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Research Article

Prognostic Effect of Immunohistochemical Scoring on Survival in Glioblastoma

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Abstract

Objectives: We aimed to show whether the scoring system we developed using IDH, p53 and Ki-67 markers has a prognostic feature on survival in glioblastoma.

Methods: Retrospective screening was conducted on 109 patients who were followed up in our clinic. IHC scoring was performed from pathology reports.

Results: Fifty-five patients (50.5%) were IDH Wild, 44 (40.4%) of them were p53 mutant, and 51 (46.8%) of them were Ki-67 >30 status. Median PFS was 6.2 months (95% CI: 5.7-6.8 months), and median OS was 10.1 months (95% CI: 7.6-12.5 months). In multivariate analysis p53 status was independent prognostic factor for both PFS and OS [(HR: 2.03 (1.14-3.61), p=0.02) and (HR: 1.86 (1.03-3.36), p=0.04), respectively]. However, Ki-67 status was an independent prognostic factor for only OS [HR: 1.94 (1.02-3.69), p=0.04]. When the patients were examined by dividing them into four IHC score groups for the combined prognostic value of IDH, p53, and Ki-67 status; differences between group 0 and the others were statistically significant.

Conclusion: This study demonstrated that p53 and Ki-67 are useful, independent prognostic markers for GBM patients. Furthermore, the combined use of these three IHC markers is a statistically significant indicator for PFS and OS.

Keywords: Glioblastoma, immunohistochemical scoring, IDH, p53, Ki-67

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In adults, glioblastoma (GBM) is the most common primary malignant central nervous system (CNS) tumor. GBM accounts for 25% of all CNS tumors and 50-55% of all glial tumors.[1] Most patients are treated with a multidisciplinary approach that includes adjuvant radiotherapy and chemotherapy following resection of the tumor.[2] Unfortunately, even with maximal treatment, it has a high recurrence rate. The three and five year survival rates of patients diagnosed with GBM do not exceed 3-5% and 0.5%, respectively.[3]

The median overall survival of patients with GBM in population-based studies is approximately 10 to 12 months.[4] Therefore, many studies have been carried out to determine prognostic markers for patient selection for treatment and treatment response for such an aggressive disease. In two patient-based nomograms of the radiation oncology treatment group (RTOG) in 2010 and 2017, clinical parameters such as patient age, gender, performance score, and tumor resection width at the time of diagnosis are shown as prog-

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nostic. However, it does not sufficiently cover tumor-based prognostic markers.[5,6]

According to World Health Organization (WHO) 2016 classification, GBM is divided into two main groups as isocitrate dehydrogenase (IDH) wild and IDH-mutant.[7] The IDH-wild group accounts for 90% of all GBMs. They are patients over 55 years of age with de-novo primary GBM, and the prognosis is poor. On the other hand, the IDH-mutant group represents the 10% better prognosis group, mostly young and with a previous history of low-grade glioma.[8,9] MGMT is an enzyme involved in DNA repair, and its methylated state is an independent prognostic factor for both progression-free survival (PFS) and overall survival (OS), independent of other clinical parameters.[10] Therefore, it is mainly used to determine the treatment type of patients at the initial diagnosis stage.[6,11]

p53 and Ki-67 are immunohistochemical (IHC) parameters involved in the pathological evaluation of glial tumors. [6] p53 is a tumor suppressor gene and is essential in cell apoptosis. Although many studies show the effect of being mutant or wild on survival in glial tumors, it is controversial whether it is an independent risk factor.[6,12] Ki-67 is a nuclear antigen that shows cell proliferation. Its high level is one of the most critical parameters that show the proliferation rate of the tumor. In glial tumors, increased Ki-67 levels are associated with tumor grade and poor prognosis.[6,13] However, there is no research in the literature on the prognostic feature of the combined use of all these IDH, p53, and Ki-67 markers.

