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“CAROL DAVILA” BUCHAREST

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“MANAGEMENT OF LOW-GRADE SUPRATENTORIAL GLIOMAS CORRELATED WITH CURRENT DATA THROUGH MAGNETIC RESONANCE IMAGING”

DOCTORAL THESIS SUMMARY

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2.6 Introduction

In recent years, neuro-oncology has made significant progress, and glioma research has become a global priority due to its complexity and major impact on patients. The chosen topic aims to explore the diversity and behavior of gliomas, as well as the effects of various therapeutic interventions on prognosis. Although advances have been made in imaging and surgical techniques, treatment remains a challenge, highlighting the need for a personalized approach.

The importance of this topic is emphasized by new classifications of central nervous system tumors, such as the 2021 WHO Classification, and the use of radiogenomic markers, like the T2-FLAIR mismatch sign. The research focuses on a comparative analysis of surgical treatment outcomes and the evaluation of the impact of radiogenomic markers on the management of low-grade gliomas. Additionally, it examines glioma-associated epilepsy, which has implications for treatment and prognosis.

The objectives include: a comparative analysis of surgical treatments for glioma subtypes, an assessment of the impact of the T2-FLAIR mismatch sign on the classification and management of low-grade gliomas, and an investigation of the implications of associated epilepsy. The research method is retrospective, based on the analysis of clinical and imaging data from patients with glioma, and the study integrates essential interdisciplinary aspects to improve treatment and clinical outcomes. The research limitations are acknowledged, but they offer opportunities for future prospective studies and randomized clinical trials.

I. GENERAL PART

1. GENERAL CHARACTERISTICS AND MANAGEMENT OF GLIOMAS

1.1. Definition

Low-grade diffuse gliomas, tumors originating from glial tissue, can progress to higher-grade gliomas over time (1).

1.2. Diagnostic and Treatment Protocols

According to the guidelines, glioma management involves a predefined algorithm. Diagnosis begins with imaging, including structural MRI with DWI, FLAIR, and T1 sequences with and without contrast. It is recommended that the management strategy be discussed within a multidisciplinary team and, where possible, that advanced MRI technologies be utilized (2).

1.3. Surgical Management Correlated with Perioperative Imaging

Surgical resection should occur within six months of diagnosis, aiming to obtain a histological diagnosis and achieve maximum tumor excision. In cases where surgical resection is not feasible, biopsy or active surveillance is recommended. Neurosurgery units should be equipped with advanced technologies, such as awake craniotomy and intraoperative monitoring (3).

2. CONTEMPORARY GUIDELINES IN THE SURGICAL MANAGEMENT OF GLIOMAS

2.1. Modern Intraoperative Techniques

The use of 5-ALA-guided surgery and intraoperative MRI is recommended for precise resections. Other techniques include intraoperative ultrasound and diffusion tensor imaging. Awake craniotomy is essential for preserving neurological functions and requires collaboration with neuropsychologists and speech therapists. Laser interstitial thermal therapy (LITT) is recognized as a minimally invasive therapeutic modality (4,5).

2.2. Epilepsy in Low-Grade Gliomas

Epilepsy in patients with glioma is associated with a reduced quality of life and may have prognostic value. The NICE guidelines identify seizure control as one of the key outcomes following surgery (6).

3. 2021 WHO CNS5 CLASSIFICATION

Current classifications of central nervous system (CNS) tumors use specific molecular markers to improve diagnostic accuracy and prognosis. The classification is based on both molecular and histological information to provide an integrated diagnosis (7).

4. CONCLUSIONS

The identification of preoperative tumor markers and the use of advanced imaging technologies will enhance the diagnosis and treatment of gliomas. Integrating the WHO CNS5 classification system is crucial for more adaptable and precise management.

II. PERSONAL CONTRIBUTIONS

3. Study Hypothesis and General Objectives

Gliomas, the most common primary brain tumors in adults, develop in the cerebral parenchyma and are classified by the World Health Organization (WHO) based on histological type, grade, and molecular information, with an increased emphasis on molecular data. Standard treatment includes surgical intervention, radiotherapy, and chemotherapy, with survival outcomes varying according to glioma type and prognostic factors. IDH-wildtype glioblastoma has a poor prognosis, whereas low-grade gliomas have a median survival of 5–7 years (8,9).

Epilepsy is common among patients with gliomas and significantly impacts their quality of life, presenting a more severe clinical course than other forms of symptomatic epilepsy. This type of epilepsy, present in over 80% of patients with low-grade gliomas and 40-60% of those with glioblastomas, requires personalized therapeutic approaches.

The research hypothesis is that significant differences exist in treatment outcomes and prognosis for glioma patients based on the tumor subtype, the presence of associated epilepsy, and the use of radiogenomic markers. The research is based on three main hypotheses. Firstly, the outcomes of surgical interventions, including survival rates and functional recovery, differ among various glioma subtypes according to specific molecular characteristics, such as IDH mutations and 1p/19q codeletion (10). Secondly, glioma-associated epilepsy influences treatment strategies and patient prognosis. It is assumed that subgroups of glioma patients, particularly those with high-grade tumors or tumors located in epileptogenic regions, require specialized management to optimize seizure control and overall prognosis (11). Thirdly, the T2-FLAIR mismatch radiogenomic marker represents a significant advance in the classification and management of low-grade gliomas, enabling more precise classification and guiding therapeutic interventions (12).

