

Role of Postoperative Conventional Radiation Therapy in the Management of Supratentorial Malignant Glioma

- with respect to survival outcome and prognostic factors -

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Purpose : To evaluate the role of conventional postoperative adjuvant radiotherapy in the management of supratentorial malignant glioma and to determine favorable prognostic factors affecting survival

Material and Methods : From Sep. 1985 to Mar. 1997, the number of eligible patients who received postoperative radiotherapy completely was 69. They ranged in age from 7 to 66 years (median, 47). Forty-two (61%) patients were glioblastoma multiforme and the other 27 (39%) were anaplastic astrocytoma. Twenty patients (29%) had Karnofsky score equal or more than 80 preoperatively. Forty-three patients (62%) had symptom duration equal or less than 3 months. Twenty-four patients (35%) had gross total resection and forty patients (58%) had partial resection, the remaining five patients (7%) had biopsy only. Radiotherapy dose ranged from 50.4 Gy to 61.2 Gy (median, 55.8; mode, 59.4) with fraction size of 1.8 Gy-2.0 Gy for 33-83 days (median, 48) except three patients delivered 33, 36, 39 Gy, respectively with fraction size of 3.0 Gy due to poor postoperative performance status. Follow-up rate was 93% and median follow-up period was 14 months.

Results : Overall survival rate at 2 and 3 years and median survival were 38%, 20%, and 16 months for entire patients; 67%, 44%, and 34 months for anaplastic astrocytoma; 18%, 4%, and 14 months for glioblastoma multiforme, respectively ($p=0.0001$). According to the extent of surgery, 3-year overall survival for gross total resection, partial resection, and biopsy only was 38%, 11%, and 0%, respectively ($p=0.02$). The 3-year overall survival rates for patients age $40>$, $40-59$, and $60\leq$ were 52%, 8%, and 0%, respectively ($p=0.0007$). For the variate of performance score $80\leq$ vs $80>$, the 3-year survival rates were 53% and 9%, respectively ($p=0.008$). On multivariate analysis including covariates of three surgical and age subgroups as above, pathology, extent of surgery and age were significant prognostic factors affecting overall survival. On another multivariate analysis with covariates of two surgical (total resection vs others) and two age ($50>$ vs $50\leq$) subgroups, then, pathology, extent of surgery and performance

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status were significant factors instead of age and 3-year cumulative survival rate for the five patients with these three favorable factors was 100% without serious sequela.

Conclusion: We confirmed the role of postoperative conventional radiotherapy in the management of supratentorial malignant glioma by improving survival as compared with historical data of surgery only. Patients with anaplastic astrocytoma, good performance score, gross total resection and/or young age survived longest. Maximum surgical resection with acceptable preservation of neurologic function should be attempted in glioblastoma patients, especially in younger patients. But the survival of most glioblastoma patients without favorable factors is still poor, so other active adjuvant treatment modalities should be tried or added rather than conventional radiation treatment alone in this subgroup.

Key Words : Postoperative Radiation Therapy, Supratentorial Malignant Glioma

INTRODUCTION

Malignant gliomas constitute 33–45% of primary brain tumor and the majority of them (up to 85%) are glioblastoma multiforme.¹⁾ Survival for these patients has been increased by adding postoperative adjuvant radiotherapy but its outcome is still poor. Despite of recent advances of therapeutic strategies such as altered fractionation,²⁾ boost of brachytherapy,³⁾ adjuvant chemotherapy,⁴⁾ addition of hypoxic cell radiosensitizer or halogenated pyrimidine analogs,⁵⁾ etc, the survival gain of these has been no real breakthrough over the conventional radiotherapy with limited success for selected patients. Pretreatment prognostic factors in malignant glioma may have an even greater effect on the outcome than minor modifications in therapy. We evaluated the role of conventional postoperative radiotherapy in the treatment of malignant glioma retrospectively in terms of survival and tried to determine any favorable prognostic factors or patient subgroups.

MATERIALS AND METHODS

1. Patient Characteristics

From Sep. 1985 through Mar. 1997, eighty-four patients with histologically confirmed supratentorial malignant gliomas were registered for the postoperative adjuvant radiotherapy at our department.

Of them, fourteen patients received incomplete radiotherapy and one patient's record was not available, so the remaining 69 patients were eligible. Various patient-related characteristics are tabulated in Table 1. Patients ranged in age from 7 to 66 years (median, 47). Performance status was scored preoperatively based on Karnofsky scale.⁶⁾ Three most common presenting symptoms are headache, motor weakness, vomiting, etc, and 26 (38%) patients had any one of the symptoms for more than 3 months before surgical intervention.

