Turk Neurosurg, 2022

Original Investigation

DOI: 10.5137/1019-5149.JTN.40005-22.2

Received: 11.03.2022
Accepted: 12.04.2022

Published Online: 20.04.2022

Analysis of the Prognosis of High-Grade gliomas in the View of New Immunohistochemistry Markers and 2016 WHO Classification

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ABSTRACT

AIM: To evaluate isocitrate dehydrogenase (IDH) mutation status and Ki67 percentages of tumors that were treated in our institution to determine whether these markers affected the initial diagnosis and survival rates.

MATERIAL and METHODS: High-grade glioma patients, who were operated in our department between 2013 and 2018, were enrolled in the study and retrospectively reviewed. New immunohistochemistry staining studies were conducted and survival analyses were performed.

RESULTS: Of 135 patients and 136 tumors, 117 were glioblastoma multiforme (GBM), 8 were grade III-IV glioma, 4 were anaplastic astrocytoma and 7 were anaplastic oligodendroglioma. One patient had two different lesions, which were GBM and anaplastic astrocytoma respectively. Mean age was 55 (7-85) years, and 88 (65%) were male and 47 (35%) were female. The most common complaint was motor deficit (56%). Fourteen patients underwent reoperation due to recurrent disease. Tumors were most commonly found in the frontal lobe (53, 39%). Magnetic resonance imaging (MRI) features showed that existence of necrosis is strongly related to GBM ($p<0.01$). Approximately 126 patients were found to be IDH-wildtype, which changed 6 patients' diagnosis to GBM, IDH wildtype from grade III-IV glioma. Five patients, who were diagnosed with anaplastic astrocytoma and anaplastic oligodendroglioma initially were found to be IDH wildtype. IDH mutation status, extend of resection, and age were found to affect survival.

CONCLUSION: IDH mutation status is important in classifying high-grade gliomas, as well as its effects on prognosis. This mutation is related to several radiological features of tumors. Extent of resection and patient age are also profoundly affect survival. Detailing the diagnosis with molecular features will help physicians to shape targeted adjuvant therapies, which would better outcomes.

KEYWORDS: High-grade gliomas, Neuropathology, WHO Classification, Integrated diagnoses, Neurooncology

ABBREVIATIONS: CNS: Central nervous system, **GBM:** Glioblastoma multiforme, **WHO:** World Health Organization, **GTR:** Gross total resection, **MRI:** Magnetic resonance imaging, **IDH:** Isocitrate dehydrogenase, **OS:** Overall survival, **PFS:** Progression free survival, **STR:** Subtotal resection

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INTRODUCTION

Gliomas are the most common primary neuroepithelial tumors of the central nervous system (CNS). Among them, glioblastoma multiforme (GBM) is the most common subtype of gliomas as well as the most common primary malignant tumor (23).

Gliomas consist of four grades according to the World Health Organization (WHO) guidelines: grade I and II are regarded as low-grade gliomas whereas grade III and IV are accepted as high-grade gliomas. High-grade gliomas involve anaplastic astrocytoma, anaplastic oligodendroglioma, and GBM (24). Recent studies on the pathophysiology of gliomas reported that there are several pathways of gliomagenesis, which cause tumors that evolve from the same path to act similarly. Thus in 2016, a revised classification system included molecular markers as the diagnostic criteria and proposed integrated and layered diagnoses (15). The recently published fifth edition of the WHO Classification of CNS Tumors comprises more molecular features of gliomas as diagnostic tools than in the 2016 edition (16). Further evaluation of molecular aspects of gliomagenesis would lead us not only to understand the pathophysiology better, but also to plan case-specific treatments.

In the present study, we present a series of 135 patients with 136 high grade gliomas, including their demographic characteristics, pathological and radiological features, and outcomes. We aimed to correlate integrated diagnoses based on 2016 WHO Classification and prognosis.

MATERIAL and METHODS

A retrospective chart analysis of patients with high-grade gliomas treated in the Department of Neurosurgery between 2013 and 2018 was performed. The patient's clinical features, radiological imaging studies, and postoperative medical treatments were evaluated. Follow-up data were collected from inpatient and outpatient clinic files, and the patients and their relatives were contacted if available. All the patients were indicated to undergo gross total resection (GTR) of the tumor, which is defined as no residual tumor on postoperative images. All patients were screened with magnetic resonance imaging (MRI) with contrast within 24 hours of surgery if not contraindicated. All patients were scheduled to receive postoperative radiotherapy and chemotherapy.

