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Analysis of the Mortality Probability of Preoperative MRI Features in Malignant Astrocytomas

Malign Astrositomlardaki Preoperatif MRI Özelliklerinin Ölüm Olasılığı Analizi

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ABSTRACT

AIM: The aim of the present study is to analyze the effects of the MRI features on the recurrence time and prognosis, and to emphasize the analyses of mortality risks in malignant astrocytomas.

MATERIAL and METHODS: The effects of preoperative MRI features on prognosis were studied for follow-up period of 45 months, from November 1999 to August 2003, on a total of 79 patients' 41 cases of total resection and 38 cases of subtotal resection diagnosed to have malignant astrocytoma subsequent to craniotomy.

RESULTS: The cases of gross total resection had 2.2 times as high survival rate as those in the subtotal resection group ($p<0.01$). The comparison of the cases in the groups in relation to their ages revealed that mortality rate rose 4.35 times ($p<0.01$) in the age group of 60 years and above, and 2.1 times in the age group of 45-59 years. When cases without necrosis were compared with the group containing necrosis of grade 1, 2, 3, it was observed that the probability of mortality increased 3.84 ($p<0.01$), 4.15 times ($p<0.01$) in the case of necrosis of grade 2 and 3, respectively by means of Cox regression model.

CONCLUSION: Necrosis in preoperative MRI of malignant astrocytomas seems to be an important clinical marker of the prognosis.

KEYWORDS: Malignant astrocytoma, Preoperative MRI features, Recurrence time, Prognosis, Degree of resection, Analysis of mortality probability

ÖZ

AMAÇ: Bu çalışmanın amacı, preoperatif MRI özelliklerinin nüks zamanına ve prognoza olan etkisini analiz etmek ve malign astositomalarda ölüm olasılığı riskine vurgu yapmaktır.

YÖNTEM ve GEREÇ: Bu çalışma kraniotomi sonrası malign astrositoma tanısı alan 79 hastanın Kasım 1999- Ağustos 2003 tarihleri arasında 45 aylık takip periyodunda gross total rezeksiyonlu 41 ve subtotal rezeksiyonlu 38 hastanın preoperatif MRI özelliklerinin prognoza etkisi analiz edildi.

BULGULAR: Cox regresyon analizinde; gross total rezeksiyon yapılan olguların subtotal rezeksiyon grubuna göre 2,2 kat hayatta kalma olasılığına sahip olduğu görüldü ($p<0,01$). Yaş gruplarında ise, 60 ve üzeri yaş grubundaki olguların ölüm olasılığının 4.4 kat arttığı ($P<0.01$), ölüm olasılığındaki bu artışın 45-59 yaş grubunda 2,1 kat olduğu tespit edildi. Nekroz içermeyen olgular 1, 2 ve 3. derece nekroz içeren grupla karşılaştırıldığında; 2. derece nekroz içeren grupta ölüm olasılığının 3,84 kat arttığı ($P<0,01$), 3. derece nekroz içeren grupta ise ölüm olasılığının 4,15 kat ($p<0,01$) arttığı görüldü.

SONUÇ: Malign astrositomalarda Preoperatif MRI'daki nekroz hastalığın prognozu açısından önemli bir klinik belirleyici olarak görünmektedir.

ANAHTAR SÖZCÜKLER: Malign astrositoma, Operasyon öncesi MR özellikleri, Tekrarlama süresi, Klinik seyir, Tümörün çıkarılma derecesi, Ölüm olasılığı analizi

INTRODUCTION

Clinical studies on malignant astrocytoma (MA) have not only studied patient features affecting the prognosis but also the contribution of the surgical and medical treatments used. Among the significant prognostic independent variables in these studies are degrees of resection, (1,12,26,33), age (6,10,22), preoperative Kanofsky performance score (KPS) (6,10,15,22), localization of tumor (10,14,22), postoperative radiotherapy (RT), and chemotherapy (6,10). There is a limited number of studies on the effects of radiological features of preoperative tumors on prognosis (16,22,27,28). In the present study, the preoperative radiological features of the tumor, and the effects of pathological diagnosis of tumor on the recurrence time have been assessed prospectively using the methods of univariate and multivariate statistical analyses.

