

GLIOBLASTOMA: IMPACT OF MOLECULAR GENETIC DIAGNOSTICS AFTER SURGICAL TREATMENT ON SURVIVAL PROGNOSIS.

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ABSTRACT

This study aimed to evaluate the impact of molecular genetic markers on overall survival (OS) and progression-free survival (PFS) in patients with glioblastoma following surgical treatment. A retrospective-prospective study included 220 patients who underwent surgery between January 2022 and May 2026. Molecular genetic analysis assessed IDH1/IDH2 mutations, MGMT promoter methylation, TERT promoter mutations, and EGFR amplification. Survival outcomes were evaluated using the Kaplan–Meier method, log-rank test, and multivariable Cox regression analysis. The results demonstrated that MGMT promoter methylation and IDH mutations were associated with longer OS and PFS. Patients with methylated MGMT and IDH-mutant tumors showed more favorable survival outcomes. Conversely, TERT promoter mutations and EGFR amplification were associated with shorter survival. Younger age and gross total tumor resection were also identified as favorable prognostic factors. These findings highlight the importance of integrating molecular genetic diagnostics with clinical and surgical data to improve prognostic assessment, personalize treatment strategies, and optimize postoperative management in patients with glioblastoma.

Keywords: glioblastoma, molecular genetic diagnostics, MGMT, IDH1/IDH2, TERT, EGFR, overall survival, progression-free survival, surgical treatment, prognostic factors.

INTRODUCTION

Glioblastoma (WHO Grade 4) is the most common and most aggressive primary tumor of the central nervous system in adults. Despite major advances in modern neurosurgery, radiotherapy, and chemotherapy, the prognosis remains unfavorable, and median overall survival rarely exceeds 15–20 months. Numerous studies have shown that the extent of tumor resection is one of the most important prognostic factors in glioblastoma. A greater extent of resection is associated with improved overall and progression-free survival. Accordingly, modern intraoperative navigation technologies are being actively introduced into neuro-oncological practice, including fluorescence-guided surgery using 5-aminolevulinic acid (5-

ALA), intraoperative magnetic resonance imaging, neurophysiological monitoring, and mapping of functionally eloquent brain areas. The use of these technologies makes it possible to significantly increase the radicality of surgery and achieve the maximum safe tumor resection. However, even after complete removal of the contrast-enhancing portion of the tumor, most patients develop disease recurrence, indicating the high biological aggressiveness of glioblastoma and infiltrative growth of tumor cells beyond the visible lesion boundaries. In recent years, it has become evident that survival outcomes are determined not only by the extent of surgery but also by the molecular genetic characteristics of the tumor. The introduction of the World Health Organization molecular classification (WHO, 2021) has substantially changed approaches to the diagnosis and prognostication of glioblastoma. Molecular markers such as IDH1/IDH2 mutations, MGMT promoter methylation, TERT promoter mutations, EGFR amplification, and other genetic alterations that directly affect tumor sensitivity to treatment and patient survival have acquired particular importance. The modern concept of personalized neuro-oncology requires the integration of clinical, neuroimaging, morphological, and molecular genetic data to determine prognosis and select the optimal treatment strategy. Therefore, studying the impact of the molecular genetic characteristics of glioblastoma on surgical treatment outcomes is of considerable scientific and practical interest.

The aim of this study was to evaluate the impact of molecular genetic markers of glioblastoma on overall and progression-free survival in 220 patients who underwent surgical treatment between 2022 and 2026.

MATERIAL AND METHODS OF RESEARCH

Study Design and Patient Selection Criteria

A retrospective-prospective study of treatment outcomes was conducted in 220 patients with morphologically verified glioblastoma treated in the neurosurgical department from January 2022 to May 2026.

The inclusion criteria were:

- age over 18 years;
- newly diagnosed glioblastoma;
- availability of preoperative contrast-enhanced magnetic resonance imaging of the brain;
- performance of surgical intervention;
- availability of molecular genetic examination results of tumor tissue;
- possibility of assessing long-term treatment outcomes.