All radiological features of tumors (localization of the tumor, corpus callosum invasion, dural invasion, intratumoral hemorrhage, invasion of adjacent gyri, existence of necrosis, gliomatosis, cyst and multifocal disease) were evaluated by a senior neuroradiologist.

All specimens were reviewed and reclassified according to algorithms of the 2016 WHO Classification account to form integrated diagnoses. Light microscopy was used to evaluate the histomorphology of the tumors and immunostaining patterns of the sections.

Paraffin-embedded tissue blocks were sectioned at 5-µm thickness on a microtome and floated in distilled water. The paraffin-embedded tissues were then deparaffinized and rehydrated using xylene. Tissue sections were incubated with primary antibody solutions by following the manufacturer-recommended steps for each stain. Light microscopy was used to evaluate the staining patterns of the sections. Isocitrate dehydrogenase (IDH) mutation status was reported as positive or negative. The Ki67 index was estimated by counting the number of immunoreactive cells and then grouped according to the percentage of staining (<5%, 5-15% and >15%).

The survival analyses were performed by the Statistical Package for Social Sciences (SPSS) version 13.0. The Kaplan-Meier analysis was used for evaluation of survival rates, and the log-rank test was used for comparing survival among the groups. Overall survival (OS) was estimated as the time interval from the date of diagnosis to the date of death from any cause or time of latest follow-up. Progression-free survival (PFS) was defined as the relapsed time between the date of diagnosis and the date of first relapse, progression or death from any cause.

The institutional ethics committee approved this study (file No. 2019/173). Informed consent was signed by patients' relatives before surgery.

RESULTS

Of the 135 patients, 88 (65%) were male and 47 (35%) were female. The mean age was 55 years (range, 7-85 years). The most common symptom during admission was motor deficit (76/135, 56%). The patients' characteristics are summarized in Table I.

The neurological examination results of 40 (30%) patients were normal at the first admission. The examination results of 32 (24%) patients improved postoperatively (23 motor

Table I: Patient Characteristics

Characteristics	Property	n	%
Sex	Male	88	65
	Female	47	35
Symptoms	Motor deficit	35	60
	Sensory deficit	25	43
	Seizures	22	40
	Speech difficulty	14	24
	Headache	8	13.7
	Cognitive decline	5	8.6
Location	Frontal	52	38.2
	Temporal	41	30
	Parietal	16	11.7
	Occipital	4	3
	Insula	5	4
	Others	18	13.2

deficits, one sensory deficit, two speech disorder, six cognitive impairment). However, the results were worse after surgery in 12 patients, which slightly improved in out-patient visits. Out of these patients, five had new developing motor deficit while four patients' existing deficits worsened. Three patients had cognitive decline while one patient developed dysphasia following surgery. Three patients died shortly after surgery: two of them had intracerebellar hemorrhages and could not be saved despite surgical evacuation of the hematoma, and one patient, whose Karnofsky score was low preoperatively with multiple comorbidities, developed an abscess in the resection site and in spite of adequate antibiotic therapy and surgical intervention, the patient died.

All radiological features of the patients were evaluated by a senior neuroradiologist. Localization of the tumor, corpus callosum invasion, dural invasion, intratumoral hemorrhage, adjacent gyri invasion, existence of necrosis, gliomatosis, cyst, and multifocal disease were assessed. Approximately 52 (38.2%) patients had frontal, 41 (30%) had temporal, 16 (11.7%) had parietal, 4 (3%) had occipital, and 5 (4%) had insular tumors. Furthermore, there were eight (6%) corpus callosum, six (4%) thalamic, one (0.5%) cerebellar, two (1%) intraventricular, and one (0.5%) septum pellucidum tumors. Tumor localizations according to histopathological diagnosis were also assessed. The most common localization of all distinct types of lesions was found to be frontal lobe (GBM 43%; grade III-IV gliomas 37.5%; anaplastic astrocytoma 50%; anaplastic oligodendroglioma 57%).