The aim of the present study was to analyze the effects on the recurrence time and prognosis of the MRI features (mass impact, degree of contrast enhancement, degree of tumor edema, necrosis degree of tumor) of preoperative tumors, one of the major dependent variables considered when determining the patients' remaining lifespan, and to emphasize the analyses of mortality risks associated with dependent variables.

MATERIAL and METHODS

This study investigated the effects of radiological features, defined prospectively and assumed to affect the prognosis, in 79 patients diagnosed with MA based on the resection subsequent to craniotomy in the Neurosurgery Clinic of the Medical Faculty of Erciyes University from November 1999 to August 2003. Of the 79 cases, 41 underwent gross total, and 38 subtotal resection. Of the cases, 28 (35.4%) were female and 51 (64.6%) were male patients. The age range of the patients was 21-76 years with a median of 48 years.

Histopathological diagnosis was assessed to be grade 3 (Anaplastic astrocytoma- "AA"), and grade 4 astrocytoma (GBM) by the World Health Organization (WHO) (20).

The data regarding the patients' radiological and clinical features as well as their treatment methods were recorded in the tumor follow-up forms specifically designed for this study group.

Patients were examined regularly every 3 months, and the clinical and radiological data were recorded in special tumor follow-up forms. On each occasion the patient reported for a check-up, an MRI was obtained and assessed in terms of recurrence and re-growth by an experienced radiologist. The relatives of the patients who had not attended the check-up sessions were contacted by telephone and questioned about their patient's neurological performance levels. As for those who had died, the dates of their death were obtained from relatives.

Imaging protocol and Statistical Analyses

Pre-operative and post-operative CT and MR imaging were routinely performed on the patients with and without contrast enhancement. Tumor-related characteristics thought to be prognostic were identified by an experienced radiologist. Mass impact, the degree of peripheral edema, retention of contrast medium, and the degree of necrosis were quantified as grade 0, 1, 2, and 3 according to the Hammoud method (16). The quantification criteria of MRI features are presented in Table I.

Table I: Preoperative MRI Features and Grades

Factor	Grade	Description
MRI Necrosis	0	No necrosis
	I	Necrosis is less than 25% of tumor volume
	II	Necrosis is between 25-50% of tumor volume
	III	Necrosis is more than 50% of tumor volume
Mass effect	0	No mass effect
	I	The midline shift is below 0.5 cm
	II	The midline shift is between 0.5-1 cm
	III	The midline shift is greater than 1 cm (uncal herniation)
Contrast enhancement	0	No enhancement
	I	Low and middle grade increase in signal
	II	High degree of signal increase
	III	Whole mass is equally contrast enhancement
Edema	0	No edema
	I	Edema is under the tumor volume
	II	Edema is equal the tumor volume
	III	Edema is greater than the tumor volume

The cumulative lifespan of the patients after the date on which they were operated on was determined using the Kaplan-Meier method. The survival curves for various subgroups were compared using Log Rank test. The effects of the multiple variables concerning the patients' survival were analyzed through the Cox regression method. The raw and processed data in this study have a confidence interval of 95%. When the quantified values affecting patients' survival times were significant, P was accepted as less than 0.05 and 0.01, and at other times P values greater than 0.05 were not accepted to be significant. The Statistical Package for the Social Sciences 10.0 (SPSS, Inc, Chicago, IL) was used for statistical analyses.

RESULTS

Demographic features of the patients

The study population consisted of 79 patients. As is shown in Table II, there were 28 (35.4%) female and 51 (64.6%) male patients. Throughout the follow-up period (45 months), 20 (25.3%) patients were alive. Of 51 male patients, 9 (17.6%) are alive with a survival time calculated to be 13 months, while 11(39.3%) of the 28 female patients are alive with a 15-month survival time. There was no statistically significant difference in survival times and survival rates between genders in terms of prognosis of the disease (P>0.05) (Table II).