This study aims to show whether the scoring system we developed using these three IHC markers, which are routinely used to diagnose glial tumors, has a prognostic feature on survival in a highly aggressive tumor such as GBM.

Methods

Study Design and Data Characteristics

Our study is retrospective, descriptive and cross-sectional. 109 GBM patients who were followed up in the Department of Medical Oncology and Radiation Oncology of Trakya University Faculty of Medicine were included between January 2013 and December 2020. All patients were 18 years or older at the time of the first resection, surgically removed material was pathologically confirmed as primary GBM, pre-and postoperative cranial imaging was available, and the pathology reports had immunohistochemical parameters required for the study. In addition, all patients received postoperative adjuvant radiotherapy, and most of them received adjuvant temozolomide (TMZ).

Using patient's follow-up files and hospital automation system records; age at diagnosis, gender, Karnofsky performance status (KPS), surgical resection width, tumor localization, tumor size, IHC characteristics of the tumor, and TMZ use in adjuvant therapy were evaluated.

In the IHC evaluation of the resection materials of the patients; Those with IDH-1 staining were considered mutant, and those without IDH-1 staining were considered wild. To determine p53 status, positivity rates were determined in 200 counted cells. Materials that were 50% or more positive were considered mutant. Below 50% were considered wild. For the Ki-67 level, the rate of positive cells in 1000 cells counted under the microscope was accepted. "30", which is the median value and also the value determined by ROC analysis, was determined as the cut-off value.

IHC scoring was performed according to the status of these three markers obtained from pathology reports. The result of IHC, which may affect the prognosis positively, was accepted as "0", while the result that could affect the prognosis negatively was accepted as "1". IDH-wild, p53 mutant, and Ki-67 high results were evaluated as "1" points each. In this way, four groups were formed with the sum of the scores ranging from "zero" to “three.”

Treatment and Follow-Up Characteristics of the Patients

After surgical resection (gross total, subtotal or excisional biopsy), the patients were treated with 30 fractions, 2 Gy/day, five days a week, 5-6 weeks for a total of 60 Gy radiotherapy and concurrently TMZ 75 mg/m^2 for seven days continuously according to the standard Stupp protocol.[2] Subsequently, it was planned to continue adjuvant TMZ for at least six cycles, the first course of 150 mg/m^2 and the continuation of 200 mg/m^2.

Cranial magnetic resonance imaging (MR) taken before the surgical treatment and within two days at the latest postoperatively was performed every 6-8 weeks on average during the treatment process and when the patient had new symptoms. After the adjuvant treatment, imaging was continued every 12 weeks. Pseudo-progression and true progression distinctions were decided at the multidisciplinary tumor council.

Statistical Analysis

The patient's progression-free survival (PFS) and overall survival (OS) times were calculated based on the date of surgical resection, the dates of the last outpatient clinic control, the dates of death, and the dates of progression. Demographic data were evaluated with descriptive statistical methods, and differences between groups were evaluated with independent t-test and chi-square test. Survival times were calculated with the Kaplan-Meier test, and the

differences in survival between groups were compared with the Log-rank test. Cox regression analysis was used to assess whether parameters were independent prognostic factors (multivariate analyses). Data evaluations were performed using the Statistical Package for the Social Science (SPSS) version 23.0. A value of $p<0.05$ was considered statistically significant.

The study was approved by the Local Ethics Committee of Trakya University Faculty of Medicine (No: TUTF/BAEK 2021/107, Date: 27/04/2021) according to good clinical practice and applicable laws and declaration of Helsinki.