Contrast enhancement patterns among tumors were assessed and defined as ring, patchy and diffuse. GBMs mostly showed ring contrast enhancement (83%), while the most common pattern among anaplastic astrocytomas was patchy (37.5%) and among anaplastic oligodendrogliomas was diffuse (57%).

Evaluation of existence of necrosis among distinct tumor types showed a statistically significant correlation between necrosis and GBMs (GBM 85%; grade III-IV gliomas 25%; anaplastic oligodendroglioma 57%, $p<0.01$). In addition, frontal and temporal lobe tumors were found to be more necrotic than others ($p=0.044$). Furthermore, ring enhancement and necrosis were found to be related to each other significantly ($p<0.01$).

The correlation between radiological features and IDH mutation status correlation showed no statistical significance. However, dural invasion and necrosis were found to be more frequent in IDH-*wildtype* tumors. Detailed radiological features of the tumors according to their localization are summarized in Table II.

Table II: Radiological Features Among Tumors

		Histopathologic diagnosis							
		GBM		Grade III-IV gliomas		Anaplastic astrocytoma		Anaplastic oligodendroglioma	
Radiologic features		**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Localization	Frontal	43	37	3	37.5	2	50	4	57
	Temporal	39	33	1	12.5	1	25	-	-
	Parietal	16	14	-	-	-	-	-	-
	Occipital	3	2.5	-	-	-	-	1	14
	Insula	2	2	2	25	1	25	-	-
	Others	14	11.5	2	25	-	-	2	28.5
Necrosis		100	85	2	25	-	-	4	57
Corpus callosum invasion		40	34	4	50	1	25	4	57
Dural invasion		36	31	5	62.5	-	-	3	43
Gliomatosis		16	13.5	-	-	-	-	1	14
Intratumoral hemorrhage		17	14.5	-	-	-	-	1	14
Cyst		14	12	-	-	-	-	-	-
Gyral invasion		18	15	1	12.5	-	-	-	-
Multifocal disease		49	42	1	12.5	-	-	4	57
Contrast pattern	Ring	97	83	3	37.5	-	-	1	14
	Patchy	6	5	3	37.5	1	25	2	28.5
	Diffuse	11	9	1	12.5	1	25	4	57
	Mix	1	0.8	1	12.5	1	25	-	-
	None	2	1.7	-	-	-	-	-	-

Table III: Patient Characteristics Among Previous Diagnosis * Since one Patient Had Two Distinct Tumors Which were Assessed Separately There are Totally 136 Tumors in 135 Patients

		GBM	Grade III-IV glioma	Anaplastic astrocytoma	Anaplastic oligodendroglioma
Mean age		57 (7-85)	44 (12-65)	40 (19-64)	46 (22-68)
Sex	Male	78 (68%)	3 (37.5%)	2 (50%)	4 (57%)
	Female	37 (32%)	6 (62.5%)	2 (50%)	3 (43%)
Extend of resection	GTR	89*	5	4	5
	STR	18	-	-	2
	Biopsy	10	2	1*	-

Table IV: Mean Ki67 Indexes among Integrated Diagnosis

IDH status	Diagnosis	Mean Ki67 percentage
IDH-wildtype	GBM	21
	Grade III-IV glioma	19.5
	Anaplastic astrocytoma	10
	Anaplastic oligodendroglioma	17.5
IDH-mutated	GBM	37.5
	Grade III-IV glioma	9.5
	Anaplastic astrocytoma	10
	Anaplastic oligodendroglioma	7.5

In total, 102 (75.5 %) patients underwent GTR, while 20 (15%) underwent subtotal resection (STR). Thirteen (10%) patients only received biopsy for histopathological confirmation. Fourteen (12.74%) patients, all of whom had GTR previously, underwent reoperation due to recurrence in our study period. Eleven patients' pathological diagnosis did not change in the second operation (nine GBMs, one grade III-IV glioma, one anaplastic oligodendroglioma). However, three patients' diagnosis upgraded (one from grade III astrocytoma to GBM, one from grade 2 oligodendroglioma to grade 3 oligodendroglioma, and one from necrosis to gliosis). None of the patients who underwent STR or tissue sampling as the first operation were reoperated on.