The primary objectives of the research are to enhance the understanding of treatment outcomes and management strategies for glioma patients by focusing on three areas: a comparative analysis of surgical outcomes among different glioma subtypes to determine variations in functional recovery and survival, an evaluation of the impact of associated epilepsy on treatment strategies and patient prognosis, and the validation of the clinical utility of the T2-FLAIR mismatch radiogenomic marker in the classification and management of low-

grade gliomas. These objectives will help refine clinical protocols and optimize personalized treatment approaches, thereby improving patient outcomes (13).

4. General Research Methodology

The research comprises three distinct studies, each addressing a specific issue in the diagnosis and management of gliomas, using various methods and analyses.

The first study focused on evaluating the T2-FLAIR mismatch radiogenomic sign using magnetic resonance imaging (MRI) in patients with low-grade diffuse glioma. The retrospective study included 45 patients and analyzed the sensitivity and specificity of the T2-FLAIR mismatch sign for diagnosing IDH-mutant astrocytomas. Data were collected from medical records and MRI imaging, assessing the clinical, demographic, and histopathological characteristics of the patients. Statistical and imaging results were compared between patients with and without the T2-FLAIR mismatch sign to establish correlations between imaging markers and tumor subtypes.

The second study examined the impact of glioma-associated epilepsy on patient treatment and prognosis through a retrospective analysis of a cohort of 38 patients with glioma and associated epilepsy. The study identified the prevalence and types of epileptic seizures and evaluated how these influenced therapeutic decisions, including the choice of antiepileptic drugs and surgical interventions.

The third study combined retrospective and prospective approaches to investigate the relationships between different imaging techniques (MRI, MR spectroscopy) and histopathological outcomes in glioma diagnosis. This study included 61 patients and applied advanced statistical analyses, such as multivariate analysis, to identify predictive factors for patient prognosis.

All three studies employed rigorous statistical methods to analyze the data and assess the research hypotheses. The most complex study included logistic regression analyses and survival analyses. These methodologies ensured the validity and reliability of the results, providing an in-depth understanding of the impact of radiogenomic markers, associated epilepsy, and various imaging techniques on the diagnosis, treatment, and prognosis of patients with glioma.

5. The New T2-FLAIR Mismatch Radiogenomic Marker in Newly Suspected Low-Grade Gliomas: Implications for Classification and Neurosurgical Management in Light of the 2021 WHO Classification of Central Nervous System Tumors (WHO CNS5)

5.1 Introduction

The T2-FLAIR (fluid-attenuated inversion recovery) mismatch sign has become an important radiogenomic marker for IDH-mutant gliomas without 1p19q codeletion, particularly for astrocytomas. The 2021 World Health Organization (WHO) classification for central nervous system tumors (WHO CNS5) consolidated all IDH-mutant diffuse astrocytic tumors under the category "Astrocytoma, IDH-mutant," assigning grades 2, 3, or 4 according to the new criteria (6). This change emphasizes the increasingly important role of molecular data in the classification of CNS tumors, highlighting the need to integrate various data types to achieve a comprehensive diagnosis.

Although promising, the T2-FLAIR mismatch sign requires further investigation to validate its clinical utility in managing low-grade gliomas. Recent studies have shown that IDH mutation and non-codeletion of 1p/19q can be predicted using conventional and advanced MRI techniques (Figure 5.1). Gadolinium-enhanced MRI is considered the preferred modality for diagnosing and managing these tumors (14).