Results

Patient's Characteristics

The median age was 59 years (range 50-66 years). Sixty-five patients (59.6%) were male, and 72 (66.1%) of them had a Karnofsky performance score (KPS) ≥70. Of the 109 patients, 55 (50.5%), 30 (27.5%), and 24 (22%) were treated with gross total resection, subtotal resection, and excisions biopsy, respectively. The most common tumor location at presentation; 34 (31.2%) temporal, 29 (26.6%) parietal, and 25 (22.9%) frontal lobes, respectively. The median tumor size was 41.5 mm, and 75 (68.8%) of patients had ≥ 41.5 mm tumors. Fifty-five patients (50.5%) were IDH Wild, 44 (40.4%) of them were p53 mutant, and 51 (46.8%) of them were Ki-67 >30 status. Eighty-four patients (77.1%) were treated with CCRT followed by adjuvant TMZ, while the others were treated only with CCRT (Table 1).

The median follow-up time was 9.2 months (range 5.6-15.2 months). At the date of the last follow-up day, 100 (91.7%) patients had a recurrence, 76 (69.7%) patients had only the best supportive care, and 97 (89.0%) of them died (Table 1).

Comparison of Study Demographics According to IDH, P53 and Ki-67 Groups

IDH molecular subtype and p53 status were grouped according to being 'wild' or 'mutant.' According to ROC analyses done for finding Ki-67 cut-off values, 30 (area under the curve (AUC):0.317, p=0.001) was found statistically significant.

Two groups were created for each IHC parameter. There were no statistically significant differences between the two groups when comparing IDH wild and mutant patients according to their clinical and demographic features. However, for the p53 wild group, most of the patients were KPS ≥70, had single lobe tumors, and Ki-67 levels were low (p=0.02, <0.01, and 0.02, respectively). According to the Ki-67 levels, most patients had KPS≥70 performance status and wild type p53 in the Ki-67 low group (p=0.03. There were no differences between other parameters (Table 2).

Table 1. Clinicopathologic features of study population

Parameters	All patients (n=109)
Age, years, n(%)	
Median (IQR)	59 (50-66)
Gender, n(%)	
Female	44 (40.4)
Male	65 (59.6)
Karnofsky performance score, n(%)	
KPS ≥70	72 (66.1)
KPS <70	37 (33.9)
Extent of surgery, n(%)	
Gross total resection	55 (50.5)
Subtotal resection	30 (27.5)
Excisional biopsy	24 (22.0)
Tumor location, n(%)	
Frontal lobe	25 (22.9)
Temporal lobe	34 (31.2)
Parietal lobe	29 (26.6)
Occipital lobe	4 (3.7)
Multicenter tumors	17 (15.6)
Radiological tumor size, n(%)	
<41.5 mm	34 (31.2)
≥41.5 mm	75 (68.8)
IDH molecular subtype, n(%)	
Mutant	29 (26.6)
Wild	55 (50.5)
Missing	25 (22.9)
P53 mutation status, n(%)	
Wild	65 (59.6)
Mutant	44 (40.4)
Ki67 status, n(%)	
≤30	58 (53.2)
>30	51 (46.8)
Adjuvant Temozolomide, n(%)	
Yes	84 (77.1)
No	25 (22.9)
Recurrence status, n(%)	
No	9 (8.3)
Yes	100 (91.7)
Treatment after recurrence, n(%)	
Re-operation	10 (9.2)
Re-radiotherapy	6 (5.5)
Systemic chemotherapy	17 (15.6)
Best supportive care	76 (69.7)
Mortality status, n(%)	
Alive	12 (11.0)
Dead	97 (89.0)

Survival Analysis

Median PFS was 6.2 months (95% CI: 5.7-6.8 months), and median OS was 10.1 months (95% CI: 7.6-12.5 months).