Pathology reports found that 117 (86%) patients had GBM, 4 (3%) had grade 3 astrocytoma, 7 (5%) had grade 3 oligodendroglioma, and 8 (6%) had grade III-IV glioma. One patient had two distinct tumors: grade 3 astrocytoma in right parietal lobe and GBM in right temporal lobe. These lesions were regarded as two different tumors, resulting in 136 tumors in 135 patients. Patient characteristics in the previous diagnosis are summarized in Table III.

Following immunostaining, 126 patients (93.3%) were found to have IDH-*wildtype* tumors. A vast majority of these tumors consisted of GBMs (115, 91% GBM; 6, 5% grade III-IV glioma; 3, 2% anaplastic astrocytoma; 3, 2% anaplastic oligodendroglioma): 82 (65%) were male and 44 (35%) were female, and the mean age was 56 (7-85) years. Of the IDH-*mutated* tumors, two (22%) were GBM, two (22%) were grade III-IV glioma, one (11%) was anaplastic astrocytoma, and four (44%) were anaplastic oligodendroglioma. There were six (67%) males and three (33%) were females, and the mean age was 44 (22-62) years.

IDH mutation status studies revealed that six patients who were previously reported as having grade III-IV gliomas actually had GBM. Furthermore, two patients' reports changed from GBM to GBM, *IDH-mutated* (previously named as secondary GBM). Out of the IDH-*wildtype* group two were anaplastic astrocytoma and three were anaplastic oligodendroglioma. Since a lack of IDH mutation in grade III tumors is a rare event, light microscopy studies were repeated. This repetition confirmed the diagnoses, leading us to change the diagnoses to anaplastic astrocytoma, *NOS* and anaplastic oligodendroglioma, *NOS.*

Statistical analyses showed that IDH mutation is more frequent in anaplastic oligodendrogliomas and both anaplastic astrocytomas and grade III-IV gliomas are more prone to have IDH mutation than GBMs ($p<0.01$). In addition, there was a statistically significant correlation between IDH mutation and insular and occipital lobe tumors ($p=0.008$).

Ki-67 staining results were not technically available for 30 patients; the mean percentage was found to be 20% in the remaining patients. The mean Ki-67 labeling index among tumors was 21.28% in GBMs, 17% in grade III-IV gliomas, 10% in anaplastic astrocytomas, and 11.78% in anaplastic oligodendrogliomas, without meaningful statistical significance between groups ($p=0.179$) (Table IV). In addition, no significance between tumor localization and Ki-67 indexes were found ($p>0.05$).

The correlation between IDH mutation and Ki-67 indexes was also evaluated. Due to an inadequate number of IDH-*mutated* tumors, data are presented as medians. Among IDH-*wild type* tumors, the median Ki67 index was 20% (2-60%) whereas among IDH-*mutated* tumors, the median Ki67 index was 10% (2-60%). A statistically significant correlation was found between a high proliferation index and more malignant tumors ($p=0.032$).

The mean follow-up period was 20 months (1-228 months). Survival analyses were performed to investigate distinct prognostic factors impacting on prognosis. The 1-,3- and 5-year OS of the patients was available for analyses. Due to the short follow-up period and unequal distribution of patients, PFS data was not suitable for statistical analyses. During the study period 108 patients died and 78 had recurrence.

The 1-year OS of GBMs was 51.3%, and 69 patients recurred at a mean time of 27 weeks. Statistics showed that GBMs had the shortest OS and PFS; furthermore, anaplastic astrocytomas and anaplastic oligodendrogliomas had better 1- year OS rates compared to grade III-IV gliomas (50%, 0% and 37.5% respectively, p=0.018).

IDH-*mutated* tumors were found to have a better OS rate compared to IDH-*wildtype* tumors (p=0.004). However, it was not possible to compare the PFS of both groups, since there were patients who died in the 1-year period without recurrence. Therefore, we only investigated the correlation of IDH mutation status to patients without recurrence in the 1-year period. Again, IDH-*mutated* patients had better prognosis (p=0.004).