2. Tumor Characteristics

Histopathologic criteria was based on WHO 4 grading system⁷⁾ and 27 (39%) patients had anaplastic astrocytoma (AA) and the other 42 (61%) had glioblastoma multiforme (GM). In the AA group, five patients were diagnosed to anaplastic mixed astrocytoma with oligodendroglial component. In GM group, one patient was a gliosarcoma in which a component of sarcoma is admixed with the glioma and its prognosis is known to be similar to that of GM.¹⁷⁾ The most frequent site of main tumor mass was frontal lobe in 26 patients (38%) and the next was parietal lobe in 20 (29%), temporal lobe in 13 (19%), basal ganglia or thalamus in seven (10%), multiple lobes in two, occipital lobe in one patient, respectively. Other tumor-related characteristics are also shown in Table 1.

Table 1. Patient and Tumor-related Characteristics

Characteristics	No. of patients(%)
Age (years)	
40>	23 (33)
40-59	32 (47)
60≤	14 (20)
Gender	
male	37 (54)
female	32 (46)
Performance score	
80≤	20 (29)
80>	49 (71)
Motor deficit	
present	37 (54)
absent	32 (46)
Change in mental status	
present	20 (30)
absent	49 (70)
Seizure	
present	6 (9)
absent	63 (91)
Symptom duration (months)	
3<	26 (38)
3≥	43 (62)
Tumor histology	
anaplastic astrocytoma (AA)	22 (32)
mixed AA	5 (7)
glioblastoma multiforme (GM)	41 (59)
gliosarcoma	1 (2)
Tumor size (cm)	
6>	34 (49)
6≤	35 (51)
Main tumor location	
frontal lobe	26 (38)
parietal lobe	20 (30)
temporal lobe	13 (19)
others	10 (13)

3. Treatment

Table 2 lists treatment-related characteristics. Radiotherapy was performed by 6-MV X-ray LINAC with daily dose of 1.8-2.0 Gy five times per week up to 50.4-61.2 Gy (median, 55.8; mode, 59.4) of total dose in most patients for 33-83 days (median, 48). But three patients were treated by 3.0 Gy fraction size with total dose up to 33, 36, 39 Gy respectively because of poor performance status postoperatively. Before the era of routine use of MRI, target volume included contrast-enhancing lesion only on preoperative CT scan with 3 cm margin and was reduced after 45-50 Gy with 1-2 cm margin. Since 1992, target volume also included edema with 1-2 cm margin on preoperative MRI

Table 2. Treatment-related Characteristics

Characteristics	No. of patients(%)
Extent of resection	
gross total	24 (35)
partial	40 (58)
biopsy	5 (7)
Radiotherapy dose(Gy)	
59.4>	40 (58)
59.4≤	29 (42)
Radiotherapy duration(days)	
45>	18 (26)
45≤	51 (74)
Surgery to radiotherapy interval(days)	
22>	25 (36)
22≤	44 (64)
Chemotherapy	
yes	15 (22)
no	54 (78)

and was reduced after 45-50 Gy including contrast-enhancing lesion only with 1-2 cm margin. Chemotherapy was delivered to 15 patients with the agents of procarbazine, vincristine, BCNU or ACNU of 1 to 6 cycles after radiation treatment, but there was no strict indication for chemotherapy. Thirty-one out of 47 patients who could be evaluated for disease progression underwent salvage treatment such as surgery, chemotherapy, radiosurgery, or combined treatment for tumor progression.

4. Follow-Up

Of total 69, sixty-four patients were followed-up (93%) and five were lost. Final follow-up was obtained in April 1998. Follow-up range was 2- 103 months (median, 14). Follow-up was performed by reviewing medical records and calling or mailing to local government office or patient's home. Forty-seven patients (68%) could be evaluated in terms of progression-free survival (PFS). The term of disease progression was named only when radiological study revealed disease progression compared to previous postoperative image or on the date of salvage operation when radiological study was unavailable.