According to the IDH mutation analysis, median PFS was 5.8

Table 2. Comparison of clinicopathologic presentation of study population according to IDH mutation, p53 and Ki67 subgroups

	IDH Wild (n=55)	IDH Mutant (n=29)	p	P53 Wild (n=65)	P53 Mutant (n=44)	p	Ki67 Low (≤30) (n=58)	Ki67 High (>30) (n=51)	p
Age, years, n (%)									
<59	22 (40.0)	11 (37.9)	0.99	34 (52.3)	18 (40.9)	0.33	29 (50.0)	23 (45.1)	0.70
≥59	33 (60.0)	18 (62.1)		31 (47.7)	26 (59.1)		29 (50.0)	28 (54.9)	
Gender, n (%)									
Female	22 (40.0)	10 (34.5)	0.65	31 (47.7)	13 (29.5)	0.07	24 (41.4)	20 (39.2)	0.85
Male	33 (60.0)	19 (65.5)		34 (52.3)	31 (70.5)		34 (58.6)	31 (60.8)	
Karnofsky PS, n (%)									
KPS <70	22 (40.0)	7 (24.1)	0.23	16 (24.6)	21 (47.7)	0.02	14 (24.1)	23 (45.1)	0.03
KPS ≥70	33 (60.0)	22 (75.9)		49 (75.4)	23 (52.3)		44 (75.9)	28 (54.9)	
Tumor location, n (%)									
Single lobe	43 (78.2)	28 (96.6)	0.03	60 (92.3)	32 (72.7)	<0.01	52 (89.7)	40 (78.4)	0.12
Multicenter tumors	12 (21.8)	1 (3.4)		5 (7.7)	12 (27.3)		6 (10.3)	11 (21.6)	
Tumor size, n (%)									
<41.5 mm	18 (32.7)	12 (41.4)	0.48	21 (32.3)	19 (29.5)	0.83	23 (39.7)	11 (21.6)	0.06
≥41.5 mm	37 (67.3)	17 (58.6)		44 (67.7)	31 (70.5)		35 (60.3)	40 (78.4)	
IDH status, n (%)									
Wild	-	-	-	27 (56.3)	28 (77.8)	0.06	30 (60.0)	25 (73.5)	0.25
Mutant				21 (43.8)	8 (22.2)		20 (40.0)	9 (26.5)	
P53 status, n (%)									
Wild	27 (49.1)	21 (72.4)	0.06	-	-	-	41 (70.7)	24 (47.1)	0.02
Mutant	28 (50.9)	8 (27.6)					17 (29.3)	27 (52.9)	
Ki67 status, n (%)									
≤30	30 (54.5)	20 (69.0)	0.25	41 (63.1)	17 (38.6)	0.02	-	-	-
>30	25 (45.5)	9 (31.0)		24 (36.9)	27 (61.4)				

months (95% CI: 3.2-8.3 months) in IDH wild group while it was 7.8 months (95% CI: 4.2-11.3 months) in the IDH mutant group (p<0.01) (Fig. 1). Median OS was 8.1 months (95% CI: 6.1-10.1 months) in IDH wild group while it was 14.1 months (95% CI: 8.2-20.0 months) in the IDH mutant group (p<0.01) (Fig. 2).

Of the p53 mutation analysis, median PFS was 8.3 months (95% CI: 6.5-10.2 months) in the p53 wild group while it was 4.5 months (95% CI: 3.3-5.6 months) in the p53 mutant group (p<0.01) (Figure 1). Median OS was 12.1 months (95% CI: 9.2-12.5 months) in the p53 wild group while it was 6.0 months (95% CI: 4.7-7.4 months) in the p53 mutant

