

Volumetric extent of resection and residual contrast enhancement on initial surgery as predictors of outcome in adult patients with hemispheric anaplastic astrocytoma

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Object. To investigate the prognostic significance of the volumetrically assessed extent of resection on time to tumor progression (TTP), overall survival (OS), and tumor recurrence patterns, the authors retrospectively analyzed preoperative and postoperative tumor volumes in 102 adult patients from the time of the initial resection of a hemispheric anaplastic astrocytoma (AA).

Methods. The quantification of tumor volumes was based on a previously described method involving computerized analysis of magnetic resonance (MR) images. Analysis of contrast-enhancing tumor volumes on T₁-weighted MR images was conducted for 67 patients who had contrast-enhancing tumors. Measurements of T₂ hyperintensity were obtained for all 102 patients in the study.

The presence or absence of preresection enhancement, actual volume of this enhancement, and the percentage of preoperative enhancement as it relates to the total T₂ tumor volume did not have a statistically significant relationship to TTP or OS. In addition to age, the volume of residual disease measured on T₂-weighted MR images was the most significant predictor of TTP ($p < 0.001$), and residual contrast-enhancing tumor volume was the most significant predictor of OS ($p = 0.003$) on multivariate analysis. In contrast to low-grade gliomas, there was no statistically significant relationship between the extent of resection and histological characteristics at the time of recurrence, that is, tumor Grade III compared with Grade IV.

Conclusions. Data from this retrospective analysis of a histologically uniform group of hemispheric AAs treated in the MR imaging era suggest that residual tumor volumes, as documented on postoperative imaging studies, may be a prognostic factor for TTP and OS for this patient population.

KEY WORDS • anaplastic astrocytoma • extent of resection • volumetric measurement • prognosis • survival

DESPITE recent advances in diagnostic and therapeutic modalities, the prognosis of AA remains poor. Only modest improvements in survival have been achieved in patients with AA despite the aggressive use of surgery, radiotherapy, and chemotherapy on initial diagnosis; and reoperation, brachytherapy, and additional chemotherapy on recurrence.¹⁸ Almost all patients treated for AA harbor progressive tumors and die of this disease.

Several prognostic factors thought to affect outcome in patients with AAs include age, neurological status, and tumor volume as well as treatment-related variables such as timing of surgical intervention, extent of resection, postoperative tumor volume, use of radiotherapy, and administration of chemotherapy. Age is a generally accepted prog-

nostic factor. As in cases of low-grade astrocytomas^{1,10} and GBMs,^{9,11,15} the prognostic role of the extent of resection in AAs is controversial given the lack of randomized controlled trials addressing this issue and the difficulty in obtaining information from available studies that have methodological limitations.¹⁸

Contrast enhancement on MR imaging due to extravasation from tumor vasculature, which lacks endothelial tight junctions, is a well-known characteristic of high-grade gliomas and positively correlates with malignancy.^{4,23} The prognostic importance of contrast enhancement, however, is not clearly defined for a homogeneous patient population harboring AAs. These lesions have heterogeneous contrast enhancement characteristics, and the enhancing tumor volume may not accurately reflect the tumor burden because infiltrative tumor exists in areas with abnormal T₂ intensity.

In this study, we analyzed in detail the prognostic significance of the presence and the volume of preoperative and postoperative contrast enhancement in patients with hemispheric AAs. To answer the question of whether the volume

Abbreviations used in this paper: AA = anaplastic astrocytoma; CI = confidence interval; GBM = glioblastoma multiforme; HR = hazard ratio; KPS = Karnofsky Performance Scale; MR = magnetic resonance; OS = overall survival; POR = percent of resection; RTOG = Radiation Therapy Oncology Group; TTP = time to tumor progression; VRD = volume of residual disease.

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of the pathological entity (represented as either enhancing volume or nonenhancing volume) at the time of initial surgery, the volumetrically assessed extent of resection, or the VRD is a predictor of outcome (that is, TTP and OS), we evaluated pre- and postoperative tumor volumes and POR as they relate to outcome in a group of adult patients who had undergone an initial surgery after the diagnosis of hemispheric AA.