Table II: Demographic and Characteristics of the Patient with Malign Astrocytoma

Factors	Variable	n=79	Mean survival time (CI 95%)	p
Median age (SD), y		48		
Age group	<45	31	**19 (15-23)**	**P<0.01[a]**
	45-59	26	**12 (9-16)**	**P<0.05[b]**
	≥60	22	6 (3-9)	
Gender	male (%)	51	13 (10-15)	p>0.05
	female(%)	28	15 (10-19)	p>0.05
MRI Necrosis grade	0	12	**21 (15-27)**	**P<0.01[q̄]**
	I	20	**16 (11-21)**	**P<0.05[q̄ q̄]**
	II	31	10 (7-13)	p>0.05
	III	16	9 (4-14)	p>0.05
Mass effect grade	0	12	**19 (14-26)**	**P<0.05[∂]**
	I	17	10 (6-14)	p>0.05
	II	29	12 (8-16)	p>0.05
	III	23	14 (9-18)	p>0.05
Edema grade	0	6	21 (11-31)	p>0.05
	I	29	13 (9-16)	**P<0.05[*]**
	II	34	10 (7-13)	p>0.05
	III	10	**22 (15-29)**	**P=0.01[**]**
Contrast enhancement grade	0	0	-	
	I	27	16 (12-21)	p>0.05
	II	52	12 (9-14)	p>0.05
	III	0	-	
Neurovavigation		67		
Rezection degree	Gross total	41	**17 (13-21)**	**P<0.01**
	Subtotal	38	10 (7-13)	
Histopathology	GBM	64	12 (9-14)	
	AA	15	**20 (14-26)**	**P<0.01**

[a]<45age group versus ≥60 age group} p<0.01,

[b]<45 age group versus 45-59 and, }p<0.05

45-59 age group versus ≥60 age group}p<0.05

[q̄]MR necrosis grade 0 versus MR necrosis grade 2 and necrosis grade 3,

[q̄ q̄]MR necrosis grade 1 versus MR necrosis grade 2 and necrosis grade 3

[∂]Mass effect grade 0 versus grade 1 p<0.05 and, Mass effect grade 0 versus grade 2and 3 p>0.05

[*]Grade 1 edema versus grade 3 edema p<0.05

[**] Grade 2 edema versus grade 3 edema p=0.01

The analysis of the factors affecting the prognosis of the 79 patients used as the database in this study is presented in Table II.

The patients' age and prognosis

The patients' age ranged between 21 and 76 years with a median of 48 years. The patients were divided into 3 groups depending on their age. Group 1 comprised the patients aged under 45, group 2 those aged 45-59, and group 3 the patients aged 60 years and over. Mean survival time (MST) was 19 months in 31 cases in group 1, and 12 months in 26 cases in group 2, compared to 6 months in 22 cases in group 3. When group 1 was compared with group 2 and 3, the MST was found to be statistically significant ($p<0.05$, $P<0.01$). MST was found to be statistically significant also in group 2 and 3 ($P<0.05$) (Table II).

Pathological Diagnosis

The numbers of the GBM and AA patients assessed together as malignant astrocytoma were 64 (81%) and 15 (19%), respectively. Throughout the follow-up period (45 months), the survival rates of the GBM and AA patients were 21.8% (14 cases) and 40% (6 cases), respectively. While MST was found to be 12 months for GBM, it was 20 months for AA. This difference between MST levels was found to be statistically significant ($p<0.01$). (Table II presents the pathological diagnosis and MST).

Tumor Characteristics in Preoperative MRI

Degree of edema: Summarized in Table II are the effects of the degree of edema in the preoperative MRG on overall survival rates. The study of the relationship between the degree of edema and the survival time revealed that the patient group with edema of grade 3, defined as the edema greater than the volume of the tumor, had longer MST's than the group with edema of grade 2, defined as edema equal in size to the volume of the tumor (22 months and 10 months, respectively). The statistical difference between MST's was significant ($P<0.05$). The patient group with edema of grade 3 survived longer than those in the group of grade 1 with edema smaller than the tumor volume (22 months compared to 13 months). This difference between grade 3 and 1 was statistically significant ($P<0.05$). The difference between the overall survival rates of the group 0, the group without edema, compared with the other groups, and the differences of survival rates between grade 1 and 2 were found to be statistically insignificant ($P>0.05$).