5. Statistical Methods

Overall survival and progression-free survival were measured from the date of surgery or biopsy to the date of death or last follow-up or local tumor progression, respectively. Statistical difference in

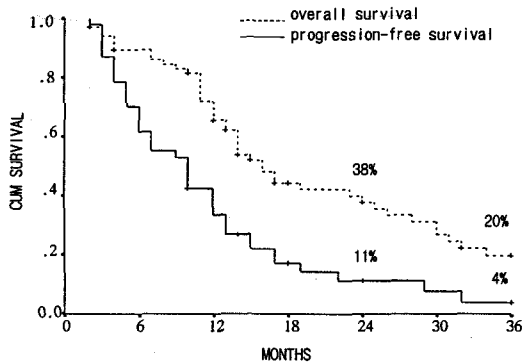


Fig. 1. Overall and progression-free survival in entire patients.

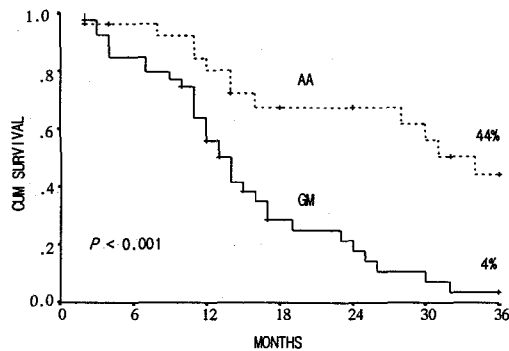


Fig. 2. Overall survival according to the histopathology.

patient proportion between groups was analyzed using Pearson χ^2 test. Estimates of overall survival and PFS were calculated by the Kaplan-Meier method. Statistical difference in survival between groups was evaluated by log-rank tests. Multivariate analysis was carried out using the stepwise Cox proportional hazard model. All these procedures were performed by SAS software version 6.12.

RESULTS

1. Overall Survival

Forty-seven patients (68%) died over the study period. Overall survival rates (OSR) at 2 and 3 years were 38% and 20%, respectively, for all patients (Fig. 1); 67% and 44%, respectively, for AA patients; and 18% and 4%, respectively, for GM

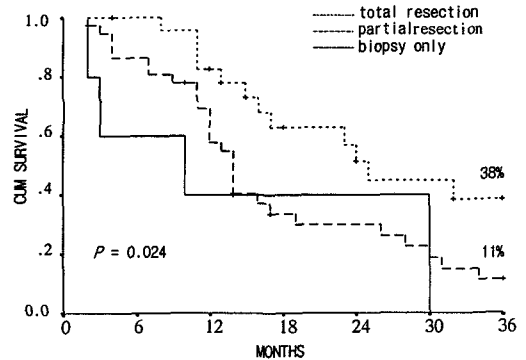


Fig. 3. Overall survival according to the extent of surgery.

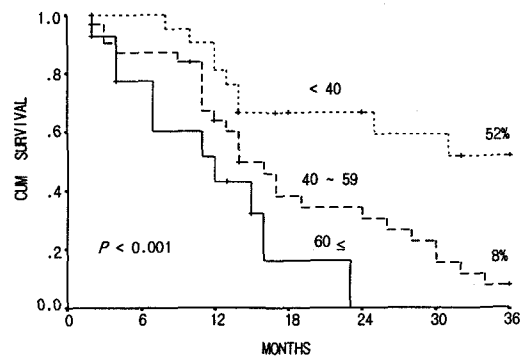


Fig. 4. Overall survival according to the age.

patients (Fig. 2). Median survival time (MST) was 16 months for all patients, 34 months for AA patients, and 14 months for GM patients and their difference was significant statistically ($p = 0.0001$). According to the extent of resection, MST were 25, 14, and 10 months and 3-year OSR were 38%, 11%, and 0% for the group of total resection, partial resection, and biopsy only, respectively (Fig. 3, $p = 0.02$). For the groups stratified by age ($40 >$ vs $40 \sim 59$ vs $60 \leq$), 3-year OSR was 52%, 8%, and 0%, respectively (Fig. 4, $p = 0.0007$). According to the performance score ($80 \leq$ vs $80 >$), 3-year OSR was 53% vs 9%, respectively (Fig. 5, $p = 0.008$). By the factor of symptom duration ($3 \text{ months} <$ vs $3 \geq$), 3-year OSR was 30% vs 13%, respectively (Fig. 6, $p = 0.03$).