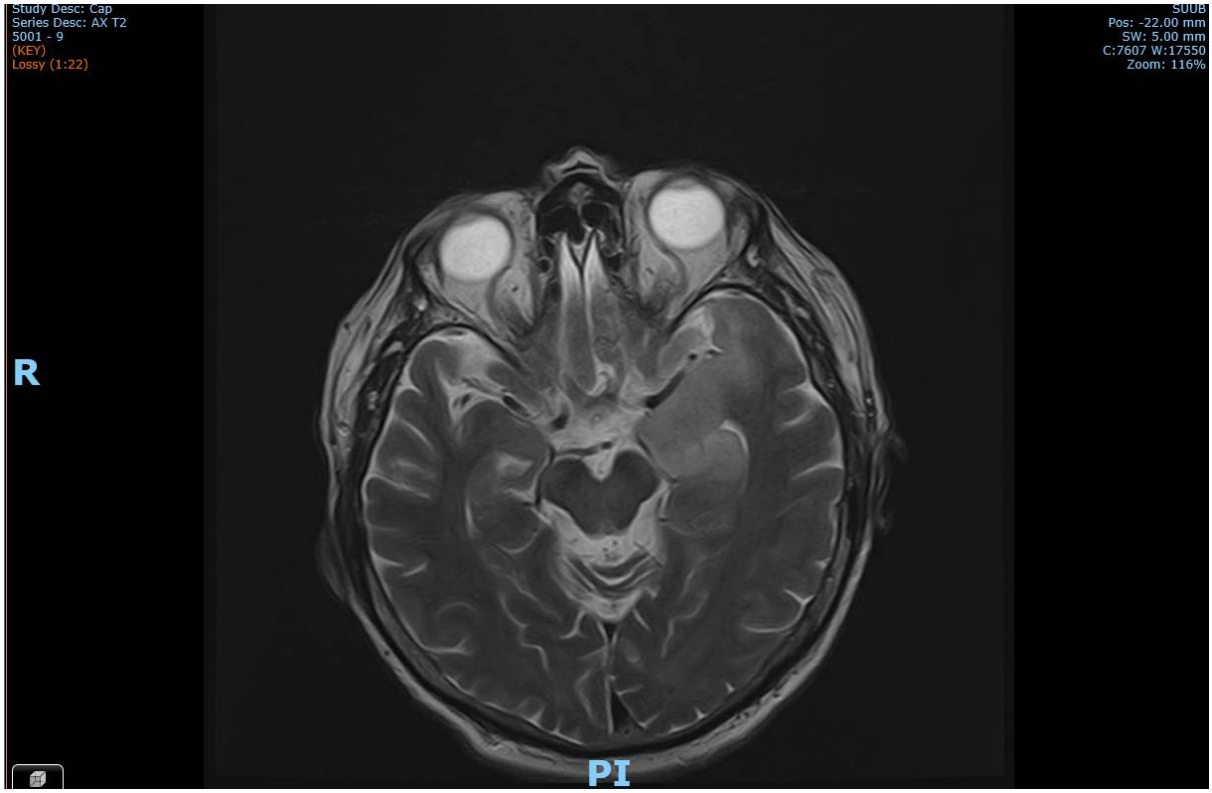

Fig. 5.1. Brain MRI Axial T2W images of 69M with final histology WHO grade 2 diffuse astrocytoma

The T2-FLAIR mismatch sign has been the subject of extensive research due to its high specificity for IDH-mutant gliomas without 1p/19q codeletion and its association with microcystic changes found in IDH-mutant astrocytomas. Radiogenomic biomarkers, such as the T2-FLAIR mismatch sign, have gained attention due to their simplicity, wide availability, and specificity in identifying IDH-mutant gliomas without 1p/19q codeletion (7) (Figure 5.2).

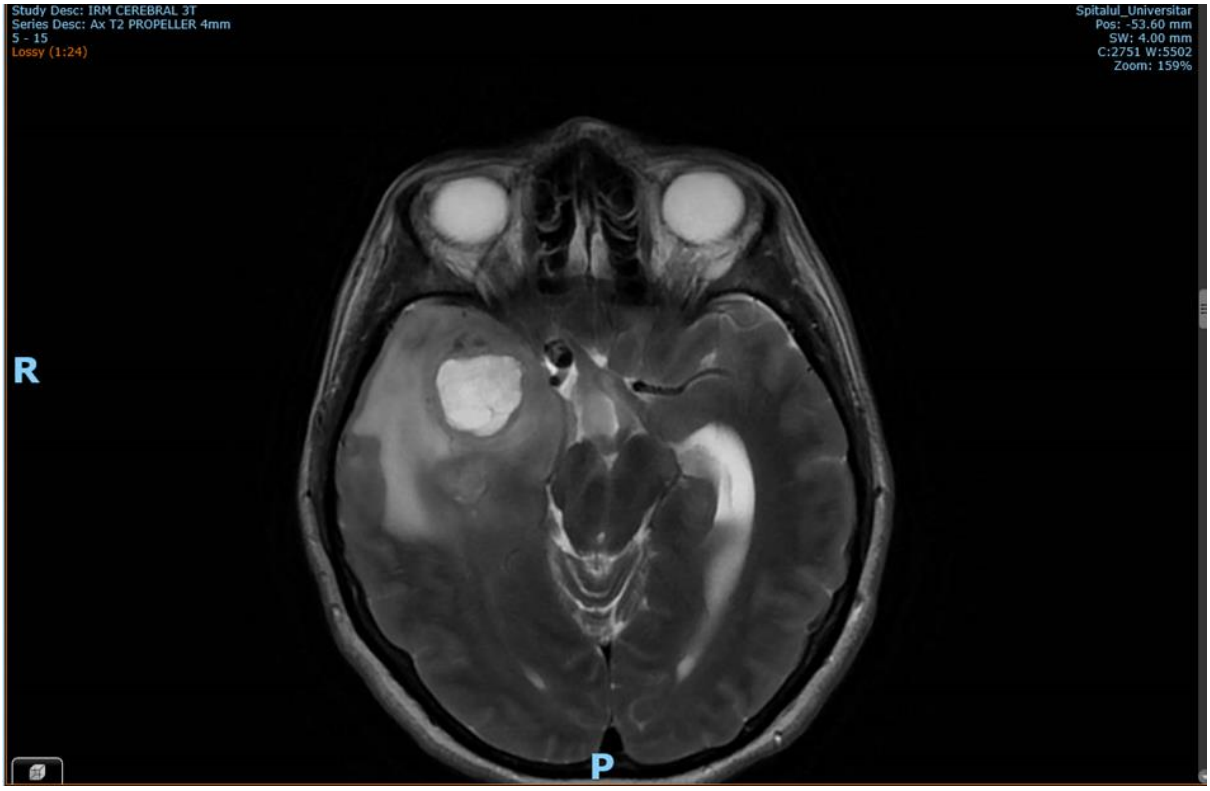

Fig. 5.2. T1W and T2FLAIR MRI images of a 46-year-old female patient diagnosed with a grade 4 glioblastoma according to WHO classification.

This marker can radiologically differentiate distinct gliomas; however, further investigations are needed to correlate it with biological characteristics (15). The present study aims to evaluate the relationship between the T2-FLAIR mismatch sign and clinical, radiological, and histological parameters according to the new WHO CNS5 Classification.