Mass impact of the lesion: When the mass impacts of lesions on survival rates were compared in neuroradiological studies, it was detected that the survival rate during the follow-up period of the group without mass impact was 50%, and their MST was 19 months. The difference between the MST of this group and that of the group (10 months) only with a mass impact of grade 1 was also found to be statistically significant ($P<0.05$). However, when the group without mass impact was compared with the other groups, it was found that the difference between their MST's did not reach a level of statistical significance ($P>0.05$). The degrees of the mass impact of the tumors, and their respective MST's are shown in Table II.

Contrast enhancement of tumors: Table II shows the contrast enhancement of the tumors on preoperative MRG and the data regarding their respective overall survival. There was no case without contrast enhancement in the 79-patient study group (for grade 0). Of the 27 patients (grade 1) with weak retention of contrast matter, 8 (29.6%) were alive and the MST's was 16 months, while in the 52-patient group (grade 2) with moderate retention, 13 (23.1%) patients were alive, their MST being 11 years. There was no case with contrast enhancement of grade 3 in the study. Statistical intergroup comparisons revealed no significant differences in survival times ($P>0.05$).

Degree of necrosis: The breadth of the central part of the tumors that does not retain contrast medium, and therefore assumed to be necrotic in preoperative neuro-radiological studies, was assessed together with the MST's of the cases and their percentage of survival (Table II). While the average survival times of patient groups with necrosis of grade 0 and 1 were found to be 21 and 16 months respectively, those of the patient group with necrosis of grade 2 and 3 were found to be 10 and 9 months, respectively. There was no significant difference between the mean survival times of the cases with necrosis of grade 0 versus grade 1, and those with necrosis of grade 2 and 3 were statistically significant. ($P<0.01$). Statistically significant differences were detected between the groups with necrosis of grade 1 and 2 ($P<0.05$), as was in the grade 1 versus grade 3 ($P<0.05$). There was no statistically significant difference in MST detected between grade 2 and 3 groups either ($P>0.05$). Table II shows the grades of necrosis and survival rates. Kaplan Meier life curves are also shown in Figure 1.

Degree of resection: The mean and median survival times together with the statistical analyses of the tumors detected on the early postoperative MRG were determined on the basis of their degree of resection, and are presented in Table II. Throughout the follow-up period, a survival rate of 43.9% was determined in the group of 41 patients who underwent total resection, while it was 5.3% in the 38-patient subtotal resection group. As for the mean survival times, these were 17 and 10 months, respectively.

When resection groups were analyzed according to their survival times, the group of gross total resection was statistically more significant and had longer survival times ($P<0.01$).

Recurrence time: Recurrence was found to have had an impact on survival in univariate analyses and recurrence time was found to be an effective prognostic factor. However, re-growth and its duration (cases in which subtotal resection was detected in postoperative MR) were found to have no effect on survival time in multivariate analyses. Therefore, only the preoperative MR features which affect recurrence time were analyzed, and the results are summarized in Table III. Of the 41