2. Progression-Free Survival

In the eligible 47 patients (68%), the median time

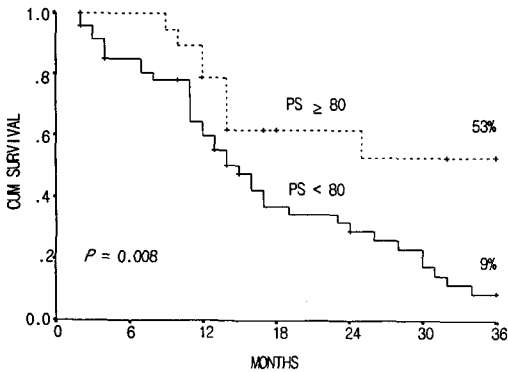


Fig. 5. Overall survival according to the performance score.

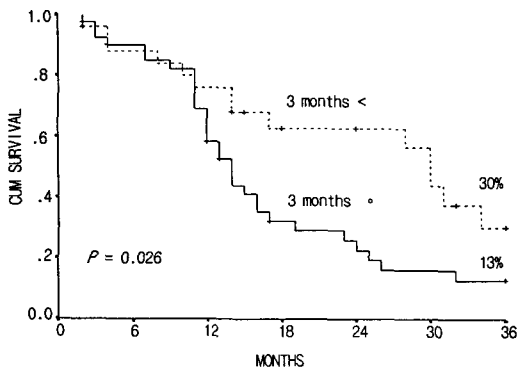


Fig. 6. Overall survival according to the number of prognostic factors.

to progressive tumor regrowth was 10 months with all patients and 13 versus 7 months for patients with AA vs GM, respectively ($p=0.003$). Median progression-free survival (MPFS) for patients with three age groups ($40>$ vs $40-59$ vs $60\leq$) were 12, 7, and 8 months, respectively ($p=0.038$). In male vs female patients, the MPFS was 10 vs 11.5 months, respectively and the difference was also significant statistically ($p=0.01$). According to the history of seizure, MPFS was 9.5 months for patients without history of seizure but the PFS for patients with seizure did not reach median ($p=0.047$).

3. Prognostic Factors

Fifteen potential prognostic variates factored into multivariate analysis were age ($40>$, $40-59$, $60\leq$), pathology (AA vs GM), tumor size ($6\text{ cm}\leq$ vs $6>$),

Table 3. Univariate and Multivariate Analysis of Potential Prognostic Factors for Overall Survival

Covariate	Univariate p -value	Multivariate p -value	Risk ratio (95% CI)
Pathology AA vs GM	<0.001	0.001	3.335 (1.598~6.958)
Extent of resection total vs partial vs biopsy	0.024	0.003	2.658 (1.505~4.693)
Age(years) 40> vs 40-59 vs 60≤	<0.001	0.003	2.178 (1.294~3.668)
Performance score 80≤ vs 80>	0.008		
Symptom duration (months) 3< vs 3≥	0.026	ns*	*

* : not significant statistically

tumor location (frontal lobe, parietal, temporal, others), gender, performance score ($80\leq$ vs $80>$), symptom duration ($3\text{ months}\geq$ vs $3<$), presence vs absence of motor deficit, mental change, and seizure, extent of surgery (gross total resection, partial resection, biopsy only), surgery to radiotherapy interval ($22\text{days}\leq$ vs $22>$), radiotherapy duration ($45\text{days}\leq$ vs $45>$), radiotherapy dose ($59.4\text{ Gy}\leq$ vs $59.4>$), adjuvant chemotherapy (yes vs no). Table 3 lists significant prognostic factors associated with improved OSR in all patients. Table 4 lists several prognostic factors in each pathology. In view of PFS, univariate analysis showed that pathology, age, gender and history of seizure were significant but only pathology and extent of surgery were significant on multivariate analysis.

4. Survival Analysis of Subgroups in AA

Survival outcomes for specific subgroups in AA are shown in Table 5. They were firstly stratified by performance status, which was the only significant variate on multivariate analysis in AA. Furthermore, in 17 patients of poor performance score ($80>$), they were again stratified by radiotherapy dose ($55\text{Gy}\leq$ vs $55>$), which was the only significant variate in this subgroup.