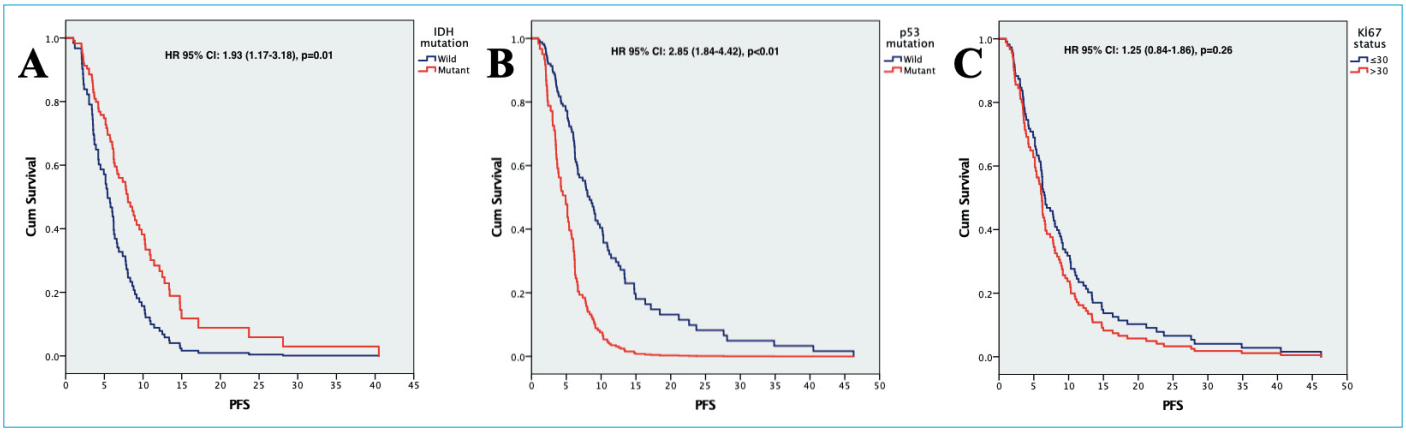

Figure 1. Kaplan-Meier survival analyses for progression-free survival **(a)** According to IDH mutation status **(b)** According to p53 mutation status **(c)** According to Ki-67 labeling index.

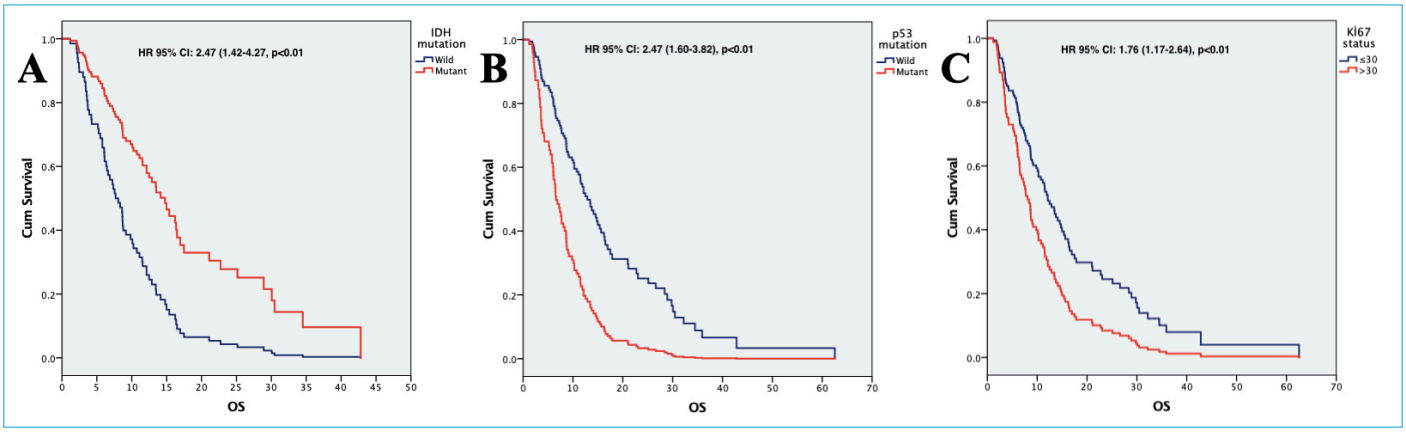

Figure 2. Kaplan-Meier survival analyses for overall survival **(a)** According to IDH mutation status **(b)** According to p53 mutation status (C) According to Ki-67 labeling index.

group (p<0.01) (Fig. 2).

