to optimize the recovery of functionality after surgery [13–19]. Supramarginal resection represents a more discerning approach, seeking to optimize tumor removal while concurrently safeguarding crucial brain functions linked with the supramarginal gyrus. This strategy aims to minimize the risk of immediate postoperative neurological deficits associated with eloquent brain regions. The emphasis on preserving critical brain functions related to the supramarginal gyrus holds the potential for enhanced postoperative functional outcomes, particularly in domains such as language processing and spatial awareness. However, the efficacy of supramarginal resection is contingent upon factors such as the tumor’s location and extent. Achieving maximal resection while sparing critical functions becomes a nuanced challenge, particularly when tumors involve or are

Considerations for optimal gross total resection

1. Advanced imaging modalities: the integration of advanced imaging modalities, such as functional MRI, diffusion tensor imaging, and 5-ALA fluorescence, plays a crucial role in optimizing gross total resection. These techniques aid surgeons in visualizing tumor margins, preserving critical structures, and improving the accuracy of resection.

2. Intraoperative monitoring: real-time neurophysiological monitoring during surgery is essential to assess and preserve critical brain functions. Monitoring helps surgeons make informed decisions about the extent of resection, especially in areas associated with eloquent brain functions.

3. Adjuvant therapies: gross total resection is often followed by adjuvant therapies such as radiation and chemotherapy. Coordination between surgical and oncological teams is vital to tailor the adjuvant treatment plan based on the extent of resection and the patient’s overall health.

The limitations associated with the infiltrative nature of the tumor, the risk of neurological deficits, and the presence of perivascular tumor satellites emphasize the need for a thoughtful and multidisciplinary approach to glioblastoma surgery. Advances in imaging, intraoperative monitoring, and collaboration among healthcare professionals continue to refine the strategies for achieving optimal gross total resection in the complex management of glioblastoma [14, 20, 21].

Comparative clinical studies

In a series of comprehensive studies exploring surgical strategies for glioblastoma, researchers have undertaken retrospective cohort and comparative analyses to discern the outcomes associated with GTR and supramarginal resection. Di Long et al. (2022) conducted a retrospective cohort study, emphasizing survival rates, progression-free survival, and postoperative functional outcomes in glioblastoma patients undergoing either GTR or supramarginal resection. The findings indicated that GTR tended to achieve higher rates of complete tumor removal, while supramarginal resection exhibited potential advantages in preserving critical brain functions [19]. Parallelly, Polonara G. et al. (2023) delved into a similar comparative investigation, echoing the evaluation of survival metrics and functional outcomes in GTR versus supramarginal resection scenarios. Their results confirmed the emerging pattern observed by Di Long et al., suggesting potential benefits associated with supramarginal resection in terms of neurofunctional preservation [17]. Moreover, Johnson et al. (2023) approached the comparative analysis from a distinct perspective, centering on the impact of GTR and supramarginal resection on patients’ quality of life. This nuanced exploration encompassed postoperative neurocognitive function, language skills, and motor abilities. The outcomes of this study underscored the potential for supramarginal resection, when individualized to patient characteristics, to yield improved functional outcomes compared to more extensive resection approaches [6]. Building on these insights, Bonosi L. et al. (2023) contributed a prospective study utilizing advanced imaging techniques to assess the efficacy of GTR and supramarginal resection. Their results suggested that while GTR achieved higher rates of macroscopic tumor removal, supramarginal resection presented a more nuanced approach, particularly in cases where preserving critical brain functions took precedence [22]. Collectively, these studies contribute to a growing body of evidence highlighting the multifaceted considerations in selecting between GTR and supramarginal resection strategies for glioblastoma management. GTR is characterized by its overarching goal to eliminate the entire visible tumor mass, providing potential relief from intracranial pressure, and ameliorating symptoms associated with mass effect. Particularly, in cases where the tumor is situated distantly from critical brain regions, GTR has the potential to minimize immediate neurological deficits. Furthermore, GTR is associated with a likelihood of improved overall survival and delayed recurrence, contributing to an extended period of enhanced functional status for select patients. But pursuit of GTR is not without limitations. Notably, GTR poses an elevated risk of neurological deficits, particularly when the tumor is located proximate to or within functionally eloquent brain areas. Surgical interventions in these regions may result in deficits involving motor skills, sensory perception, or language functions. The potential for postoperative neurological deficits consequently has implications for functional outcomes, necessitating comprehensive rehabilitation and supportive care strategies to optimize the recovery of functionality after surgery [13–19]. Supramarginal resection represents a more discerning approach, seeking to optimize tumor removal while concurrently safeguarding crucial brain functions linked with the supramarginal gyrus. This strategy aims to minimize the risk of immediate postoperative neurological deficits associated with eloquent brain regions. The emphasis on preserving critical brain functions related to the supramarginal gyrus holds the potential for enhanced postoperative functional outcomes, particularly in domains such as language processing and spatial awareness. However, the efficacy of supramarginal resection is contingent upon factors such as the tumor’s location and extent. Achieving maximal resection while sparing critical functions becomes a nuanced challenge, particularly when tumors involve or are
in close proximity to essential brain regions. This delicate balance between tumor removal and function preservation may pose difficulties, and there remains a potential risk of neurological deficits. Additionally, the challenge extends to the possibility of a higher risk of tumor recurrence compared to GTR, introducing considerations that could impact long-term functional outcomes for patients undergoing supramarginal resection [5–12].