Table 4. Prognostic Factors in Each Pathology

Covariate	Univariate <i>p</i> -value	Multivariate <i>p</i> -value	Risk Ratio (95% CI)
Anaplastic astrocytoma			
Performance score (80≤ vs 80>)	0.02	0.016	8.296 (1.068–64.419)
Gender	0.03	ns [†]	*
Extent of surgery (total resection vs others)	0.03	ns	*
Pure AA* vs mixed AA	0.04	ns	*
Radiotherapy dose (55Gy< vs 55>)	<0.001	ns	*
Age (40> vs 40–59 vs 60≤)	0.08	ns	*
Glioblastoma multiforme			
Extent of surgery (total vs partial vs biopsy)	<0.001	0.017	5.076 (2.045–12.597)
Age (40> vs 40–59 vs 60≤)	0.25	0.006	2.647 (1.288– 5.441)
Tumor size (6 cm≤ vs 6>)	0.08	0.027	2.418 (1.083– 5.398)
Tumor site	0.02	ns	*
Performance score (80≤ vs 80>)	0.28	ns	*

*: anaplastic astrocytoma, †: not significant statistically

Table 5. Survival Outcome for Patients with AA* by the Most Significant Factor of Performance score (No. of patients: 27)

Subgroups	No. of patients	Median survival (months)	2-year survival (%)	<i>p</i> -value
Performance score				
80 ≤	10	NE [†]	89	
80 >				
RT [‡] dose 55 Gy ≤	17	28	56	0.01
55 Gy >	12	31	75	<0.01
	5	12	0	

*: anaplastic astrocytoma, †: no median estimable, ‡: radiation therapy

Table 6. Survival Outcome for Patients with GM* by the Most Significant Factor of Extent of Surgery (No. of patients: 42)

Subgroups	No. of patients	Median survival (months)	2-year survival (%)	<i>p</i> -value
Gross total resection	13	17	22	
Partial resection	26	12	17	
Age (years)				
40>	6	NE [†]	50	
40–59	15	14	16	
60≤	5	7	0	0.001
Biopsy	3	3	0	<0.001

*: glioblastoma multiforme, †: no median estimable

5. Survival Analysis of Subgroups in GM

Survival outcomes for specific subgroups in GM are shown in Table 6. They were firstly stratified by the variate of extent of surgery, which was the most significant variate on multivariate analysis in GM. After this, in 26 patients with partial resection, they were again stratified by age variate, which was the most significant variate on multivariate analysis in

this subgroup. On the other hand, when GM patients are stratified to two surgical extents (resection vs biopsy), their median survival were 14 vs 3 months, respectively. Of them, in 39 patients who had resection, tumor size (6 cm≤ vs 6>) was the only significant factor and their median survival were 13 vs 16 months, respectively (*p*=0.03).

Table 7. Survival Outcome for Patients by the Number of Favorable Prognostic Factors Including Pathology(AA), Performance score(80≤), and Gross Total Resection

No. of factors	No. of patients	Median survival (months)	3-year survival (%)
3	5	NE*	100
2	13	NE	54
1	30	16	9
0	21	11	0

p-value < 0.001, *: no median estimable

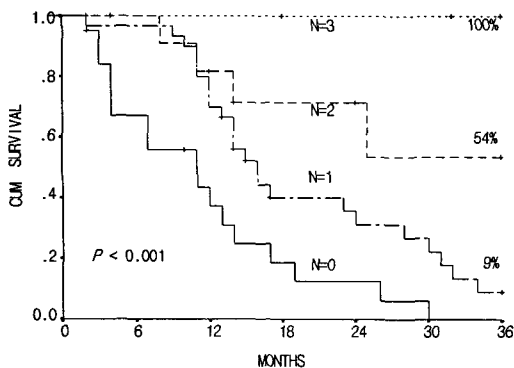


Fig. 7. Overall survival according to the duration of symptom.

6. Survival Analysis of Subgroups According to the Number of Prognostic Factors

Another multivariate analysis was performed with different splitting nodes of extent of surgery (total resection vs others) and age (50≤ vs 50>) from original three surgical and age subgroups so as to have only two subgroups in each variate, then, pathology of AA, total resection, and good performance score (80≤) were three favorable prognostic factors. The overall cumulative survival rate of five patients having all these three factors was 100% at 3 years (Table 7, Fig. 7) and they survived at the follow-up 18, 32, 36, 46, and 103 months, respectively, and they had suffered no serious treatment-related sequela until the end date of this study.