According to the Ki-67 status, median PFS was 7.8 months (95% CI: 6.0-9.6 months) in 67 ≤30 group while it was 6.0 months (95% CI: 5.0-7.0 months) in p53 mutant group (p=0.26). (Figure 1). Median OS was 12.1 months (95% CI: 10.1-14.2 months) in Ki-67 ≤30 group while it was 7.3 months (95% CI: 5.1-9.6 months) in Ki-67 >30 group (p<0.01) (Fig. 2).

Univariate and Multivariate Analyses

In the univariate analysis of PFS, KPS, surgery type, tumor location, IDH mutational status, p53 status, treatment with adjuvant TMZ, and any recurrence treatment were associated with PFS. In the multivariate analyses, surgery type, tumor location, p53 status, treatment with adjuvant TMZ, and any recurrence treatment were statistically significant (Table 3).

In the univariate analysis of OS, KPS, surgery type, tumor location, tumor size, IDH mutational status, p53 status, Ki-67 level, treatment with adjuvant TMZ, recurrence treatment were both associated with survival. In addition, the multivariate analysis for OS, surgery type, p53 status, Ki-67 level, treatment with adjuvant TMZ, and any recurrence treatment was statistically significant (Table 3).

As seen in multivariate analysis p53 status was independent prognostic factor for both PFS and OS [(HR: 2.03 (1.14-3.61), p=0.02) and (HR: 1.86 (1.03-3.36), p=0.04), respectively]. However, Ki-67 status was an independent prognostic factor for only OS [HR: 1.94 (1.02-3.69), p=0.04] (Table 3).

Combined Prognostic Analysis of IHC Scoring System

The patients were examined by dividing them into four IHC score groups for the combined prognostic value of IDH, p53, and Ki-67 status. IDH-wild, p53 mutant, and Ki-67 high results were evaluated as "1" points each. In this way, four groups were formed with the sum of the scores ranging from "zero" to "three." When the univariate analysis was done to find the prognostic effect of groups according to select '0' point as an indicator, 1,2 and 3 points had hazard ratios for PFS and OS, as seen in Figure 3. Differences between group 0 and the others were statistically significant (p values were in Figure 3).

Discussion

To our knowledge, this study was the first to investigate the prognostic role of combined analysis IHC markers in GBM patients. One hundred and nine patients were examined in this study and it was found that the p53 mutant and Ki-67 high status in the study population were statistically significantly associated with poor prognosis. In addition to determining the statistical value of IHC parameters alone, our data also demonstrated an independent association of combined IHC scoring of these markers with survival.

On the contrary, being a rare disease, brain tumors are the leading cause of cancer death.[1] Previously, surgery was the only treatment for GBM. Then, radiotherapy and the addi-

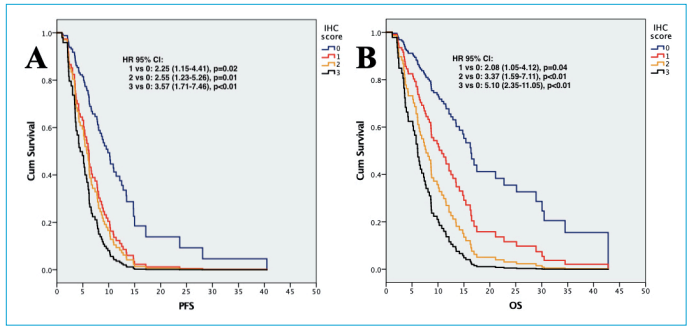

Figure 3. Kaplan-Meier curves between prognostic groups according to IHC scoring system. **(a)** For progression-free survival **(b)** For overall survival.

Table 3. Univariate and multivariate analysis of progression free survival and overall survival in study population.