Clinical Material and Methods

Patient Population

The study population consisted of 102 adult patients with AAs located in the cerebral hemispheres. All patients underwent initial surgery at the University of California, San Francisco, Medical Center between 1994 and 2001. The patient population had a median age of 49 years (range 22–84 years) and included 48 women (47%) and 54 men (53%). The predominant tumor location was the frontal lobe (38 patients [37%]), followed by the parietal lobe (34 patients [33%]), temporal lobe (28 patients [28%]), and occipital lobe (two patients [2%]). Slightly more tumors were located in the left cerebral hemisphere (57 patients [56%]). The aim of surgery was maximal tumor resection; to achieve this goal with minimal morbidity, cortical and subcortical stimulation mapping techniques were used when necessary.¹² Only patients with a KPS score of 70 or higher were included in the study. Patients with recurrent AA were not included in this analysis. Pathological material was reviewed, and only those patients for whom the histological diagnosis of AA was confirmed using the current World Health Organization criteria were included.¹³ Patients with other Grade III gliomas (including Grade III mixed gliomas) were excluded because of these lesions' natural history and prognosis, which is different from pure Grade III astrocytomas.⁵ All patients (100%) received postoperative radiotherapy; and 94% of the patients (96 of 102), chemotherapy. Follow-up evaluation was uniform in all patients, that is, neurological examination and control MR images obtained at regular intervals.

This study was conducted with approval from the University of California, San Francisco, Committee on Human Research.

Determination of Tumor Volumes and Disease Progression

All patients underwent MR imaging preoperatively and within the first 48 hours postoperatively. The T₁-weighted Gd-enhanced and T₂-weighted MR images were digitized and used to measure pre- and postoperative tumor volumes by using a previously described method of image analysis⁶ with the aid of computer software (Scion Image Beta for Windows, version 4.02; Scion Corp., Frederick, MD). Briefly, this method consists of defining the dimensions on the software by using the scale on the digitized MR image and then delineating the tumor area. Given that the slice thickness is known, the volume of disease adjacent to each brain section is calculated, and these volumes are added to determine the total tumor volume. The tumor volume was considered to be the contrast-enhancing area on T₁-weighted images and the area of hyperintensity on T₂-weighted images, including any region of central necrosis. The resection

cavity was not included in the volume measurement. From these data, the POR was calculated based on T₂-weighted MR images for all patients and on T₁-weighted MR images for patients who had a contrast-enhancing lesion.

Tumor progression was assessed on follow-up MR images. For contrast-enhancing lesions, disease progression was defined as a 25% or greater increase in the product of the largest perpendicular diameters of contrast enhancement of any lesion or any new enhancing tumor on MR images. The same criteria were applied to areas of T₂ hyperintensity for patients with nonenhancing lesions. In questionable cases (for example, if the patient had undergone radiosurgery or high-dose focal radiotherapy) our standard of practice was to use MR spectroscopy, positron emission tomography, or biopsy procedure rather than radiation necrosis to confirm the presence of tumor. The TTP and OS were calculated from the time of initial diagnosis.

Statistical Analysis

Our approach to statistical analysis consisted of determining the prognostic significance of preoperative contrast enhancement, pre- and postoperative T₂ volumes and PORs, and the significance of postoperative contrast enhancement, as they related to outcome (that is, TTP and OS). We first analyzed variables in each of these three groups to evaluate their prognostic significance, and then put all variables that had a statistical significance level of less than 0.05 into a multivariate stepwise model to determine those with the most significant impact on TTP and OS. Radiotherapy was not included in the model because all patients had received postoperative focal external-beam radiotherapy (total dose 60 Gy) as part of the initial treatment. Only six patients (5.9%) in the study population did not receive chemotherapy. Because the standard chemotherapy regimen changed in 2000 (the predominant chemotherapy regimen was nitrosourea based before 2000 and temozolomide based thereafter), we determined whether there was a difference in outcome between these time periods by using a Cox proportional hazards model. Because there was no statistically significant difference in either TTP or OS, no adjustment for chemotherapy was made in the analyses included in this report.