DISCUSSION

Our results also confirmed the role of radiotherapy in the management of malignant glioma in that postoperative adjuvant conventional radiotherapy improved outcome from 4-6 months treated by surgery alone of historical data⁸⁾ to 16 months of this study in terms of median survival. Median survival of our patients with AA and GM were comparable to those of other studies which reported 15-46 months for AA and 7-14 months for GM, respectively.^{4, 15, 16)}

There are several well-known prognostic factors affecting overall survival in malignant glioma^{1, 8)} such as pathologic grade, performance status, age, extent of surgery, duration of symptom, etc, all of which are also found to be significant on univariate analysis in our study. It is well known that anaplastic astrocytomas appear to be distinct and respond differently than GM. The relationship between age and survival outcome may in part reflect a greater proliferative potential of malignant glioma in older patients.⁸⁾ Performance status is of prognostic value by virtue of its dependence on the quantity and quality of neurologic defect.⁹⁾ The duration of symptom appears to be indicative of the rate of tumor growth.⁹⁾ Radical tumor removal has been known to be favorable to progression-free survival, overall survival, and improving functional status despite the terminology describing the extent of resection varying from surgeon to surgeon.¹⁰⁾ In our study, performance score and symptom duration lost statistical significance after adjustment for age and pathology. In fact, the variate of performance status was dependent on age variate with older patients having worse performance score (p=0.001) and the factor of symptom duration was dependent on pathology with AA patients having longer duration of symptom (p=0.001). As a result of multivariate analysis, three favorable factors affecting overall survival in entire patients are AA, gross total resection, and age younger than 40, and the eight patients with all these factors survived 87.5 % at 3 years.

In view of progression-free survival, history of seizure was one of the significant variates on univariate analysis. The history of seizure may predate the clinical diagnosis by months to years in patients with slowly growing tumors.¹¹⁾ Of six patients having history of seizure in our study, five had histology of AA and four had symptom duration more than 3 months (mean, 18months). But this variate has not been consistently observed to be significant across all historical data. Only pathology and extent of surgery were significant variates of multivariate analysis affecting progression-free survival.

We tried to determine the survival outcome for the most favorable subgroups in each pathology criteria. Patients were stratified by the most significant variate on multivariate analysis in each pathology and again patients of subgroup were further stratified by another most significant variate on multivariate analysis in each subgroup and eventually we were able to construct the tree of subgroups by the order of significance of prognostic factors. In AA group, because performance status remained only significant factor after adjustment for all factors, the patients were firstly stratified by performance status. In the subgroup of good performance score ($80 \leq$), there was no further variate by which these patients could be stratified. But in subgroup of poor performance score ($80 >$), the patients were further stratified by radiotherapy dose which was only significant on multivariate analysis in this subgroup when we made a different node of dose ($55\text{Gy} >$ vs $55 \leq$) from original node ($59.4\text{Gy} >$ vs $59.4 \leq$). On the contrary, all ten patients in subgroup of AA and good performance score ($80 \leq$) received radiotherapy dose more than 55 Gy. It was likely that patients with good performance score were relatively younger than those with poor performance score (median, 33.5 vs 47 years) and this allowed them the full course of radiotherapy. From this result, we could again validate that radiotherapy for AA requires a total dose of at least 55 Gy by conventional fractionated radiation schedule. The presence of oligodendroglial component (mixed AA) was one of the significant variates on univariate

analysis in AA. Several reports said that there were better survival outcomes in AA patients with oligodendroglial component as well as in GM patients than in each pure pathology.^{12, 13)} The 2-year survival rates of mixed AA and pure AA patients in our study were 100% vs 59%, respectively ($p=0.04$). But on multivariate analysis, all variates including this mixed pathology lost their significance except performance status only and actually all these mixed AA patients were included in favorable performance status ($80 \leq$).

In GM group, when patients were stratified by extent of surgery, the most significant factor on multivariate analysis in GM, there was no further significant variate in total resection group or biopsy only group possibly because of the small number of patients. But in 26 patients with partial resection group, they were again stratified to three age subgroups which was the most significant variate on multivariate analysis in partial resection group of GM. Among them, six patients with at least partial resection and younger than 40 survived 50% at both 2 and 3 years and median was not reached. With extent of surgery, main tumor site was also significant in univariate analysis in GM patients. Simpson, et al, said that frontal lobe was the favorable factor in multivariate analysis affecting survival in GM.¹⁴⁾ Also, our result shows that median survival times for patients of frontal, parietal, temporal lobe and other site were 17, 11.5, 17, and 10 months, respectively ($p=0.02$), but the survival for patients of frontal and temporal lobe were similar and this factor of tumor site lost its significance after adjustment for other variates including the extent of surgery.

When multivariate analysis was performed with different nodes of extent of surgery (total resection vs others) and age ($50 \leq$ vs $50 >$) in all patients, then, pathology, extent of surgery, and performance score remained the three significant covariates instead of age. It seems that the significance of age disappeared because the power of age variate, which is a continuous variate in nature, weakened after age was stratified to more discrete subgroups from 3 to only 2.