Future directions and implications

The future directions and implications of GTR and supramarginal resection in treating glioblastoma involve ongoing advancements in neurosurgical techniques, technology, and personalized medicine. These developments aim to improve the extent of tumor removal while minimizing neurological deficits and optimizing patient outcomes. Here are some potential future directions and implications [9, 10, 12, 23–25]:

1. Precision medicine and personalized approaches: advancement in molecular profiling. Future research may focus on integrating advanced molecular profiling techniques to identify specific genetic and molecular characteristics of glioblastoma tumors. This information can guide surgeons in tailoring the surgical approach based on the unique biological features of each patient’s tumor.

2. Integration of intraoperative imaging: continued improvement in imaging technologies. Ongoing research may lead to the development of more advanced intraoperative imaging techniques, such as real-time functional MRI, to enhance the visualization of tumor boundaries and critical brain structures during surgery. This can assist in achieving a more precise and thorough resection.

3. Innovative navigation systems: development of enhanced neuronavigation systems. Future advancements may involve the integration of artificial intelligence and augmented reality into neuronavigation systems. This could improve the accuracy of surgical planning, allowing for more effective GTR or supramarginal resection while minimizing the risk of damage to eloquent brain regions.

4. Targeted therapies and adjuvant treatments: emerging targeted therapies. Research into targeted therapies and immunotherapies may complement surgical interventions by addressing residual tumor cells after resection. The integration of novel adjuvant treatments could further improve the long-term outcomes for glioblastoma patients.

5. Neuromodulation and neuroprotection: neuromodulation strategies. Future research may explore neuromodulation techniques aimed at preserving and even enhancing neurological functions during surgery. These approaches could involve real-time monitoring and modulation of neural circuits to mitigate the risk of postoperative deficits.

6. Combination therapies and multimodal approaches: integration of multimodal therapies. The future may see an increased emphasis on combining surgical interventions with other treatment modalities, such as targeted radiation therapies, to achieve synergistic effects and improve overall survival rates.

7. Patient-centered outcome measures: focus on quality of life. Future studies may prioritize patient-centered outcomes, including quality of life assessments, to evaluate the impact of GTR and supramarginal resection on the daily functioning and well-being of glioblastoma patients.

Conclusions

In conclusion, the advancement of glioblastoma therapy relies on the convergence of state-of-the-art technology, tailored medical approaches, and a comprehensive understanding of the molecular and genetic attributes of the tumor. Anticipated developments include advancements in intraoperative imaging, precision medicine, and augmented reality neuronavigation devices. The primary objective is to enhance surgical procedures for optimal tumor removal while minimizing any adverse effects on the nervous system. The use of novel targeted therapeutics and multimodal treatment strategies, together with a strong focus on patient-centered outcome measures, is expected to improve both overall survival and quality of life. The translation of these achievements into clinical practice will heavily rely on collaborative research activities and active involvement in clinical trials. The management of glioblastoma is progressing towards a more refined and individualized approach, offering better outcomes and a more optimistic future for those dealing with this difficult diagnosis. The prospects and consequences of using GTR and supramarginal resection for the treatment of glioblastoma are positioned to take advantage of state-of-the-art technology, personalized medicine, and a thorough comprehension of the molecular and genetic characteristics of tumors. The primary objective is to enhance surgical procedures, reduce negative effects after surgery, and improve overall patient outcomes in the intricate and demanding field of glioblastoma treatment. The future of glioblastoma therapy will be influenced by ongoing research and breakthroughs in the area.

References


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Поза межами: оцінка необхідності та часу супрамаргінальної резекції при лікуванні гліобластоми

Резюме. Гліобластома, класифікована Всесвітньою організацією охорони здоров'я як астроцитома IV ступеня, продовжує залишатися дуже агресивним типом раку, який вимагає комплексної стратегії, що включає хірургічне втручання, променеву та хіміотерапію. Традиційно загальна резекція в першу чергу націлена на контрастні ділянки, показані на T1-зважених магнітно-резонансних зображениях. Однак у сучасних дослідженнях пропонують більш агресивний підхід, який зосереджується на видаленні ділянок навколо пухлинні та назвивається супрамаргінальною резекцією. Ця інноваційна стратегія прагне вийти за рамки традиційних границь, пропонуючи можливі переваги для виживання. Однак це також викликає занепокоєння щодо видалення тканини мозку, яка має вирішальне значення при виконанні важливих функцій. Надзвичайно поганий прогноз гліобластоми, що характеризується середнім періодом виживання 10 місяців, підкреслює нагальну потребу в нових підходах до лікування.

Мета дослідження полягає в тому, щоб оцінити вплив резекції з запасом, який виходить за рамки контрастного посилення, на виживання деяких пацієнтів із гліобластомою. Потенційні переваги, здоказовані в попередніх серіях випадків, узгоджуються з концепцією індивідуалізованого прийняття хірургічних рішень, коли під сумнів ставиться переважаючий підхід досягнення максимально можливого видалення пухлини при посиленні контрастом. Тим не менш потенційні неврологічні ризики слід ретельно оцінити. Завдання цього дослідження полягає в тому, щоб надати суттєву інформацію про покращення лікування гліобластоми шляхом детального вивчення компромісу між агресивним видаленням пухлинні та збереженням неврологічних функцій у конкретних групах пацієнтів.

Ключові слова: супрамаргінальна резекція; загальна резекція; гліобластома; гліома; гліома високого ступеня злоякісності