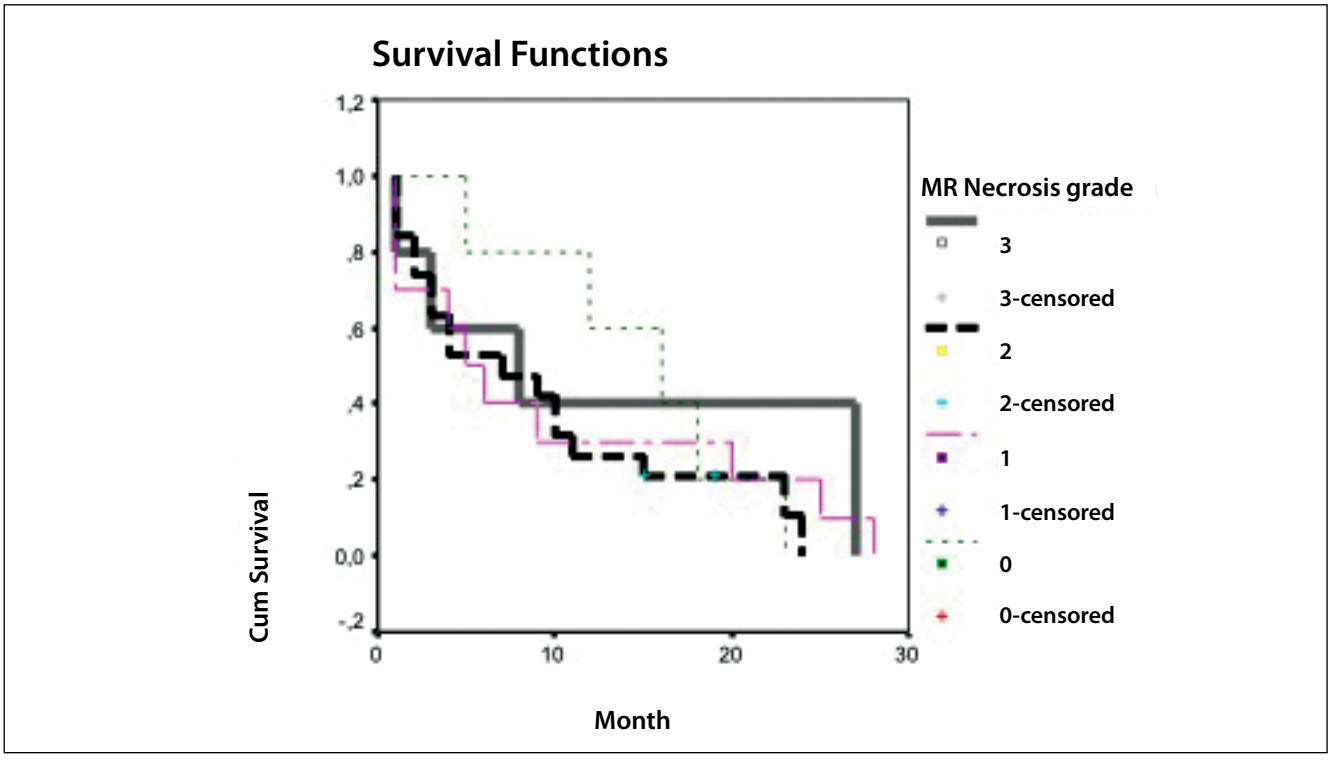

Figure 1: Preoperative MR necrosis grade and Kaplan Meier life curves.

cases in the gross total resection group, 27 (34.2%) recurred. Of these cases, 15 (55.6%) were alive. As for the 14 cases without relapse, only 3 (21.43%) were alive. The comparison of mean survival times in the recurrence and non-recurrence group, 21 months and 7 months, respectively, yielded statistically significant differences ($p<0.01$)

Preoperative MRI features and recurrence times

Necrosis and recurrence times: Table III shows the analysis of the effect of the degree of necrosis in preoperative MRI on survival times. It was determined that the mean recurrence times for the group with no necrosis, for the group with necrosis of grade 1, and for the group with necrosis of grade 2 were 15, 12 and 7 months, respectively. As for the group with necrosis of grade 3, it was 3 months. Statistical analyses of the intergroup differences revealed that the group with no necrosis had significantly longer recurrence times than both groups of necrosis of grade 2 and 3 ($P<0.05$ and $P<0.01$ respectively). No significant difference was found between the group with necrosis of grade 1 and the group without necrosis ($P>0.05$). Similarly, the groups with necrosis of grade 2 and 3 did not differ significantly ($P>0.05$). The difference in recurrence times between the groups with necrosis of grade 1 and 2 was significant ($P<0.01$), in contrast to the groups with necrosis of grade 2 and 3 ($P<0.05$).

Contrast Enhancement and Recurrence Times: The analysis of the effect of the medium contrast enhancement in preoperative MRG on recurrence times showed that the mean recurrence time in the 12-case group with a retention rate of grade I was 13 months compared with 7 months. The difference between recurrence times in relation to contrast enhancement was found to be statistically significant ($p<0.05$). Table III shows contrast enhancement and recurrence times.