In conclusion, we confirmed the role of post-operative conventional radiotherapy in the management of this tumor by improving survival as compared with historical data of surgery only. Patients with anaplastic astrocytoma, good performance score, gross total resection and/or young age survived longest. Maximum surgical resection with acceptable preservation of neurologic function should be attempted in glioblastoma patients of especially younger age. But the survival of most glioblastoma patients without favorable factors is still poor, so other active adjuvant treatment modalities (i. e., hyperfractionation, concurrent chemotherapy, stereotactic radiosurgery, brachytherapy, etc) should be tried or added rather than conventional radiation treatment alone in this subgroup.

REFERENCES

1. **Leibel SA, Scott CB, Pajak TF.** The management of malignant gliomas with radiotherapy: Therapeutic results and research strategies. In: Tepper JE, eds. *Seminars in radiation oncology*. Philadelphia, PA: WB Saunders Co. 1991; 1:32-49
2. **Werner-Wasik M, Scott CB, Nelson DF, et al.** Final report of a phase I/II trial of hyperfractionated and accelerated hyperfractionated radiation therapy with Carmustine for adults with supratentorial malignant gliomas, RTOG 83-02. *Cancer* 1996; 77: 1535-1543
3. **Sneed PK, Lamborn KR, Larson DA, et al.** Demonstration of brachytherapy boost dose-response relationships in glioblastoma multiforme. *Int J Radiat Oncol Biol Phys* 1996; 35:37-44
4. **Fine HA, Dear KGB, Loeffler JS, et al.** Meta-analysis of radiation therapy with or without adjuvant chemotherapy for malignant gliomas in adults. *Cancer* 1993; 71:2585-2597
5. **Prados MD, Scott CB, Rotman M, et al.** Influence of bromodeoxyuridine radiosensitization on malignant glioma patient survival: a retrospective comparison of survival data from Northern California Oncology Group(NCOG) and Radiation Therapy Oncology Group trials(RTOG) for glioblastoma multiforme and anaplastic astrocytoma. *Int J Radiat Oncol Biol Phys* 1998; 40:653-659.
6. **Rubin P, McDonald S, Keller JW.** Staging classification of cancer: a unified approach. In: Perez CA, Brady LW, eds. *Principles and practice of radiation oncology*. 2nd ed. Philadelphia, PA: Lippincott Co. 1992; 163-172
7. **Zulch KL.** Histologic classification of tumors of the central nervous system. *International histologic classification of tumors*. No. 21, Geneva, World Health Organization, 1979
8. **Leibel SA, Scott CB, Loeffler JS.** Contemporary approaches to the treatment of malignant gliomas with radiation therapy. In: Yarbro JW, eds. *Malignant Astrocytomas. Seminars in oncology*. Philadelphia, PA: WB Saunders Co. 1994; 21:198-219
9. **Walker MD, Green SB, Byar DP, et al.** Randomized comparison of radiotherapy and nitrosourea for the treatment of malignant gliomas after surgery. *N Eng J Med* 1980; 303:1323-1329
10. **Berger MS.** Malignant astrocytoma: surgical aspects. In: Yarbro JW, eds. *Malignant Astrocytomas. Seminars in oncology*. Philadelphia, PA: WB Saunders Co. 1994; 21:172-185
11. **Levin VA, Leibel SA, Gutin PH.** Neoplasms of the central nervous system. In: DeVita VT, Hellman S, Rosenberg SA, eds. *Cancer: principles and practice of oncology*. 5th ed. Philadelphia, PA: Lippincott Co. 1997; 2022-2082
12. **Donahue B, Scott CB, Nelson JS, et al.** Influence of oligodendroglial component on the survival of patients with anaplastic astrocytomas: a report of Radiation Therapy Oncology Group 83-02. *Int J Radiat Oncol Biol Phys* 1997; 38:911-914
13. **Nelson JS, Petito CK, Scott CB, et al.** Glioblastoma with oligodendroglial features (GBM-OL). report from RTOG trial 83-02. (Abstr.) *Lab Invest* 1996; 74: 141A
14. **Simpson JR, Horton J, Scott C, et al.** Influence of location and extent of surgical resection on survival of patients with glioblastoma multiforme: results of three consecutive Radiation Therapy Oncology Group(RTOG) clinical trials. *Int J Radiat Oncol Biol Phys* 1993; 26:239-244
15. **Choi DH, Lee HK, Hong SE.** Radiotherapy results of malignant astrocytoma and glioblastoma multiforme. *J Korean Soc Ther Radiol Oncol* 1992; 10:163-169
16. **Chang SK, Suh CO, Lee SW, et al.** Analysis of prognostic factors in glioblastoma multiforme. *J Korean Soc Ther Radiol Oncol* 1996; 14:181-189
17. **Bruner JM.** Neuropathology of Malignant glioma. In: Yarbro JW, eds. *Malignant Astrocytomas. Seminars in oncology*. Philadelphia, PA: WB Saunders Co. 1994; 21:126-138

