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Original Research

Subventricular zone involvement and cortico-spinal tract infiltration as predictors of outcome in Glioblastomas: a distinct surgical, clinical and prognostic entity

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Highlights

- Motor+SWZ glioblastomas show the poorest survival.
- Combined involvement significantly limits extent of resection.
- Motor+SWZ tumors display persistently worse functional outcomes.
- Anatomical–functional integration improves prognostic stratification.
- Preoperative identification may guide tailored surgical strategies.

Abstract

Background

Glioblastomas (GBMs) involving the subventricular zone (SVZ) and eloquent motor pathways represent a major surgical and prognostic challenge. While SVZ contact and motor-area involvement have been independently associated with poor outcome, the combined prognostic impact remains poorly defined.

Methods

We retrospectively analyzed 200 consecutive patients with newly diagnosed IDH-wildtype GBM treated between 2018 and 2024. Four anatomical subgroups were identified: non-motor/non-SVZ (n=79), non-motor/SVZ (n=58), motor/non-SVZ (n=34), and motor/SVZ (n=39). Overall survival (OS), progression-free survival (PFS), extent of resection (EOR), and functional outcome assessed by Karnofsky Performance Status (KPS) were compared using Kaplan–Meier analysis, Cox regression, and longitudinal mixed-effects modeling.

Results

The lowest gross-total resection rate was observed across the motor/SVZ subgroup (58%; p=0.008). Median OS and PFS were significantly shorter in the motor/SVZ subgroup (OS 8.0months; PFS 5.0months) compared with the other anatomical groups (OS 11.0–15.0months; PFS 4.0–7.5months; OS: p=0.020, PFS: p=0.041). In multivariable Cox analysis, combined motor and SVZ involvement was independently associated with reduced OS (HR 1.63, 95% CI 1.02–2.74, p=0.047). Patients with motor/SVZ tumors consistently exhibited the lowest postoperative and follow-up KPS values, indicating persistently worse functional status. The adverse prognostic effect of motor/SVZ involvement was confirmed in sensitivity analyses.

Conclusions

GBMs involving both eloquent motor pathways and the SVZ may represent a high-risk anatomical subgroup associated with reduced resectability, poorer postoperative functional recovery, and shorter survival. Given the small motor/SVZ sample size, these findings should be considered hypothesis-generating and require validation in larger multicentric cohorts. Nevertheless, they support the potential value of integrating anatomical and functional parameters in surgical decision-making and prognostic stratification.

Introduction

The 2021 World Health Organization (WHO) Classification of Tumors of the Central Nervous System (CNS) identifies more than 100 different subtypes of malignancies, wherein glioma represent the most histologically heterogeneous and aggressive ones. IDH-wt, of all mainstream brain tumors, is the subtype of the glioblastoma (GBM, IDH-wildtype), which is the most aggressive subtype, accounting for 55–60% of all glioma cases, with a median overall survival (OS) of 14–18months regardless of a multimodal treatment approach, including surgery, radiotherapy, and chemotherapy alone or in combination [1].

Based on current literature, the clinical outcome is remarkably influenced the tumour's anatomical relationship, which may restrain surgical resection and increase progression. Indeed, extension to the subventricular zone (SVZ) and the cortex were significantly associated to non-local recurrence patterns and tumor multifocality, supporting the concept of SVZ anatomy as distinct clinical phenotype [2]. Furthermore, tumour invasion of eloquent cortical areas, notably the motor region, represents an unmet surgical challenge that hinders the extent of resection (EOR) to an unfavourable outcome-wise [3], [4], [5].

Accordingly, SVZ involvement (or lateral-ventricle contact as an imaging proxy for periventricular/SVZ adjacency) in GBMs as a predictor of worse outcomes has been extensively studied [6], [7], [8]. In a cohort study Jafri et al., 2013 analyzed SVZ-contact-only and SVZ+cortical involvement patterns, which were linked to reduced OS and progression-free survival (PFS) [9]. Subsequently, these findings were confirmed by Mistry et al., 2017 through a meta-analysis, wherein GBMs contacting the lateral ventricle were associated with lower survival, potentially beyond common prognostic covariates [10]. Despite improvements in molecular characterization and treatment, SVZ involvement has consistently been reported as an independent negative prognostic factor for OS and PFS [8], [9].