Degree of Edema and Recurrence Times: The analysis or recurrence times in relation to the degree of edema on preoperative MRG in table 3 shows that the mean recurrence time was 14 months for the group with no edema (grade 0), 9 months in the group with edema of grade I, 5 months in the group with edema of grade II, and 12 months in the group with edema of grade III. Intergroup comparisons yielded a statistically significant influence of recurrence times ($p>0.05$)

Mass Impact and Recurrence Times: The recurrence time in the group with no mass impact in relation to the degree of the preoperative mass impact was 11 months, followed by 5 months in the group with a mass impact of grade I, 9 months in the group with a mass impact of grade II, and 8 months for grade III. These findings were not statistically significant ($p>0.05$). Table III shows recurrence times in relation to the degree of mass impact.

Analysis of mortality probability

When the effects of independent variables on mortality probability were analyzed by means of Cox regression model, it was seen that the cases of gross total resection had 2.20 times greater survival chance than the cases of subtotal resection group ($P<0.01$). It was also observed that the mortality probability of cases in the age group of 60 years and over increased by 4.35 times ($P<0.01$) compared to the age

group of under 45 years. This increase in mortality probability was 2.1 fold in the 45-59 age group versus the age group of under 45 years (p<0.05). When the cases without necrosis were compared with the groups with necrosis of grade 1, 2, and 3, it was found that mortality increased 3.84 fold in the group with necrosis of grade 2 (P<0.01), while it increased 4.15 times in the group with necrosis of grade 3 (P<0.01). Table IV shows the analysis of the probability of mortality with regard to the variables in Cox regression analysis.

Contrast retention, the degree of mass impact, histopathological subgroups, recurrence, re-growth, and the degree of edema on preoperative MRI appear, as judged by the results of Cox regression analyses, not to raise the probability of mortality or to have any effect on survival.

The degree of surgical resection appears in Cox regression model as a prognostic factor but seems to lose its statistical significance with the inclusion of recurrence time in analyses.

Table III: Preoperative MRI Features Affect on Nux Time

Factors	Variable	Mean nux time (CI 95%)	Survi rate %	P value
MRI Necrosis grade	0	**15 (10-19)**	**71.4**	**p<0.05 *** **p<0.01****
	I	12 (8-15)	80.0	**p<0.01"**
	II	7 (3-10)	25.0	p>0.05
	III	3 (1-5)	16.7	p>0.05
Mass effect grade	0	11 (6-17)	62.5	p>0.05
	I	5 (0-11)	14.3	p>0.05
	II	9 (5-14)	46.2	p>0.05
	III	8 (4-12)	46.2	p>0.05
Contrast enhancement grade	0	-	-	-
	I	**13 (10-17)**	**58.3**	**p<0.05**
	II	7 (4-10)	37.9	p>0.05
	III	-	-	-
Edema grade	0	14 (8-21)	75	p>0.05
	I	9 (5-13)	35.7	p>0.05
	II	5 (2-9)	35.3	p>0.05
	III	12 (7-17)	57.1	p>0.05

** p<0.05 MR necrosis grade 0 versus necrosis grade 2*
***p<0.01 MR necrosis grade 0 versus necrosis grade 3*
"p<0.01 MR necrosis grade 1 versus necrosis grade 2 and 3
P>0.05 MR necrosis garade 0 versus 1 and MR necrosis grade 2 versus 3
p>0.05 MR necrosis grade 0 versus grade 1 and MR necrosis grade 1, 2 and 3 versus each other.

Table IV: The Analysis of the Probability of Mortality with Regard to the Variables in Cox Regresssion Analysis

variable		B coefficient	Standard error	OR	OR 95%CI	P
Age	<45					**<0.01**
	45-59	- 0.74	0.33	*0.48*	0.25 - 0.90	**<0.05**
	≥60	- 1.47	0.35	*0.23*	0.12 - 0.45	**<0.01**
Necrosis	0					**=0.01**
	I	0.68	0.51	1.98	0.73 - 5.34	**>0.05**
	II	1.35	0.47	*3.84*	1.52 - 9.72	**<0.01**
	III	1.42	0.50	*4.15*	1.56 - 11.09	**<0.01**
Gross total resection						
Subtotal resection		0.79	0.27	2.20	1.3 - 3.7	**<0.01**

As for necrosis, edema, mass impact on preoperative MRI, and histopathological subgroups, these are all, as independent variables, in interaction with recurrence time.