The prognostic significance of preoperative and postoperative contrast enhancement and preoperative and post-resection tumor volumes were analyzed using a Cox proportional hazards model. All analyses were adjusted for age and KPS score.

Preoperative Contrast Enhancement. To determine the prognostic significance of contrast enhancement at the time of diagnosis, we defined and analyzed three variables related to contrast enhancement on preoperative MR images. These variables comprised the presence or absence of contrast enhancement (yes or no), the actual volume of enhancement (cm³), and the percent of enhancing volume, which was defined as the volume of enhancement (cm³) divided by the total volume of T₂ hyperintensity (cm³).

Preoperative and Postresection Tumor Volumes. To assess the prognostic significance of tumor volumes (pre- and postresection) and POR, the analyzed variables included tumor volume measurements of preresection T₂ volume, postresection T₂ volume, and POR based on these two T₂-based measurements.

TABLE 1
Patient and tumor characteristics*

Variable	Median Value (range)
age (yrs)	49 (22–84)
KPS score	90 (70–100)
preresection T ₂ vol in cm ³ (102 patients)	30.49 (4.09–138.10)
preresection T ₁ CE vol in cm ³ (67 patients w/ preop enhancement)	15.20 (1.10–51.70)
postresection T ₂ vol in cm ³ (102 patients)	11.75 (0–34.50)
postresection T ₁ CE volume in cm ³ (50 patients w/ residual enhancement)	7.25 (1.40–22.30)
POR based on T ₂ vols (102 patients)	61.4 (9.3–100.0)
POR based on T ₁ CE vol (67 patients w/ enhancing area)	64.1 (7.1–100.0)
TTP (wks)	103.8 (8.5–600.1)
OS (wks)	163.8 (14.2–696.4)

* CE = contrast-enhancing.

Postoperative Contrast Enhancement. To determine the prognostic significance of postresection contrast enhancement, we defined and analyzed three variables related to contrast enhancement on early postoperative MR images. These variables consisted of the presence or absence of contrast enhancement (yes or no); the actual volume of enhancement (cm³), including 0 for those with no enhancement; and the percent of enhancing volume, again defined as the volume of enhancement (cm³) divided by the total volume of T₂ hyperintensity (cm³).

Histological Characteristics at the Time of Progression. For the subset of patients for whom tumor tissue was available at the time of progression (43 patients), we determined

TABLE 2
Results of statistical analysis of contrast enhancement and volume variables*

Variable	End Point	p Value	HR	95% CI
preresection enhancement				
contrast enhancement (yes/no)	TTP	0.955	0.988	0.674–1.509
	OS	0.937	1.018	0.651–1.592
CE vol	TTP	0.351	0.993	0.979–1.008
	OS	0.430	0.993	0.977–1.010
CE vol/vol on T ₂ MRI	TTP	0.786	1.104	0.541–2.254
	OS	0.557	1.256	0.587–2.690
vol-related variables				
preresection T ₂ vol	TTP	0.659	0.998	0.988–1.008
	OS	0.880	0.999	0.989–1.010
postresection T ₂ vol	TTP†	<0.001	1.081	1.037–1.127
	OS†	0.012	1.041	1.009–1.074
POR based on T ₂ vols	TTP†	0.015	0.990	0.983–1.017
	OS	0.138	0.994	0.986–1.002
postresection enhancement				
contrast enhancement (yes/no)	TTP	0.153	1.347	0.895–2.025
	OS	0.421	1.195	0.774–1.844
CE vol	TTP†	<0.0001	1.088	1.041–1.137
	OS†	0.002	1.072	1.025–1.120
CE vol/vol on T ₂ MRI	TTP†	0.029	2.049	1.078–3.895
	OS†	0.028	2.172	1.086–4.345

* All models include age and KPS score.

† Statistically significant, $p < 0.05$. These variables were later analyzed with a forward stepwise Cox regression model to determine the most significant prognostic predictor for TTP and OS, respectively.