	Progression free survival analyses				Overall survival analyses			
	Univariate analysis		Multivariate analysis		Univariate analysis		Multivariate analysis	
	HR (95% CI, Lower - Upper)	p	HR (95% CI, Lower - Upper)	p	HR (95% CI, Lower - Upper)	p	HR (95% CI, Lower - Upper)	p
Age, years,								
<59	Ref.	0.41			Ref.	0.22		
≥59	1.18 (0.79-1.76)				1.29 (0.86-1.93)			
Gender,								
Female	Ref.	0.54			Ref.	0.16		
Male	0.88 (0.59-1.32)				0.75 (0.50-1.12)			
Karnofsky PS,								
KPS ≥70	Ref.	<0.01	Ref.	0.80	Ref.	<0.01	Ref.	0.58
KPS <70	2.97 (1.94-4.55)		0.92 (0.50-1.71)		4.32 (2.79-6.69)		1.22 (0.61-2.44)	
Surgery,								
Gross total resection	Ref.	<0.01	Ref.	<0.01	Ref.	<0.01	Ref.	<0.01
Subtotal or biopsy	6.06 (3.62-10.16)		4.88 (2.33-10.22)		7.73 (4.61-12.98)		4.26 (2.01-9.0)	
Location,								
Single lobe	Ref.	<0.01	Ref.	0.02	Ref.	<0.01	Ref.	0.08
Multicenter tumors	4.34 (2.47-7.62)		2.37 (1.15-4.85)		7.05 (3.87-12.85)		2.02 (0.92-4.40)	
Tumor size,								
<41.5 mm	Ref.	0.06			Ref.	<0.01	Ref.	0.12
≥41.5 mm	1.54 (0.99-2.41)				2.43 (1.53-3.87)		1.73 (0.87-3.45)	
IDH status,								
Mutant	Ref.	0.01	Ref.	0.44	Ref.	<0.01	Ref.	0.08
Wild	1.93 (1.17-3.18)		1.27 (0.69-2.34)		2.47 (1.42-4.27)		1.57 (0.81-3.05)	
P53 status,								
Wild	Ref.	<0.01	Ref.	0.02	Ref.	<0.01	Ref.	0.04
Mutant	2.85 (1.84-4.42)		2.03 (1.14-3.61)		2.47 (1.60-3.82)		1.86 (1.03-3.36)	
Ki67 status,								
≤30	Ref.	0.26			Ref.	<0.01	Ref.	0.04
>30	1.25 (0.84-1.86)				1.76 (1.17-2.64)		1.94 (1.02-3.69)	
Adjuvant TMZ,								
Yes	Ref.	<0.01	Ref.	<0.01	Ref.	<0.01	Ref.	<0.01
No	16.16 (8.28-31.5)		6.77 (2.73-16.77)		18.64 (9.25-37.5)		5.11 (1.98-13.22)	
Recurrence tx,								
Any treatment	Ref.	0.03	Ref.	<0.01	Ref.	<0.01	Ref.	<0.01
BSC	1.62 (1.06-2.48)		3.14 (1.63-6.05)		3.66 (2.31-5.80)		3.22 (1.53-6.76)	

tion of TMZ as maintenance therapy improved survival.[2] And then, the MGMT status of the tumor was accepted as a vital factor in the efficacy of TMZ.[10] Furthermore, molecular biological procedures have opened the door to personalized medicine.[14] However, because it is a rare disease compared to other tumor types and newly developed diagnosis and treatment methods are not cost-effective and challenging to access, it seems that GBM treatment with traditional methods will continue for a while in the coming years. So, the older prognostic markers like IHC evolution are still crucial for GBM patients.

The presence of IDH mutation is one of the earliest validated prognostic indicators for GBM. IDH mutation confers a two- to threefold improvement in survival compared with IDH-wild type tumors.[7] A study by Sanson et al. included 400 gliomas that were 183 of them GBM, and the presence of IDH1 mutation were associated with significantly improved median survival 27 versus 14 months.[8] In another study, Hartmann et al., 300 GBM patients, IDH mutations were identified in 34 percent of patients surviving >36 months after diagnosis, compared with 4 percent of those IDH wild who survived <36 months.[9] Our study showed this advantage in the IDH mutant group also. Median OS was 14.1 versus 8.1 months in the IDH mutant group, which was statistically significant ($p<0.01$). However, IDH was not an independent prognostic marker in multivariate analysis (HR: 1.57 (0.81-3.05), $p=0.08$). We thought that there was missing data as 22.9% of patients, which might affect the statistical results.