5.2 Materials and Method

The study included histologically confirmed supratentorial gliomas, classified as WHO grades 2-3, identified retrospectively (2013-2018, n = 18) and prospectively (2019-2023, n = 27). Comprehensive clinical, radiological, and histological data were collected for both cohorts.

The primary objective was to investigate the association between the T2-FLAIR mismatch sign and various clinical factors, as well as to evaluate its diagnostic reliability and correlation with histological diagnosis and magnetic resonance spectroscopy (MRS).

5.3 Results

Of the 45 patients included, 30 were diagnosed with diffuse astrocytoma of grades 2 or 3 (IDH-mutant), 6 with glioblastoma (IDH-wildtype), 8 with oligodendroglioma (IDH-mutant,

1p/19q codeletion), and one with a brain abscess. The T2-FLAIR mismatch sign was present in 20% of patients with IDH-mutant astrocytoma, with a sensitivity of 20% and a specificity of 98.6%.

In conclusion, the T2-FLAIR mismatch sign has the potential to aid in the diagnosis and management of gliomas, but further validation is required in the context of the new WHO CNS5 classification.

5.4 Discussions

Until recently, the classification of central nervous system (CNS) tumors was primarily based on histological characteristics. The integration of specific molecular markers has made a significant contribution by providing valuable prognostic information. As a result, molecular data have become essential criteria in tumor classification, allowing for a more accurate estimation of prognosis for different types of tumors.

According to some studies, the T2-FLAIR mismatch sign does not influence the extent of resection in IDH-mutant diffuse astrocytomas, and its association with survival is not clearly defined. Its specificity is high, ranging from 96.0% to 100.0% for IDH-mutant astrocytomas. Although specific, the T2-FLAIR mismatch sign is rarely observed in IDH-mutant gliomas with 1p/19q codeletion (oligodendrogliomas) and has been identified in some low-grade pediatric brain tumors. Despite its low sensitivity (27.1% - 51.0%), its use in combination with other diagnostic tools may improve diagnostic accuracy (16).

Future research should include larger cohorts and utilize a wider range of advanced imaging techniques, such as apparent diffusion coefficient (ADC) and cerebral blood volume (CBV), to better clarify the prognostic significance of the T2-FLAIR mismatch sign (17).

5.5 Conclusions

In this study, the T2-FLAIR mismatch sign was not associated with clinical characteristics, prognosis, or patient outcomes. However, it was confirmed as a reliable and specific marker for IDH-mutant astrocytomas. Rapid advances in identifying non-invasive tumor markers and the use of advanced imaging sequences are essential for improving preoperative diagnostic capabilities. Integrating the WHO CNS5 classification system into standard clinical practice is vital for more effective management of CNS tumors.

6. Glioma-Related Epilepsy - Features and Implications for Treatment and Prognosis in the Context of the Latest Brain Tumor Management Guidelines

6.1 Introduction

Low-grade gliomas, tumors originating from glial tissue, tend to progress to higher-grade tumors, complicating clinical management due to their diagnostic and therapeutic complexity. Glioma-associated epilepsy is an important clinical marker, significantly influencing treatment strategies and patient prognosis (4).

This retrospective study analyzed 38 patients with low-grade glioma (WHO grade 2 or 3) treated between 2013 and 2023, focusing on the incidence and management of epileptic seizures and reviewing NICE guidelines to highlight recent recommendations and therapeutic strategies. The aim was to investigate the correlation between the extent of surgical resection and seizure control, hypothesizing that more extensive resection would lead to better clinical outcomes (Table 6.1).

Table 6.1: Engel Seizure Classification Table

Class	Characteristics	Sub-Class	Description
I	No disabling seizures	A	Completely seizure-free since surgery
I	No disabling seizures	B	No disabling seizures; only simple partial seizures since surgery

I	No disabling seizures	C	Some disabling seizures after surgery, but seizure-free for at least 2 years
I	No disabling seizures	D	Generalized seizures only with discontinuation of antiepileptic medication (AED)
II	Rare disabling seizures (almost seizure-free)	A	Initially seizure-free, but rare seizures currently
II	Rare disabling seizures (almost seizure-free)	B	Rare disabling seizures since surgery
II	Rare disabling seizures (almost seizure-free)	C	More than rare disabling seizures since surgery, but rare seizures in the last 2 years
II	Rare disabling seizures (almost seizure-free)	D	Only nocturnal seizures

III	Significant improvement	A	Significant reduction in seizures
III	Significant improvement	B	Prolonged seizure-free intervals, comprising more than half of the follow-up period, but not less than 2 years
IV	No significant improvement	-	No significant improvement

6.2 Materials and Method

The study included 38 patients diagnosed with low-grade glioma (LGG), classified as WHO grades 2-3, who were treated in our neurosurgery department between 2013 and 2023. We analyzed the incidence of glioma-associated epileptic seizures and the anticonvulsant medication protocols used, supplemented by a detailed review of the existing literature.

The investigation included an analysis of clinical and imaging data, diagnostic methods, and treatment modalities. Patients were monitored both preoperatively and postoperatively, using the Engel classification to evaluate postsurgical outcomes.

6.3 Results

Of the 38 patients, 30 had diffuse astrocytoma (grades 2 and 3), and 8 had oligodendroglioma. The average age was 50 years, with a female predominance of 60%. The tumors were predominantly located in the frontal lobe (24 cases) and the dominant hemisphere (28 cases). Epilepsy was a prevalent symptom, present in 25 patients (ranging from focal seizures to generalized convulsions).