TABLE 3
Results from forward stepwise multivariate Cox proportional hazards model*

End Point	p Value	HR	95% CI
TTP			
age	0.001	1.022	1.009–1.034
VRD-T2	<0.001	1.079	1.046–1.112
KPS score	NS	1.005	0.987–1.023
OS			
age	<0.001	1.026	1.012–1.040
VRD-T1c	0.003	1.070	1.023–1.119
KPS score	NS	1.006	0.988–1.025

* NS = not significant; VRD-T1c = volume of residual disease measured on contrast-enhanced T₁-weighted MR images; VRD-T2: volume of residual disease measured on T₂-weighted MR images based on T₂ hyperintensity.

whether the histological features were upgraded to GBM. To assess whether smaller residual tumor volumes and more radical resections at the time of initial therapy are associated with a lower likelihood of histological upgrading, we compared these variables—that is, VRD and POR—using the Wilcoxon rank-sum test for patients who did and did not have an upgrade.

Results

Patient characteristics are outlined in Table 1. All patients had tumor progression, and 86% (88 of 102 patients) died within the study period.

Volumetric analysis of tumor volumes on T₁-weighted MR images was conducted for 67 patients with contrast-enhancing tumors. We also measured T₂ hyperintensity for each patient in the study population (102 patients). In all analyses, patient age at diagnosis was a statistically significant predictor of outcome, that is, TTP and OS. Although the KPS score did not reach statistical significance, it was retained in the statistical model. Results for individual variables are outlined in Table 2, including HRs and 95% CIs.

Preoperative Contrast Enhancement

None of the three variables analyzed—that is, the presence or absence of enhancement, the actual volume of enhancement, and the percentage of enhancement as it relates to the total T₂ tumor volume—had a statistically significant impact on TTP or OS (Table 2).

Volume-Related Variables

Analyzed variables included preresection T₂ volume, postresection T₂ volume, and POR based on the previous two T₂-based measurements. Results were adjusted for patient age and KPS score. In addition to age, the VRD on T₂-weighted MR images was the only statistically significant variable in this group, for both TTP and OS (Table 2).

Time to Tumor Progression: Multivariate Model

For the entire patient population (102 patients), the median TTP was 104 weeks (range 8.5–600 weeks). When data were analyzed according to the hyperintensity on T₂-weighted MR images for all patients, age and VRD were statistically significant factors for TTP ($p = 0.001$ and $p <$

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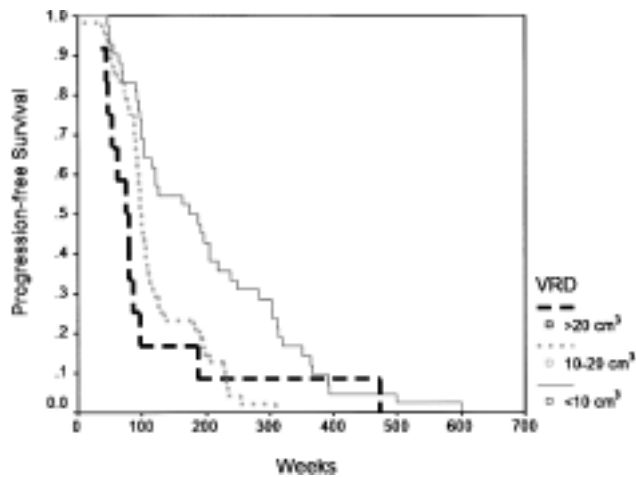


FIG. 1. Kaplan–Meier curve showing the TTP as it relates to the three subgroups of residual tumor volumes ($< 10 \text{ cm}^3$, $10\text{--}20 \text{ cm}^3$, and $> 20 \text{ cm}^3$) defined as hyperintensity on postoperative T_2 -weighted MR images. $p < 0.001$.