In addition, SVZ/ventricular adjacency may limit the maximal extent of resection (EOR) and may increase the likelihood of subtotal resection (ST), which may be implicated in leptomeningeal dissemination (LMD) [2]. Indeed, current cohort studies defined ST as an independent risk factor for decreased OS and increased LMD [12], [13]. However, in a multi-institutional retrospective study, Shimoda et al., 2015 observed that VE did not affect complications or non-locale recurrence [8]. More recently, Ahi-Kang et al., 2020 found that ependymal contact increases leptomeningeal invasion and shorter survival, while ventricular bleeding itself does not affect these outcomes [14]. These findings underline the importance to precisely determine tumour-ventricle relationship as well as intraoperative ventricular opening.

Moreover, since the degree surgical resection significantly affects the overall prognosis, EOR standardization is essential. Accordingly, the RANO research group defined MRI-based prognostic categories to improve its interpretation and comparability across studies [15].

Therefore, given the unpredictable nature of outcome determinants in GBMs, the integration of anatomical, biological, and functional parameters has become essential in prognostic stratification.

Accordingly, the need to define the interplay among tumour location, functional eloquence, and SVZ involvement is essential. The purpose of this study is to identify clinical outcomes, extent of resection, and survival in GBMs involving the motor area with subventricular zone contact, thus providing further insight into the onco-functional balance, which represents a cornerstone in glioma surgery.

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Objective of the study

While SVZ involvement and eloquent motor area invasions' contribution in GBMs have been independently linked with limited extent of resection (EOR) and worse outcome, the combination of both critical factors in prognosis determination remains poorly characterized. Therefore, the purpose of this study is to investigate the prognostic and functional significance of SVZ involvement in GBMs extending to the motor area. The motor designation is intended to capture not only primary motor cortex and ...

Participants and eligibility

A retrospective observational study was performed, including a series of adult patients suffering from histologically confirmed GBM, according to the updated WHO classification [1]. The cohort included 200 consecutive patients treated in our institutions between September 2018 and September 2024. The inclusion criteria were:

- Availability of preoperative and early postoperative MRI studies ...
- Eligibility to receive adjuvant treatment according to the standard STUPP protocol ...
- Completion of a standard ...

...

Ethical Considerations

The study protocol was approved by the Institutional Review Board of our Institution. Before the surgical procedure, all the patients gave informed written explicit consent after being provided with appropriate information. Data reported in the study have been completely anonymized. The study was conducted in accordance with the Declaration of Helsinki of Ethical principles for medical research on humans. ...

Descriptive data

The final cohort included 200 patients. SVZ-Motor (four-subgroups) classification was available in 195 cases with 5 missing, a patient who was counted but excluded from the final set of analysis (Table 1). The group distribution was:

- non-motor/non-SVZ (n=79; ...
- non-motor/SVZ (n=57; ...
- motor/non-SVZ (n=34; ...
- motor/SVZ (n=30; ...

Baseline demographic characteristics were comparable across groups with respect to age (51.0–52.0 years; n=196; p=0.947). Female sex distribution differed significantly ...

Discussion

The purpose of this study was to investigate the prognostic impact of SVZ involvement in patients with Grade IV GBMs involving eloquent motor areas, with a specific focus on the extent of resection, preoperative functional status, and survival outcomes. Patient stratification accurate according to eloquent motor area involvement and SVZ proximity, resulting in four subgroups of analysis (Groups A-D). Therefore, we aimed to determine whether the combination of these two critical anatomical ...

Conclusions

In conclusion, GBMs extending to the SVZ and motor-systems may represent a high-risk anatomical subgroup associated with reduced resectability, poorer postoperative functional recovery, and reduced overall survival. However, since the motor/SVZ group was limited in sample size, these findings should be considered as hypothesis-generating and warrant further validation in larger multicentric cohort studies. Nevertheless, these findings highlight the potential need to integrate functional status, ...

Credit authorship contribution statement

Ioannisini Giorgio: Methodology, Data curation. **Palmieri Mauro:** Methodology, Data curation. **Aurelii Lorenzo:** Conceptualization, Methodology, Formal analysis, Writing – original draft. **Nevegeo Federica:** Data curation, Investigation. **Ian Kaiai:** Project administration. **Da Rex Valeria:** Investigation. **Armacida Daniele:** Formal analysis. **Santoro Antonio:** Visualization, Methodology. **Salvati Maurizio:** Writing – review & editing, Methodology. **Fratt Alessandro:** Supervision, Methodology, Conceptualization, ...

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper. ...

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