Kaplan-Meier analyses showed that both the OS and PFS of IDH-*mutated* patients were better than those of IDH-*wild type* patients (OS: p=0.017, log-rank chi square:5.67; PFS: p=0.012, log-rank chi square:6.37). Similarly, 3-year and 5-year OS datas were also better in IDH-*mutated* patients (3-year OS p=0.005, log-rank chi square:7.862; 5-year OS p=0.004, log-rank chi square:8.173) (Figure 1).

We evaluated patient age as a prognostic factor on survival. Older patients had shorter OS and PFS compared to younger patients (p<0.01). The mean age of patients who died and survived in the 1-year period was designated according to the mean age of the subgroup. The mean age of the patients who survived was 50 years, whereas for the patients who died, it was 61 years; in other terms, older age was defined as older than 50 years for the surviving patients and vice versa.

The extent of resection was another prognostic factor that we assessed. Approximately 64 out of 102 patients who underwent GTR died, whereas 14 patients died in the STR group and 13 in the biopsy group. The 1-year-OS of patients who underwent GTR was 62.7%, for STR it was 30%, and for biopsy it was 15.4%. GTR was found to be a statistically significant factor affecting prognosis (p<0.01).

Tumor localization and radiological features were not found to have any effect on survival.

In the postoperative period, 84 (62.22%) patients received both radiotherapy and temozolomide, 32 (23.7%) patients received only radiotherapy, and 3 (2.22%) patients received only chemotherapy. Fifteen patients did not receive neither radiotherapy nor chemotherapy due to comorbidities.

DISCUSSION

Gliomas, the most common primary malignant tumors of the CNS, are classified not only according to their histopathological diagnosis but also to their molecular features. In the 2016 WHO classification, molecular features of CNS tumors were added into integrated diagnoses, since these properties are closely related to the natural course and prognosis of tumors (12,15). We aimed to review surgically treated high grade glioma cases in our institution, reevaluate them in order to form integrated diagnoses suggested by the WHO and investigate whether molecular features correlate with survival.

In total, 135 patients were enrolled in our study including 136 tumors to be investigated. Of these, 117 (86%) were GBM, 8 (6%) were grade III-IV glioma, 4 (3%) were anaplastic astrocytoma, and 7 (5%) were anaplastic oligodendroglioma. Rates of grade III tumors were similar to the literature however, our number of GBM patients was higher than previous studies (9,22). This inconsistency is explained by the fact that our series had only included high grade glioma patients.

The most common tumor localization was the frontal lobe for all four types of tumors in our series (GBM: 37%, grade III-IV glioma: 37.5%, anaplastic astrocytoma: 50%, anaplastic oligodendroglioma 57%). Our results are similar to those from previous studies, except in the case of anaplastic oligodendroglioma, which is reported to originate from the temporal lobe most frequently (7). Recent studies have shown that tumor localization has an impact on prognosis. Zhang