0.001, respectively; Table 3). The KPS score was included in the model. The TTP curves for groups of patients with different VRDs based on T_2 -weighted MR images ($< 10 \text{ cm}^3$, $10\text{--}20 \text{ cm}^3$, and $> 20 \text{ cm}^3$) are presented in Fig. 1. For comparison, TTP curves for groups of patients with different VRDs based on contrast-enhancing T_1 -weighted MR images ($< 5 \text{ cm}^3$, $5\text{--}10 \text{ cm}^3$, and $> 10 \text{ cm}^3$) are presented in Fig. 2.

Survival: Multivariate Model

For the entire patient population, the median OS was 164 weeks (range 14.2–696 weeks). Age and VRD based on T_1 contrast enhancement were selected as the significant predictors of OS ($p < 0.001$ and $p = 0.003$, respectively; Table 3). Survival curves for groups of patients with different VRDs based on T_2 -weighted MR images ($< 10 \text{ cm}^3$, $10\text{--}20 \text{ cm}^3$, $> 20 \text{ cm}^3$) are presented in Fig. 3. For comparison, survival curves for groups of patients with different VRDs based on contrast-enhancing T_1 -weighted MR images ($< 5 \text{ cm}^3$, $5\text{--}10 \text{ cm}^3$, and $> 10 \text{ cm}^3$) are presented in Fig. 4.

Histological Characteristics at Tumor Progression

All patients showed tumor progression within the study period. Of the 43 patients (42%) for whom we had a tissue diagnosis at the time of progression, 27 (63%) had a histologically confirmed GBM. As expected, the median TTP was shorter for patients with tumors that showed malignant differentiation (92 weeks, range 37–303 weeks) compared with patients who had a histologically verified AA at the time of recurrence (median TTP 211 weeks, range 68–393 weeks). Results of our analysis, however, failed to show a statistically significant relationship between the extent of resection (that is, POR and VRD) and histological characteristics at the time of recurrence.

Discussion

The available literature on the extent of the resection of AAs as a distinct histological group is very limited, and

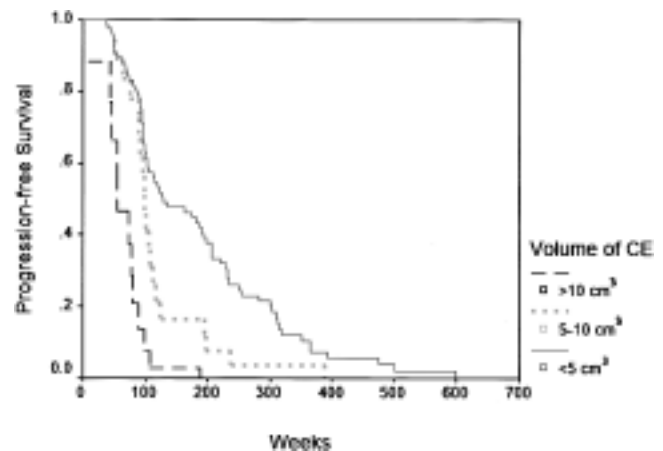


FIG. 2. Kaplan–Meier curve depicting the TTP as it relates to the three subgroups of contrast-enhancing residual tumor volumes ($< 5 \text{ cm}^3$, $5\text{--}10 \text{ cm}^3$, and $> 10 \text{ cm}^3$) as depicted on postoperative T_1 -weighted MR images. CE = contrast enhancement.

there is no randomized study in which the authors have specifically evaluated the prognostic significance of the extent of resection for hemispheric AAs. Design-related problems are common in studies focused on the evaluation of the extent of glioma resection, and thus limit the scientific strength of currently available literature.^{8,10,18} These design limitations include factors related to patient selection and histological heterogeneity among patient populations, that is, the inclusion of AAs, GBMs, anaplastic oligodendrogliomas, and anaplastic mixed gliomas with no adjustment for histological characteristics in statistical analysis. Additional limitations include treatment selection bias, nonvolumetric (and therefore subjective) assessment of the extent of resection, variability in adjuvant therapies, and the small number of patients in most studies, which lower statistical power. To minimize these methodological limitations, we chose to evaluate only adult patients with histologically reconfirmed hemispheric AAs who had a KPS score of 70 or higher and who had undergone surgery as part of the initial treatment. Our patient population was also uniform with respect to adjuvant therapy, and the statistical analysis was conducted in a way to adjust for known prognostic factors for AAs. The determination of preoperative and postresection tumor volumes was quantitative and objective. Despite careful planning and data analysis, our study does have the limitation of being a retrospective analysis, and the results and conclusions provide Class II data regarding a problem where there are no Class I data available in the literature. An additional limitation is the number of cases with a histological diagnosis at the time of progression, as detailed in *Results*.