DISCUSSION

While the effect of necrosis in preoperative MRI on the recurrence time and on prognosis, in particular, has been stressed primarily in the present study, the effects on the prognosis of other important independent variables such as degree of resection, age, pathological diagnosis, mass impact in MRG studies and contrast medium retention have been analyzed secondarily.

Degree of Resection

The degree of an optimal resection in any patient depends upon the size and locality of the tumor, the patients' general and neurological condition, and the surgeons' experience. In addition to studies which report that the larger the reaction the longer the survival time (1,6,22,36), there are also studies maintaining that the size of the resection has no impact on survival time (10,15,21,28).

The mean survival time of the 38 cases of subtotal resection was 10 months whereas it was 17 months in the 41 cases of gross total resection in this study, indicating that gross total surgical resection affects patient prognosis significantly.

The Age of the Patient

A strong association was observed between survival and the patients being young. The patients in the group aged under 45 years and in the group aged between 45-59 years had significantly longer survival times than those in the group aged 60 years and over, the mean survival time decreasing with advancing age.

There exists strong evidence for the correlation between the patient being young and longer survival times in patients with MA (6,10,21,22,31,32). Therefore, the age of the patient is an independent variable affecting the choice of surgical method, and thus survival time (2,32,35).

As age increases, the mortality risk also increases. Aggressive therapeutic modalities are not so effective in prolonging survival time as they are in younger patients (5, 6,19).

Tumor Pathology

The mean survival time of the 15 cases with AA was found to be 20 months while it was 12 months in 64 cases with GBM. In univariate analyses, patients with AA seemed to have statistically significantlylonger survival times. However, in multiple analyses, it was seen that the effect of histopathological differences on prognosis was statistically insignificant. It is natural that patients with MA differed in survival rates from the patients in the histopathological subgroup. Although different survival rates have been reported because of the different histopathological classification, cases with AA have longer survival rates in the literature (23, 29). As for GBM, it may present a pattern with longer survival in its subgroups without necrosis (4, 8, 11, 25).

Tumor Characteristics in Preoperative MRI

Necrosis: It was detected that the absence of necrosis in imaging studies was an important prognostic variable corroborating Hammound's finding (16).

Barker (4) reported that the presence of necrosis had an adverse effect on prognosis. As a result of the studies which have demonstrated the importance of necrosis and pointed to MA patients' comparatively shorter survival times (4, 8, 11, 25), necrosis has become an important diagnostic criterion in GM for many pathologists. The presence or absence of necrosis is a key criterion in diagnosing the most anaplastic form of GBM (25). However, the proportion of GBM without histopathological necrosis is reported to be 8-34% in the literature (4).

Necrotic areas of low density inside MA are a frequent histopathological feature, and they are believed to be the signs of oncoming rapid growth and malignant behavior (34). On the other hand, a direct relationship has been found between necrosis and age: in other words, the probability of the tumor developing necrosis is higher in the elderly (4).

It is theorized that cases with GBM without necrosis but with vascular endothelial proliferation have longer survival times than necrotic cases with GBM (4). The mean survival times of patients with AA ranges between 3.3 and 4 years (23, 29), which are much higher levels than the upper limit of the survival times (12.5 months) in the GBM patient group without necrosis (4).

Pope et. al. (28) reported that necrosis in astrocytomas of grade III was prognostically and statistically significant but not in astrocytomas of grade IV. Additionally, some studies report that necrosis is an unfavorable prognostic factor (16,22,27).

In the present study all the patients diagnosed to have GBM had necrosis in their pathological studies. The fact that the cases with necrosis radiologically graded as 0 and 1 had longer survival times of statistical significance than the necrotic cases of grade 2 and 3 in univariate and multivariate analyses is corroborative of the relevant literature.