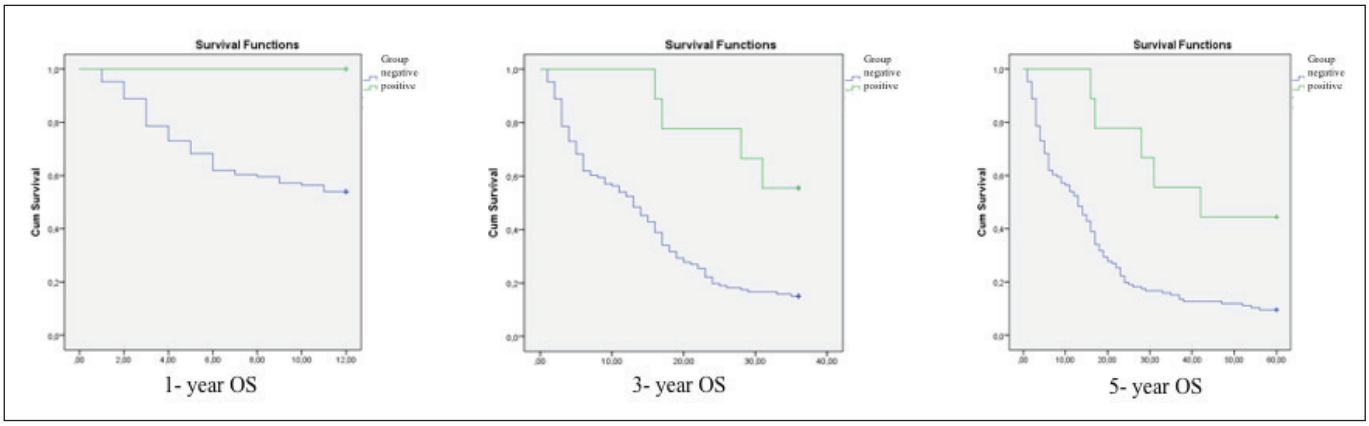

Figure 1: Kaplan Meier analyses of OS of patients according to their IDH mutation status.

et al reported that tumors located far from subventricular zone are related to a better prognosis (34). In contrary to the literature, there was no statistically significant association between tumor location and prognosis in our series (p=0.325).

An assessment of various radiological features showed that GBMs were more prone to have ring enhancement, which supports necrosis, as in our series (85%) (32). However, in our series, anaplastic oligodendroglioma patients also had high numbers of necrosis (57%), which is in contrast to the literature (3).

As it is crucial to detect IDH mutation status in glioma patients, recent radiogenomic studies have focused on determining the mutation status noninvasively prior to surgery. A novel diffusion MRI technique (diffusional variance decomposition-DIVIDE) is now being used to differentiate glioma grades and molecular features. Li et al. published statistically significant results on determining IDH mutation status using various parameters with the DIVIDE technique. They were also able to find a positive correlation between the Ki67 index and MRI features (13). Unfortunately, our study does not include advanced diffusion MRI evaluation of tumors due to technical deficiencies. Additionally, Zhang et al reported significant difference in enhancement patterns, cystic change, and intratumoral hemorrhage between various glioma subtypes (33). It is known that ring enhancement is a predictor of IDH-*wildtype* tumors. Similarly, in our series, 99 out of 126 IDH-wildtype tumors had ring enhancement (78.5%), while only 2 out of 9 IDH-*mutated* tumors had the same contrast enhancement pattern (22%). However, the remaining radiological features showed no significant association to IDH mutation status.

Similar to previous reports, the mean ages according to different tumors was 57 (7-85) years for GBMs, 44 (12-65) years for grade III-IV gliomas, 40 (19-64) years for anaplastic astrocytomas and 46 (22-68) years for anaplastic oligodendrogliomas. Patient age was found to be a positive prognostic factor for OS, which is consistent with the literature (21). Sex distribution among different tumors was also similar to the literature for GBM patients (male 68%; female 32%) (1). However, there was an equal sex distribution in anaplastic astrocytomas and slight male dominance in anaplastic oligodendrogliomas, which is in contrast to the fact that there is a reported profound male dominance in grade III gliomas (20,29). We explain this discordance by our inadequate sample size and that grade III gliomas are rare lesions. Furthermore, it is reported that male gender is related to a shorter OS and PFS; however, in our series there was no statistically significant difference between genders.

The extent of resection is a well-known prognostic factor for glioma survival (5,8,30). Recent studies have focused on achieving supratotal resection (including hyperintense areas around the tumor in FLAIR sequence), and it is reported that supratotal resection leads to longer OS and PFS (14). Pessina et al reported that with supratotal resection, the 2-year OS rates increased from 12% to 54% compared to STR (25). Various modalities are being introduced into routine surgery in order to accomplish safe maximal resection such as intraoperative imaging systems, intraoperative ultrasonography, and different augmented reality systems (17,31). Our results were similar to those of previous reports: the 1-year OS of patients who underwent GTR was found to be 62.7%. (1-year OS; STR: 30%; biopsy: 15.4%). Therefore, GTR was found to have statistically significant impact on survival (p<0.01).

GTR is also a positive prognostic factor for recurrent gliomas (4). Recently, Montemurro et al reported that the OS of the patients who underwent GTR initially and for the recurrence is significantly longer than the patients who underwent STR initially or for the reoperation (GTR+GTR: 42.6 months, GTR+STR: 19 months, STR+GTR: 17 months, p=0.0004) (18). Yet in our series, it was not possible to evaluate the impact of GTR in the second reoperation on survival, since all 14 patients who were reoperated for recurrent tumors underwent GTR.