Significance of Contrast Enhancement

Given that an MR image obtained in a patient with AA may or may not be contrast enhancing at the time of initial diagnosis, we chose first to evaluate whether the presence or absence of contrast enhancement had any prognostic significance in patients with AA. Note that AAs constitute the majority of nonenhancing malignant gliomas, that is, up to 86% in a recent population-based study.²³ Given that 34% of our patient population (35 of 102 patients) harbored nonenhancing AAs, our goal was to determine whether

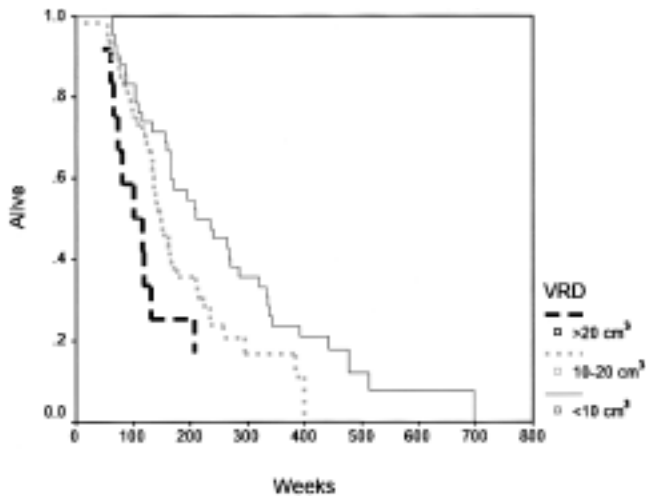


FIG. 3. Kaplan-Meier curve indicating survival from the time of initial surgery as it relates to the three subgroups of residual tumor volumes ($< 10 \text{ cm}^3$, $10\text{--}20 \text{ cm}^3$, and $> 20 \text{ cm}^3$) defined as hyperintensity on postoperative T_2 -weighted MR images.

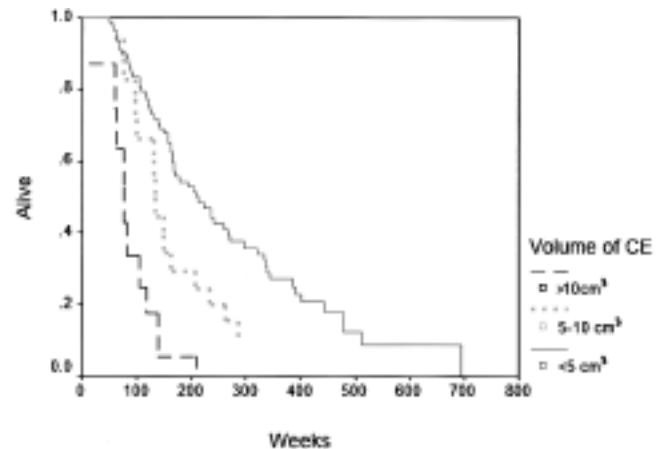


FIG. 4. Kaplan-Meier curve demonstrating survival from the time of initial surgery as it relates to the three subgroups of contrast-enhancing residual tumor volumes ($< 5 \text{ cm}^3$, $5\text{--}10 \text{ cm}^3$, and $> 10 \text{ cm}^3$) as depicted on postoperative T_1 -weighted MR images. $p = 0.003$.

our statistical analysis model should include enhancement characteristics. Our data show that when adjusted for other prognostic variables (age and KPS score), none of the enhancement-related variables (the presence or absence of contrast enhancement preoperatively, the actual volume of preoperative contrast enhancement, or the percentage of enhancing tumor volume), had prognostic importance in a histologically uniform group of AAs. Postresection enhancement, however, did have a statistically significant unfavorable effect on survival.