The exclusion criteria were:

- absence of morphological verification of the diagnosis;
- incomplete clinical or molecular genetic data;
- absence of follow-up data.

Surgical Treatment

All patients underwent surgery aimed at achieving maximum safe tumor resection. The extent of resection was determined on the basis of postoperative contrast-enhanced magnetic resonance imaging performed within the first 72 hours after surgery.

Depending on the extent of tumor removal, patients were divided into the following groups:

- gross total resection (more than 95% of tumor volume);
- subtotal resection (80–95%);
- partial resection (less than 80%);
- stereotactic biopsy.

For tumors located in functionally eloquent brain regions, surgery was performed using neuronavigation and intraoperative neurophysiological monitoring.

Molecular Genetic Examination

After surgical treatment, all patients underwent histopathological and molecular genetic examination of the surgical specimen.

The following molecular genetic markers were assessed:

- IDH1/IDH2 mutations;
- MGMT promoter methylation;
- TERT promoter mutations;
- EGFR amplification;
- other molecular alterations according to the WHO 2021 classification (when data were available).

The obtained results were used to stratify patients into prognostic groups and to assess the impact of the tumor molecular profile on survival outcomes.

Survival Assessment

Overall survival (OS) was defined as the period from the initial surgical intervention to the patient's death or the date of last follow-up.

Progression-free survival (PFS) was defined as the period from the date of surgery to the first radiologically confirmed disease progression.

Follow-up MRI examinations were performed 3 months after surgery and subsequently every 3–6 months in accordance with clinical recommendations.

Disease progression was assessed according to the RANO (Response Assessment in Neuro-Oncology) criteria.

Statistical Analysis

Statistical analysis was performed using Statistics software (IBM Corp., USA). Overall and progression-free survival were estimated using the Kaplan–Meier method. Survival curves were compared using the log-rank test. Multivariable Cox regression analysis was used to identify independent prognostic factors. Differences were considered statistically significant at $p < 0.05$.

Ethical Considerations

The study was conducted in accordance with the principles of the Declaration of Helsinki and was approved by the local institutional ethics committee. All patient data were de-identified before analysis.

Study Results

The study included 220 patients with newly diagnosed glioblastoma who underwent surgery between 2022 and 2026. Of these, 138 (62.7%) were men and 82 (37.3%) were women. The mean patient age was 42.0 ± 11.6 years.

After surgical treatment, all patients underwent morphological and molecular genetic examination of tumor tissue. The analysis included determination of IDH1/IDH2 status, MGMT promoter methylation, TERT promoter mutations, and EGFR amplification.

Table 1. General characteristics of the patients

Parameter	Value
Total number of patients	220
Men	138 (62,7%)

Women	82 (37,3%)
Mean age	42.0 ± 11.6 years
Gross total resection	148 (67,3%)
Subtotal resection	54 (24,5%)
Partial resection	18 (8,2%)

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Total number of patients	220
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Table 2. Distribution of molecular genetic markers

Marker	Number of patients	%
MGMT methylated	108	49,1
MGMT unmethylated	112	50,9
IDH-mutant type	32	14,5
IDH-wildtype	188	85,5
TERT mutation	146	66,4
TERT without mutation	74	33,6
EGFR amplification	98	44,5
EGFR without amplification	122	55,5

Analysis of the molecular genetic profile showed that TERT promoter mutations (66.4%) and IDH-wildtype status (85.5%) were the most common findings. MGMT promoter methylation was detected in 49.1% of patients.

Table 3. Overall survival according to molecular genetic profile

Parameter	Median OS (months)	p
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MGMT methylated	24	<0,001
MGMT unmethylated	14	
IDH-mutant type	31	0,002
IDH-wildtype	16	
TERT without mutation	23	0,018
TERT mutation	15	
EGFR without amplification	20	0,041
EGFR amplification	15	

Analysis of overall survival showed the most favorable outcomes in patients with a methylated MGMT promoter and an IDH mutation. Median overall survival in these groups was 24 and 31 months, respectively.