Management varied: biopsy (8%), total resection (40%), subtotal resection (32%), and partial resection (20%). No significant correlation was identified between seizures and tumor

characteristics, but the extent of resection significantly improved seizure control at six months postoperatively (76% of patients with total resection were seizure-free).

6.4 Discussions

Glioma-associated epilepsy significantly affects the quality of life but may also indicate a favorable prognosis for progression-free survival and overall survival. Seizure control primarily depends on the tumor location and the extent of surgical resection (18).

The integration of molecular markers in prognosis and treatment is becoming crucial. Recent studies show that gliomas with IDH mutations, for example, have a better prognosis and a higher incidence of epilepsy. The use of advanced surgical techniques and new antiepileptic drugs may improve seizure control and overall patient outcomes (19,20) (Figure 6.1).

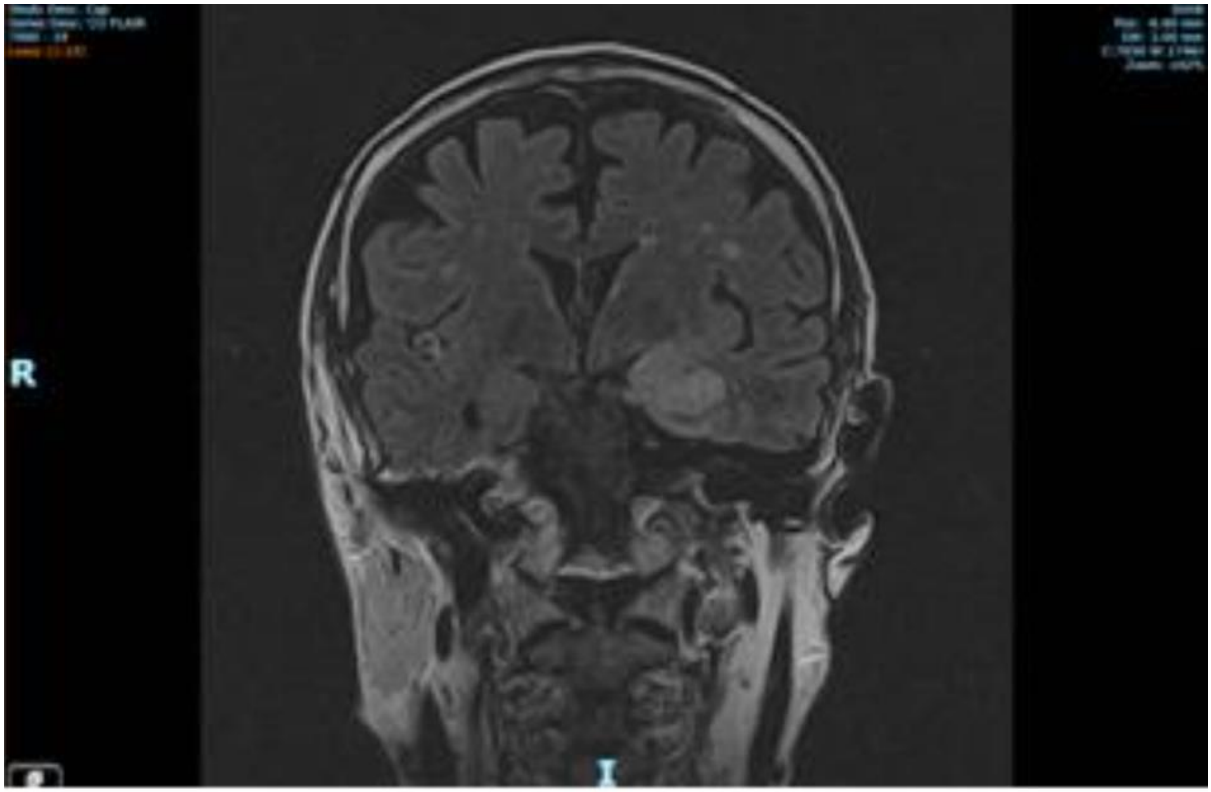

Fig. 6.1. Coronal FLAIR images of a 69-year-old patient with a grade 2 diffuse astrocytoma according to the WHO classification (Left Temporal Lobe).

6.5 Conclusions

Early and maximal surgical resection of low-grade gliomas provides dual benefits: it controls tumor progression and improves epilepsy-related outcomes. Integrating advanced diagnostic and treatment methods, including the use of molecular markers and careful management of epilepsy, remains essential for optimizing patient care (21).

7. Comparative Analysis of Treatment Outcomes in Glioma Subtypes: Personal Contributions in a Retrospective Study on Surgical Interventions and Functional Outcomes

7.1 Introduction

Gliomas are a diverse group of primary brain tumors that originate from glial cells, which are essential for the central nervous system. They range from low-grade tumors, such as oligodendrogliomas, to highly malignant tumors, like glioblastomas. Despite advances in diagnosis and treatment, managing gliomas remains challenging due to their heterogeneity and varied prognosis. Current treatments involve a combination of surgery, radiation, and chemotherapy; however, the optimal approach, particularly regarding surgical resection, is still debated for different glioma subtypes (22).