The Ki-67 index determines the aggressive growth potential of any tumor in percent.[11] Whether Ki-67 is an independent prognostic factor for glioblastomas is conflicting based on the data in the literature. Studies correlating between the Ki-67 index and outcome in glioblastoma patients showed conflicting results.[13] Some studies demonstrated a positive correlation between the Ki-67 index and survival in GBM patients. In a study, with eligible 71 GBM patients, Ki-67> 22% group (n=36), 5-year survival was approximately 30% compared to 5% in those with Ki-67 ≤ 22% (n=35) ($p=0.04$). In this study, Wong et al. suggested that a high proliferation index may predict more responsiveness to chemo/radiotherapy.[15] However, some studies showed a negative predictive effect of Ki-67 on survival. In a study of Alimohammadi et al., 153 GBM patients, Ki-67<25 patients had 20.9 months OS versus 13.0 months OS in Ki-67>25 patients.[16] Other studies have found no association between the proliferation index and outcomes due to differences in mitotic activity between different tumor sites.[17] In a meta-analysis of 52 glioma studies, only ten studies consist of GBM patients and Ki-67 correlation. Ki-67 cut-off values differs from 1.5% to 35%. According to this analysis, seven studies demonstrated a statistically significant difference in PFS; none of them showed a difference in OS.[18] Our study showed that a high Ki-67 index (>30) correlated with a shorter OS but not PFS. All of these studies use median Ki-67 values as a cut-off. In our study, we used ROC curve analysis to show the predictive effect of Ki-67 on OS.

p53 is a tumor suppressor gene that plays an essential role in promoting tumor cell apoptosis.[12] In addition, it plays a role in protecting cells from DNA damage. p53 mutations can thus lead to tumor progression through genomic instability (19-21). There is a controversy in the correlation between p53 immunoreactivity and the survival outcome of GBM patients (P). In a recently published study, 153 patients with GBM, the presence of P53 mutation was associated with significantly decreased median survival 12.0 versus 21.1 months ($p<0.001$).[16] In our study, p53 mutation status was an independent prognostic factor for PFS and OS ($p=0.02$ and $p=0.04$, respectively). In addition, P53 mutation was correlated with a shorter PFS and OS.

Our hypothesis also evaluated the prognostic effect of the combined use of IHC parameters. There was no study about combination scoring and its prognostic effect on the survival of GBM patients in the literature. Our study demonstrated that the patients whose IHC scores' zero' point had prolonged PFS and OS than the other scoring groups. Significantly, the patients whose IHC scores' three' points progressed 3.57 times before and dead 5.10 times before the 'zero' point patients group ($p<0.01$ for both). This situation showed us that combined use of these three IHC markers was more critical than single only.

Our current study had some limitations. First, this was a retrospective study performed at a single oncology center. Thus, this may cause selection bias for the patient population. Second, we were unable to assess patients' MGMT status due to the largely incomplete data in the patient files. Therefore, more large-scale multicenter prospective studies are needed to confirm the prognostic impact of the use of these IHC parameters alone or in combination in GBM patients.

Conclusion

This study demonstrated that p53 and Ki-67 are useful, independent prognostic markers for GBM patients. Furthermore, the combined use of these three IHC markers is a statistically significant indicator for PFS and OS. Combined IHC scoring is cost-effective and easy to evaluate from pathology results routinely performed in these patients. The combined use of IHC parameters can guide clinicians in estimating survival and providing more individualized treatment approaches for GBM patients.

Disclosures

Ethics Committee Approval: The study was approved by the Local Ethics Committee of Trakya University Faculty of Medicine (No: TUTF/BAEK 2021/107, Date: 27/04/2021).

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