Table 4. Progression-free survival according to molecular genetic profile

Parameter	Median PFS (months)	p
MGMT methylated	13	<0,001
MGMT unmethylated	7	
IDH-mutant type	17	0,004
IDH-wildtype	8	
TERT without mutation	12	0,026
TERT mutation	7	
EGFR without amplification	11	0,049
EGFR amplification	8	

Analysis of progression-free survival demonstrated similar patterns. The longest period without evidence of progression was observed in patients with an IDH mutation and a methylated MGMT promoter.

Multivariable Cox regression analysis showed that MGMT promoter methylation, IDH mutation, younger patient age, and gross total tumor resection were independent factors associated with a favorable prognosis.

Thus, the molecular genetic characteristics of glioblastoma have a substantial impact on overall and progression-free survival after surgical treatment and should be considered when predicting disease course and selecting subsequent treatment strategy.

RESULTS AND DISCUSSION

Despite major advances in modern neuro-oncology, glioblastoma remains one of the most aggressive tumors of the central nervous system and is characterized by an extremely unfavorable prognosis. The primary goal of surgical treatment is maximum safe tumor resection while preserving the patient's neurological functions. Numerous studies have shown that a greater extent of resection improves overall and progression-free survival. However, even after complete removal of the contrast-enhancing portion of the tumor, recurrence develops in virtually all patients, indicating the presence of additional factors that determine the biological behavior of glioblastoma. In recent years, particular attention has been paid to the molecular genetic characteristics of the tumor, which have substantially changed approaches to diagnosis, prognostication, and treatment. According to the WHO 2021 classification, the molecular profile is an integral component of glioblastoma diagnosis and enables more accurate assessment of disease prognosis.

The results of our study confirm the important role of molecular genetic markers in determining treatment outcomes in patients with glioblastoma. The most favorable overall and progression-free survival outcomes were observed in patients with a methylated MGMT promoter and an IDH mutation. These findings are consistent with major international studies in which these molecular alterations are considered independent favorable prognostic factors.

MGMT promoter methylation reduces the activity of the DNA repair enzyme and increases the sensitivity of tumor cells to alkylating agents, particularly temozolomide. Consequently, patients with methylated MGMT demonstrate greater efficacy of adjuvant chemoradiotherapy and longer survival than patients without methylation of this gene. The IDH1/IDH2 mutation status is of particular interest. In our study, patients with IDH-mutant tumors had the most favorable prognosis, which is consistent with the international literature. The presence of an IDH mutation is associated with a less aggressive disease course, slower tumor growth, and a better response to multimodal treatment.

In contrast, the presence of a TERT promoter mutation and EGFR amplification was associated with a more aggressive disease course and reduced overall survival. These molecular alterations contribute to increased proliferative activity of tumor cells, enhanced invasive growth, and the development of resistance to treatment.

An important finding of the present study is confirmation that the extent of surgery is not the only prognostic factor. Even among patients who underwent gross total tumor resection, substantial differences in survival were observed depending on the molecular genetic profile of the neoplasm. This indicates that prognosis is determined not only by the degree of surgical cytoreduction but also by the biological characteristics of the tumor.

The obtained results emphasize the need for mandatory molecular genetic testing in all patients with newly diagnosed glioblastoma. Integration of clinical, morphological, and molecular data allows more accurate prediction of disease course, assessment of the expected efficacy of adjuvant therapy, and development of an individualized treatment strategy.

CONCLUSION

Thus, the results of this study confirm that the molecular genetic markers MGMT, IDH, TERT, and EGFR are important independent prognostic factors in patients with glioblastoma after surgical treatment. Their use in routine clinical practice improves prognostic accuracy and supports the development of a personalized approach in modern neuro-oncology.

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