IDH mutation is a positive prognostic factor for gliomas, since it is not found in primary de novo GBMs, which have a worse prognosis (10). In our series, 93% of the patients were IDH-wildtype whereas 7% were found to be IDH-mutated. The majority of IDH-wildtype tumors are GBMs (44%). The 1-year OS of IDH-wildtype tumors were found to be worse than IDH-mutated tumors, which is similar to that reported in the literature (p=0.004). Furthermore, Kaplan-Meier analyses showed statistically better survival of IDH-*mutated* patients in the 3- and 5-year follow-ups (p=0.005 and p=0.004 respectively) (10). IDH mutation status and PFS correlation could not be evaluated since there were patients who died in the 1-year period without recurrence.

The Ki67 labeling index, in contrast, reflects the proliferation rate of a tumor, thus its malignancy. It is shown to be related with malignant transformation and a shorter recurrence period (26). The WHO reports increasing Ki67 values correlated with the glioma grade (diffuse astrocytomas 4%; anaplastic astrocytomas 5-10%, GBM 15-20%) (15). In addition, there are reports that higher Ki67 labeling indexes are associated with higher grades of gliomas (19,27). However, since there is no precise algorithm for predicting glioma survival using the Ki67 value and overlapping results occur between grades, the Ki67 index is not routinely used for glioma grading (28). Recent studies have focused on the impact of the Ki67 labeling index on recurrent gliomas. Li et al reported that Ki67 expression (low, middle, high) along with the WHO grade are independent prognostic factors to predict PFS (11). No statistically significant difference could be found between the mean Ki67 values and different high-grade gliomas in our series (mean Ki67 indexes: 21.28% in GBMs, 17% in grade III-IV gliomas, 10% in anaplastic astrocytomas, 11.78% in anaplastic oligodendrogliomas, p>0.05). However, there was a significant difference between Ki67 values of IDH-wildtype, and IDH-mutant tumors. IDH-wildtype tumors had higher Ki67 values, significant owing to their more aggressive nature (p=0.032).

In the literature, it is reported that IDH-mutated tumors are more prone to be located in the frontal lobe (6,33). However, contrary to what is reported, IDH-mutated tumors were localized in occipital lobe and insula in our series. There are

a limited numbers of reports investigating the relationship between tumor localization and the Ki67 index in high-grade gliomas. Altieri et al reported that gliomas located in the frontal lobe are associated with lower Ki67 indexes (2). Nevertheless, we could not find any relationship between localization and the Ki67 index.

LIMITATIONS

This study has several limitations. It is a retrospective evaluation from a single center and the number of patients and follow-up period are limited. Furthermore, we could not include all molecular markers that were defined in the WHO classification in our study due to financial burdens.

CONCLUSION

Gliomas are the most common primary neuroepithelial tumors of the CNS. The most common subtype of gliomas is GBM, which is also the most common primary malignant tumor of the CNS. The 2016 WHO classification added molecular features of tumors as diagnostic criteria, along with the histomorphological properties, in order to form an integrated diagnosis. For gliomas, the most important molecular feature, according to integrated layered diagnosis, is IDH mutation status, which is not only useful for glioma classification but also to estimate the natural course of the disease and prognosis. This study reports the demographics, clinical characteristics and outcomes of high-grade glioma patients treated in a university hospital. We aimed to evaluate the impact of different prognostic factors as well as molecular features on survival. Further studies with larger groups, longer follow-up periods, and more molecular markers are needed to reveal the gliomas' exact pathophysiology, natural course, and prognosis, which would lead physicians to plan case-specific treatments to improve survival rates.

AUTHORSHIP CONTRIBUTION

Study conception and design: DD, AS

Data collection: DD, TA, MO

Analysis and interpretation of results: DD, ID, TCU

Draft manuscript preparation: DD, AA, PAS

Critical revision of the article: DD, BB, YA

Other (study supervision, fundings, materials, etc...): DD, AS

All authors (DD, TA, ID, TTCU, AA, MO, PAS, YA, MBB, AS) reviewed the results and approved the final version of the manuscript.

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