Since the study of Chamberlain, et al.,² who showed that some AAs lack contrast enhancement on computed tomography scans, several MR imaging-based studies have confirmed this imaging characteristic of AAs.^{7,14,23} Although results of these studies concord with the fact that non-enhancement does not indicate a low-grade glioma, that a significant proportion of nonenhancing gliomas may have anaplastic features, and that enhancement per se is associated with histological malignancy, none of these studies were focused on a histologically uniform group of AAs or whether the presence or absence of enhancement has prognostic significance. The prognostic effect of contrast enhancement has been specifically evaluated in anaplastic oligodendrogliomas.⁴ The authors of this study found that the median survival time was 3 years as opposed to 11 years, the 5-year survival rates were 21% rather than 81%, and the 8-year survival rates were 7% rather than 59%, for enhancing and nonenhancing tumors, respectively. This study was non-volumetric, and contrast enhancement was only evaluated as present or absent. In addition, the authors might have refined their analysis by evaluating the status of contrast enhancement postoperatively.

In another report that included 69 AAs that were studied using computed tomography, the authors found preoperative ring enhancement to be associated with longer survival.²⁵ Two other studies focused on dynamic MR imaging included AAs.^{17,26} In evaluating malignant gliomas, Wong, et al.,²⁶ showed that higher maximum Gd uptake rates were associated with shorter survival. Lev, et al.,¹⁷ compared nor-

malized cerebral blood volume maps generated using dynamic spin echo MR imaging with conventional MR imaging enhancement. Although the correlation with survival was stronger for normalized cerebral blood volume maps, enhancement on preoperative MR images correlated with an unfavorable prognostic effect on survival.¹⁷ In neither of these studies were AAs analyzed separately.

Our data suggest that the prognosis of AA does not depend on the preoperative contrast-enhancement characteristics of the tumor; that is, in patients with a diagnosis of AA according to the current histological criteria, outcome is independent of the presence or absence of preoperative contrast enhancement. The volume of postresection enhancement does, however, have a statistically significant unfavorable relation to survival, and this finding confirms the importance of extensive resection of the enhancing portion of the tumor. In addition, future studies directed at the analysis of the prognostic significance of contrast enhancement may be strengthened by the evaluation of not only the preoperative enhancement features but also the postoperative enhancement characteristics of the residual tumor. In a recent MR spectroscopy study in 28 patients with GBM, enhancing residual disease was associated with shorter survival on univariate analysis but not on multivariate analysis.²⁰

Extent of Resection and VRD

In the literature, AAs have been typically reported in high-grade glioma series together with GBMs and other anaplastic gliomas. Most of these studies have not involved the analysis of the subgroup of AAs separately in terms of the prognostic importance of the extent of resection.²⁴ There are a few studies, although none volumetric, in which the extent of resection for AAs has been analyzed.^{3,19}

Based on 109 AAs and 24 anaplastic mixed gliomas included in an RTOG study (83-02) in patients who had undergone gross-total or subtotal resection, median survival time was 6 years compared with 1.5 years in patients who had undergone a biopsy procedure alone ($p < 0.0001$).⁵ The

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determination of the extent of resection in this study was nonvolumetric, and the AA data excluding the 24 mixed gliomas were not separately analyzed. In a study based on 103 patients in whom “astrocytoma with anaplastic foci” had been diagnosed and who had been identified from the radiotherapy carmustine arms of three RTOG malignant glioma trials (including the RTOG 83-02 report⁵ mentioned previously), surgery involved biopsy procedure in 30%, partial resection in 56%, and total resection in 14% of patients.³ The median survival time in those who had undergone partial or total resection was 49 months compared with 18 months in those who had undergone a biopsy procedure only ($p = 0.002$). On multivariate analysis, however, the extent of surgery did not prove to be predictive of outcome. The authors of this nonvolumetric analysis concluded that “the close correlation between young age and extensive surgery obscures the survival advantage for greater surgery seen with univariate analysis.”²³

In another study that included 33 AAs, the authors found that the survival rates in patients who had undergone total resections were significantly higher than those in patients who had undergone subtotal or partial resection ($p < 0.01$).¹⁹ Note, however, that there was no significant difference in the survival rates between patients treated with subtotal and partial resection, which was defined as more or less than 75% resection, respectively.