The 2021 WHO classification for gliomas integrates molecular diagnostics with traditional histology, leading to more precise tumor subtypes based on genetic and clinical characteristics. In adults, gliomas are categorized into three main subtypes: astrocytoma, IDH-mutant; oligodendroglioma, IDH-mutant with 1p/19q codeletion; and glioblastoma, IDH-wildtype. In pediatric patients, gliomas are classified into low-grade and high-grade subtypes based on molecular characteristics. The updated classification highlights the heterogeneity of gliomas and supports personalized treatment approaches for better outcomes (23).

This classification is crucial because it accounts for the heterogeneity of glioma subtypes, enabling more accurate prognoses and personalized treatment approaches. Integrating molecular data helps clinicians tailor therapies to the specific characteristics of the tumor, thereby improving patient outcomes (23).

Although gliomas are relatively rare, certain subtypes are associated with significant mortality and morbidity. Survival time after a glioma diagnosis varies widely depending on the grade, with glioblastoma multiforme (GBM) having the most unfavorable outcomes. Several inherited monogenic Mendelian cancer syndromes are associated with a higher incidence of certain specific glioma subtypes. Progress in identifying risk factors for gliomas is ongoing, but further research is needed (24).

This study hypothesizes that treatment outcomes in glioma patients, as measured by functional status and recurrence rates, vary significantly depending on the glioma subtype and the type of surgical intervention. The study aims to identify which subtypes benefit most from specific surgical approaches and to explore how clinical characteristics influence outcomes, with the goal of guiding clinical decisions and improving patient management.

7.2 Material and Method

7.2.1 Study Design and Population

This study is a retrospective analysis of 61 patients diagnosed with various glioma subtypes at the Bucharest University Emergency Hospital. The study included patients who underwent surgical interventions for gliomas, with data retrospectively extracted from electronic medical records. The glioma subtypes included were oligodendroglioma, high-grade gliomas, diffuse astrocytoma, and oligoastrocytoma. The included patients were those who underwent surgical procedures such as stereotactic biopsy, subtotal resection, or total resection.

7.2.2 Data Collection

Data were extracted from medical records and included demographic variables (age, sex), clinical variables (neurological deficits, Karnofsky Performance Status scores at admission and discharge), tumor recurrence status, glioma subtype classification, and type of surgical intervention.

7.2.3 Definition of Treatment Success

Treatment success was defined as the stability or improvement of the Karnofsky Performance Status (KPS) score at discharge compared to admission and the absence of documented tumor recurrence in follow-up clinical records.

7.2.4 Statistical analysis

Statistical analyses were performed using Python, employing descriptive statistics to characterize the demographic and clinical features of the cohort. Pearson and Spearman correlation tests were conducted to explore relationships between continuous variables, Mann-Whitney U tests were used to compare independent groups, and Chi-square tests were applied

to assess associations between categorical variables. Multiple linear regression analysis was used to examine the impact of clinical factors on Karnofsky scores at admission and discharge.

7.3 Results

7.3.1 Patient Characteristics and Distribution of Glioma Subtypes

The study cohort included 61 patients diagnosed with various glioma subtypes, such as oligodendroglioma, high-grade gliomas, and diffuse astrocytoma. The patients underwent different surgical interventions, including stereotactic biopsy, total surgical resection, and subtotal resection. No significant differences were found in baseline characteristics, such as age or sex, among the glioma subtypes.

7.3.2 Demographic Data

Of the 61 patients, 39 (63.9%) were female, and 22 (36.1%) were male. The age of the patients at the time of diagnosis ranged from 19 to 74 years, with a mean age of 43.5 years. The Karnofsky Performance Status (KPS) score was measured at admission for all participants, ranging from 60 to 100, with a significant concentration of patients in the 70-80 range (Figure 7.1).