Contrast enhancement: Contrast enhancement, unlike in previous studies, was not found to be an independent variable indicating an increasing number of patients' shorter survival time. While no difference was observed in survival in relation to contrast enhancement in univariate and multivariate analyses, it was observed that contrast enhancement acted on recurrence time and thus, survival time. It was found that the cases with contrast enhancement of grade 1 had significantly longer recurrence time compared to the cases with a contrast enhancement of grade 2 (13 months vs. 7 months). Since the recurrence time was determined to be a prognostic factor in multivariate analyses, it was concluded that contrast enhancement was negatively correlated with recurrence time and thus with survival time,

The negative correlation between contrast medium enhancement and the patients' survival can be explained

by the fact that the blood-brain barrier is broken with the penetration of contrast medium. The histopathological basis of contrast enhancement of tumors has been linked to pathological neovascularization and vascular endothelial proliferation (13). Therefore, a poor prognosis associated with greater contrast enrichment may be ascribed to vascular endothelial proliferation and an impaired blood-brain barrier (13,22).

It has been proven histopathologically that the prominence of the areas in scans performed subsequently to contrast enhancement largely depends on the dense cellular and hypervascular texture of the tumor. The limits of contrast enhancement therefore show the macroscopic margin of malignant gliomas (1,7,9,17).

The association of increasing contrast enhancement and shorter survival times has also been reported in other studies (16, 22, 28). In the current study, there was no case with contrast medium retention of grade 0 or 3. There was no statistically significant difference of survival rates between the patients in the group with contrast enhancement of grade 1 and the group of grade 2. In multivariate analysis, contrast enhancement did not appear to be a significant factor.

Edema: The area of high density in T2 A MRG imaging, thought to be traditional edema, has been demonstrated to have a variable tumor texture (13, 17, 22).

It was observed in the current study that the area assumed to be edema, based on intraoperative USG, contained tumor, and that surgical observation corroborated with the USG. In the study, the mean survival times in relation to the degree of edema were 21 months in 6 cases of grade 0, 13 months in 29 cases of grade 1, 10 months in 34 cases of grade 2, and 22 months in 10 cases of grade 3. In univariate analysis, it was found that the cases with peritumoral edema of grade 3 in preoperative MRG studies were associated with statistically longer survival times than cases of peritumoral edema of grade 1 and 2. In multiple analyses, however, it was found that the degree of edema was statistically insignificant in terms of the patients' survival times.

It is reported in the literature that the patient group with edema of grade 0 and 1 in preoperative MRI enjoyed statistically longer survival times than the patient group with edema of grade 2 and 3, but in statistical analyses with multiple variables the difference was insignificant (22).

Pope et al. (28) reported that edema, as an unfavorable prognostic factor, was significant in univariate and multiple analyses, and that there was a negative correlation between contrast medium retention and edema. They have stressed, in the light of literature, that young patients tend to have tumors unretentive to contrast medium and with less edema.

In the present study, long survival rates in cases with edema of grade 3 in univariate analyses differ from those in the literature. We believe that this could be attributed to the favorable effect on the prognosis of the relatively large size of the area to cover the edema and to undergo post-surgical radiotherapy

Mass impact: In this study the mean survival time for 12 cases without mass impact was found to be 19 months in contrast to 10 months for 17 cases with a mass impact of grade 1, the difference being statistically significant. However, when compared with groups with a mass impact of grade 2 and 3, statistical differences were not detected. In a study of mass impact in preoperative MRI on prognosis, mass impact, as a dependent or independent variable, has been reported to have no effect on the survival times of the patients (22).

As is known, MA is not a local but extensive neural tissue disease (6,7,17,18,24). The most important of the goals to be achieved in the surgical treatment of MA is the elimination of mass impact, followed by the principles that the tumor mass should be reduced, which enhances the effect of adjuvant therapies, and the diagnosis should be made correctly (1,3,21,22,24,30).

Mass impact in cases with MA is an important factor that determines the risk of tentorial herniation. Displacement of midline structures formed by tumor mass and peripheral edema gives rise to focal neurological deficits in patients. The most natural result of this deficit is functional impairment.

CONCLUSION

In the light of these findings, the increasing degree of necrosis on preoperative MRI has been assessed as a poor prognostic sign. We are of the opinion that the tumor-related characteristics of patients' preoperative MRI could be used, in connection with histopathological diagnosis, as a diagnostic marker, since MRI is practical and replicable. However, we feel that the goal in the surgical treatment of MA should be a surgical resection as large as possible, also considering neurological functions.

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