= 국문 초록 =

천막상부 악성 신경교종에서 수술 후 방사선 치료의 역할 - 생존율과 예후인자 분석 -

전남대학교 의과대학 방사선종양학교실

남택근 · 정웅기 · 안성자 · 나병식

목 적 : 천막상부 악성 신경교종의 치료로서 수술 후 방사선 치료의 역할을 생존율을 중심으로 평가하며 그 예후 인자를 분석한다.

대상 및 방법 : 1985년 9월부터 1997년 3월까지 수술 후 방사선 치료를 받은 69례의 환자를 대상으로 분석하였고 나이의 범위는 7세에서 66세이며 중앙값은 47세였다. 42례(61%)는 다형성 교모세포종 이었고 27례(39%)는 악성 성상세포종이었다. 20례(29%)는 Karnofsky 역할수행 능력 점수가 80점 이상이였다. 43례(62%)는 수술 전 3개월 이내에 증상을 호소하였다. 24례(35%)는 육안 상 완전 절제를, 40례(58%)는 부분 절제를, 나머지 5례(7%)에서는 뇌경위 조직검사만 시행하였다. 총 방사선 조사량은 50.4-61.2Gy(중앙값, 55.8; 최빈값, 59.4)로 하루 1.8-2.0 Gy 씩 33-83일 동안(중앙값, 48) 치료하였다. 단 3례는 수술 후 전신 상태의 불량으로 하루 3.0Gy 씩 각각 33, 36, 39Gy 까지 치료하였다. 추적 관찰율은 93%였고 중앙값은 14개월이었다.

결 과 : 전체 환자의 2년 및 3년 생존율과 중앙 생존기간은 각각 38%, 20%, 16개월이었다. 악성 성상세포종과 다형성 교모세포종의 중앙생존기간은 각각 34, 14개월이었다($p=0.0001$). 완전 절제, 부분절제, 뇌경위 조직검사군에서의 3년 생존율은 각각 38%, 11%, 0%였다($p=0.02$). 연령이 40세 미만, 40-59, 60세 이상 군의 3년 생존율은 각각 52%, 8%, 0%였다($p=0.0007$). 역할수행 능력점수 80점 이상과 80점 미만군의 3년 생존율은 각각 53%, 9%였다($p=0.008$). 상기와 같이 절제 정도에 따른 3개의 수술 군과 3개의 연령 군을 포함한 다요인 분석에서 병리학적 등급, 수술 정도, 연령이 유의한 인자였다. 그러나 2개의 수술 군(완전 절제와 비완전 절제)과 2개의 연령 군(50세 미만과 50세 이상)을 공변량으로한 다요인 분석에서 연령대신 병리학적 등급, 수술 정도, 역할수행 능력이 유의한 인자였고, 이들 세 가지 요인을 갖춘 5례는 치료와 관련한 심각한 부작용 없이 3년 누적생존율이 100%로 생존하고 있다.

결 론 : 악성 신경교종의 치료에서 수술 후 방사선치료를 추가함으로써 기존의 수술 단독의 생존율을 향상시키는 역할을 확인할 수 있었다. 악성 성상세포종 환자 중, 특히 양호한 역할수행 능력과 완전 절제를 받은 환자군의 생존율이 가장 양호하였다. 다형성 교모세포종 환자에서는 특히 젊은 나이인 경우 적절한 신경학적 기능보존과 함께 최대한의 중앙 절제가 선행되어야 할 것으로 생각된다. 그러나 양호한 예후 인자를 갖지 못한 대부분의 다형성 교모세포종 환자군의 생존율은 여전히 좋지 않아 이 환자 군에서는 수술 후 통상적인 방사선 치료보다는 다른 적극적인 치료가 추가 또는 시도되어야 할 것으로 생각된다.