Recent data from the Glioma Outcomes Project included 147 Grade III gliomas.¹⁶ Although data were analyzed separately for Grade III and IV tumors, the exact number of AAs within the group of Grade III gliomas was not reported. In addition, the determination of the extent of resection was not based on imaging studies. The authors reported that patients with Grade III tumors who had undergone a biopsy procedure had a median survival time of 52 weeks compared with 87 weeks in patients who had undergone craniotomy and an unspecified amount of resection. The difference was statistically significant ($p < 0.0001$).

Analysis of our data showed that both residual tumor volume on T_2 -weighted MR images and residual contrast-enhancing tumor volume as depicted on T_1 -weighted MR images were statistically significant predictors of outcome (Table 2). When adjusted for age and KPS scores and analyzed in a stepwise multivariate statistical model, VRD on T_2 -weighted MR images was the most significant volume-related predictor of TTP, whereas the volume of residual contrast enhancement was the most significant predictor of OS (Table 3). Note that in a recent MR spectroscopy study, metabolically active tumor extended outside the T_2 region in 88% of patients by as much as 28 mm, and T_1 -weighted MR images suggested a lower volume and different location of active disease compared with MR spectroscopy.²² Therefore, our data suggest that patients with AAs may benefit from a resection that targets the hyperintensity depicted on T_2 -weighted MR images. Importantly, the location of the tumor relative to functional brain tissue may affect the extent of resection. To minimize morbidity while achieving extensive resections and adhering to a meticulous surgical technique, the use of preoperative functional imaging (for example, magnetic source imaging and diffusion tensor imaging) as well as intraoperative technologies such as neuro-navigation, sononavigation, cortical and subcortical stimulation mapping, and intraoperative MR imaging are crucial.

Our results on AAs show some differences from the nat-

ural history of low-grade astrocytomas. First, the importance of preoperative tumor volume, which has been shown to have a negative effect on outcome in patients with low-grade gliomas,^{10,21} does not appear to be a prognostic factor for AAs. In addition, the risk of malignant transformation, which is minimized with less residual tumor volume¹ in low-grade astrocytomas, does not seem to apply to AAs. These differences suggest that even a relatively small pre-resection tumor volume means a dismal AA prognosis and that even a relatively small residual tumor volume carries the risk of progressing to a GBM.

The current study represents a comprehensive analysis of a histologically uniform AA series along with a detailed analysis of contrast-enhancement characteristics and volumetrically assessed tumor volumes on MR imaging. Because prospective randomized studies addressing these issues are unlikely, a more feasible approach would be to conduct retrospective matched studies or to plan prospective observational trials including patients from institutions favoring different management strategies. These studies, if adequately planned—that is, taking into consideration multiple variables that influence the outcome in patients with AA—are likely to further our knowledge.

Conclusions

Our data show that in adult patients with hemispheric AAs, the VRD following the initial surgery as measured on T_2 -weighted MR images is a significant predictor of TTP. Although the presence or absence of preoperative contrast enhancement does not indicate outcome—possibly because of the presence of tumor cells beyond the enhancing volume—the actual volume of postresection contrast enhancement appears to be a statistically significant predictor of OS. Our data show that patients with hemispheric AAs who have a higher residual volume of contrast-enhancing tumor have a poor outcome when compared with those who have less enhancing residual tumor. Complete or near-complete resection of the area of T_2 hyperintensity, however, seems to be the most important therapeutic variable related to prognosis. Overall, these results suggest that adult patients with hemispheric AAs may benefit from an extensive initial surgery to achieve maximal resection of the contrast-enhancing volume with the minimal volume of residual disease possible on T_2 -weighted MR images.

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