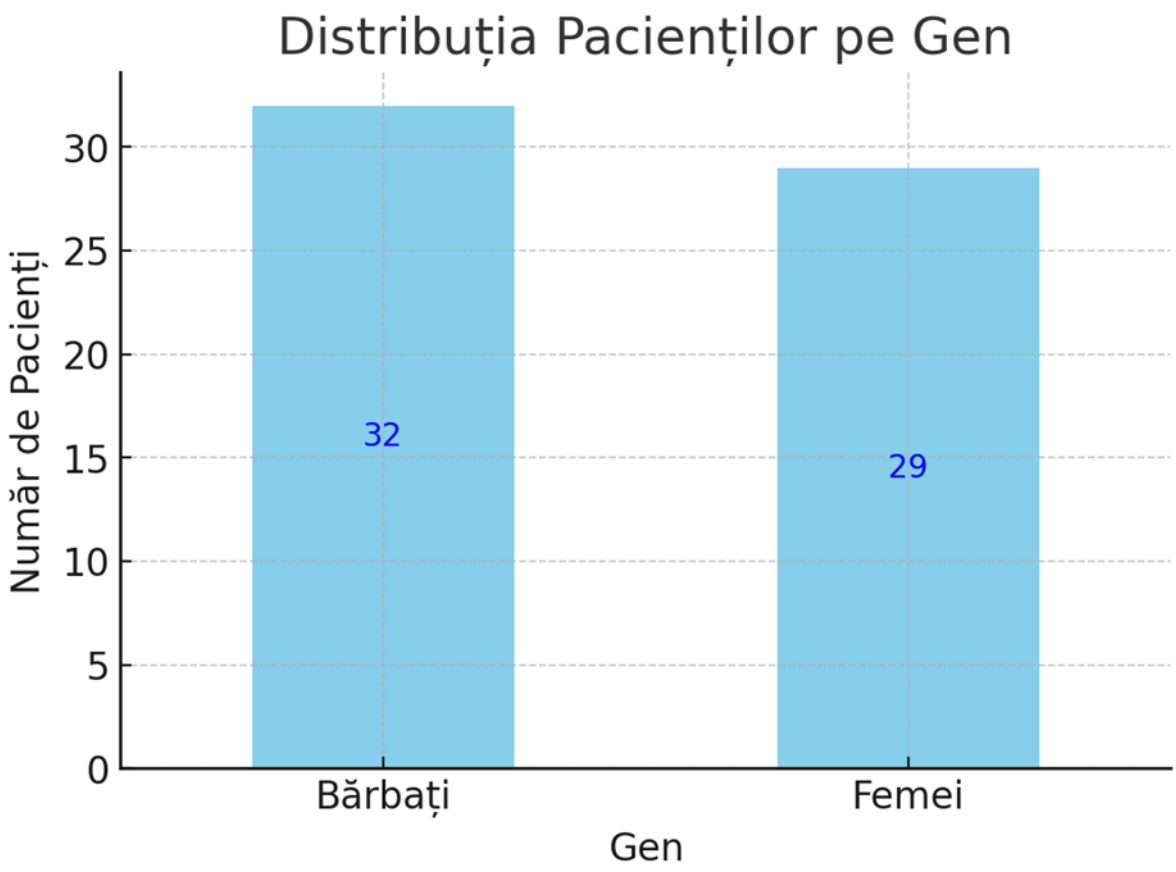

Fig. 7.1: Patient Distribution by Gender

7.3.3 Correlation Analysis

Spearman and Pearson correlation analyses did not identify strong correlations between age and Karnofsky scores, suggesting that age does not significantly influence functional status in this cohort. There is a strong positive correlation (0.83) between the Karnofsky score at admission and discharge, indicating that patients with better functional status at admission tend to maintain this status at discharge (Figure 7.2).

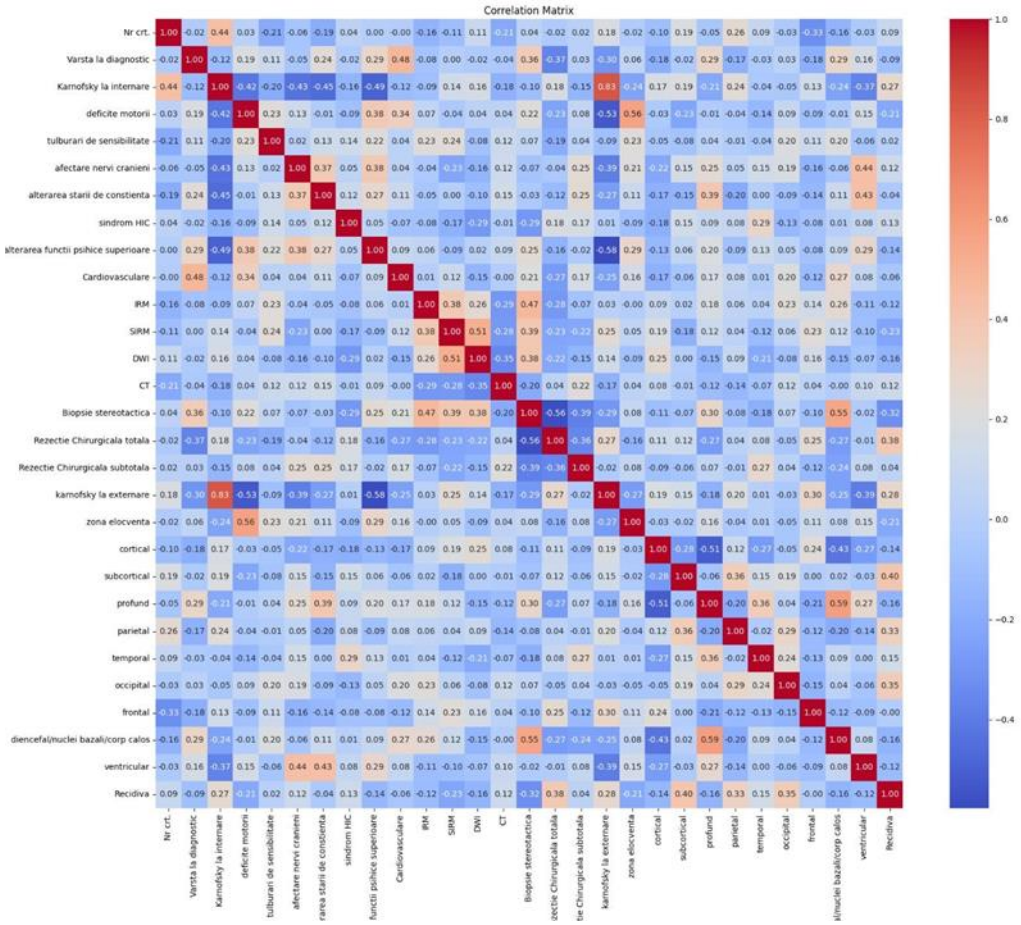

Fig. 7.2. Correlation matrix

7.3.4 Functional Outcomes Based on Surgical Interventions

The Mann-Whitney U test for the Karnofsky score showed statistically significant differences between the groups with and without Stereotactic Biopsy ($p = 0.047$) and between the groups with and without Total Surgical Resection ($p = 0.038$), indicating that the type of surgical intervention significantly influences functional outcomes.

7.3.5 Predictors of Functional Outcomes

The results of multiple linear regression analysis showed that both motor deficits and cranial nerve involvement are significant predictors of lower Karnofsky scores at admission. The coefficient for motor deficits was -10.24 ($p = 0.001$), and for cranial nerve involvement, it was -12.34 ($p = 0.001$), suggesting that the presence of these clinical factors leads to significant decreases in Karnofsky scores.

7.3.6 Comparison between Imaging Diagnosis and Histopathological Diagnosis

The Chi-square test of independence between the variables "Imaging Diagnosis" and "Histopathological Diagnosis" did not find a significant association between the two categories, indicating that imaging techniques alone cannot reliably predict the histopathological characteristics of gliomas.

7.4 Discussions

The results indicate that total surgical resection significantly improves functional outcomes, while stereotactic biopsy is associated with less favorable results. Motor deficits and cranial nerve involvement are significant determinants of reduced functional status at admission. The lack of a significant correlation between imaging and histopathological diagnoses underscores the need for a multimodal evaluation for accurate diagnosis.

7.5 Conclusions

This study highlights the significant impact of surgical and diagnostic strategies on the functional outcomes of patients with gliomas. Total surgical resection significantly improves functional status at discharge, while less invasive procedures are associated with less favorable outcomes. The study emphasizes the importance of a personalized approach based on the individual characteristics of the patient and tumor biology, supported by a multidisciplinary team. These findings provide essential guidance for neurosurgeons and oncologists in decision-making regarding the extent of resection and improving patient outcomes.

2.8 Conclusions and Personal Contributions

This research was conducted to explore critical aspects of the diagnosis and management of gliomas, with the aim of optimizing therapeutic strategies and improving clinical outcomes. The study focused on three main areas: (1) the effectiveness of surgical interventions based on glioma subtypes and molecular markers, (2) the impact of glioma-associated epilepsy on treatment and prognosis, and (3) the role of the T2-FLAIR mismatch radiogenomic marker in the classification and management of low-grade gliomas.

2.8.1 Conclusions

The study achieved its proposed objectives, contributing to a deeper understanding of how the clinical and molecular characteristics of gliomas influence therapeutic decisions and long-term outcomes.

Achievement of Scientific Research Objectives:

The comparative analysis of surgical interventions revealed significant differences among glioma subtypes, demonstrating that IDH mutations and 1p/19q codeletion influence treatment response. Patients with IDH-mutant astrocytomas and IDH-mutant oligodendrogliomas with 1p/19q codeletion showed longer survival and better functional outcomes than those with IDH-wildtype glioblastoma. The study confirmed the importance of a personalized approach based on the molecular characteristics of the tumor. For glioma-associated epilepsy, it was demonstrated that optimal management, including careful selection of medications and appropriate surgical planning, improves patient quality of life and survival. The clinical utility of the T2-FLAIR mismatch radiogenomic marker was also validated as an important tool for identifying IDH-mutant astrocytomas, improving tumor classification accuracy and guiding therapeutic decisions.

Technical-Economic Advantages and Disadvantages:

The research highlighted the advantages of a personalized approach based on the molecular and radiogenomic characteristics of tumors, such as better-tailored treatment planning, reduced complications, and improved patient prognosis. Disadvantages include the increased costs associated with advanced imaging and molecular testing technologies, the need for well-coordinated multidisciplinary teams, and limited access to resources in certain regions.

Unresolved Issues:

The study identified the need for clearer standardization of guidelines for the management of glioma-associated epilepsy and further validation of radiogenomic markers, such as the T2-FLAIR mismatch sign, in multicenter clinical trials. Additionally, a more detailed exploration of the interaction between different molecular markers and other clinical characteristics, such as response to adjuvant therapies, is needed.

Future Research Directions:

Further research is recommended to expand the use of radiogenomic and molecular markers in clinical practice through large-scale prospective clinical studies, the exploration of new therapeutic targets, and the development of more effective management protocols for glioma-associated epilepsy.

2.8.2 Personal Contributions

The personal contributions of this research are significant and are reflected in various parts of the thesis.

In evaluating the role of the T2-FLAIR mismatch marker (Chapter 5, Paragraph 4), I demonstrated the value of this radiogenomic marker as a diagnostic and prognostic tool for IDH-mutant astrocytomas, proposing its inclusion in standard clinical protocols.

In analyzing the impact of epilepsy on the treatment and prognosis of glioma patients (Chapter 6, Paragraph 2), I assessed the prevalence and types of epileptic seizures, emphasizing the importance of rigorous epilepsy management to improve patient quality of life.

My contributions to the personalization of treatment based on the molecular profile of the tumor (Chapter 4, Paragraph 3) showed that a personalized approach, grounded in the molecular characteristics of the tumor, can significantly improve treatment outcomes and reduce complications.

Regarding the integration of new imaging techniques and molecular markers into clinical practice (Chapter 5, Paragraph 6), I proposed incorporating radiogenomic and molecular markers into diagnostic and treatment guidelines, providing evidence for their clinical benefits.

Finally, in developing a methodological framework for future studies (Chapter 7, Paragraph 1), I proposed a framework for future research, based on the results of this study, to explore the use of radiogenomic and molecular markers and personalized therapeutic approaches in glioma management.

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