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Treatment Results of Glioblastoma during the Last 30 Years in a Single Institute

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Abstract

Treatment results of glioblastoma (GB) during the last 30 years in Tohoku University were analyzed to identify any improvements in patient outcome in all 332 histologically proven cases of newly diagnosed GB treated consecutively in our department between 1982 and 2011. These 30 years was divided into 5 treatment eras, Group 1 (1982–1988, without preoperative evaluation by magnetic resonance [MR] imaging, n = 46), Group 2 (1989–1996, with preoperative MR imaging, n = 41), Group 3 (1997–1999, additionally underwent intraoperative functional brain mapping and neuronavigation system, n = 38), Group 4 (2000–August 2006, underwent 30 Gy of whole brain radiation followed by 30 Gy of extended local accelerated hyperfractionated radiation therapy, n = 96), and Group 5 (September 2006–2011, adjuvant usage of temozolomide [TMZ], n = 111). Overall survival (OS) was calculated from the date of surgery to the death from any cause. The median survival time/2-year OS/5-year OS of Groups 1 to 5 were 10.7 months/10.9%/0%, 17.3 months/26.2%/6.9%, 15.9 months/23.7%/5.3%, 20.1 months/34.8%/15.5%, and 20.9 months/45.5%/19.7%. The prognosis for patients with GB improved significantly after the introduction of MR imaging. Younger GB, defined as patients aged below 60 years, or total tumor resection with all ages in Group 5 had 5-year 0S of 31.0% and 30.1%, respectively. The prognosis of GB was improved significantly after the introduction of TMZ for elderly GB, recursive partitioning analysis class 5, or totally resected GB. Introduction of MR imaging and TMZ, and total resection of the tumor were important in the improvement of outcome for patients with GB.

Key words: glioblastoma, magnetic resonance imaging, surgery, survival, temozolomide

Introduction

Glioblastoma (GB) is the most common primary brain tumor and also has the poorest outcome, often with median survival time (MST) of only around a year. Analysis of 625 patients who underwent surgery for histologically confirmed GB between 1993 and 2004 in Atkinson Morley's Unit concluded that the survival of patients with GB had not changed.[12] Overall MST was 189 days (6.3 months). Assessment of patterns

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of diagnosis and relative survival rates across time with respect to the histological type of tumor using the population-based data from the Surveillance, Epidemiology, and End Results (SEER) Program of the US National Cancer Institute (1973–1999) revealed that patients with GB continued to have the poorest survival times.[1] Therefore, the survival times of patients with GB had not changed for more than two or three decades, despite neurosurgical advances, before the introduction of temozolomide (TMZ).[1,4,12]

Further analysis using the SEER database of 34,664 patients aged 20 years or older treated under a diagnosis of GB during the years 1973 to 2008 found that patients diagnosed with GB during the years 2000 to 2008 had a superior survival rate compared with earlier decades ($p \leq 0.001$).[13] A randomized clinical trial (European Organisation for Research and Treatment of Cancer (EORTC)/National Cancer Institute of Canada (NCIC) 22981/26981) in 2005 showed that TMZ administered with radiation therapy (RT) followed by adjuvant TMZ was effective.[11] MST could be prolonged to 14.6 months compared to 12.1 months in the control arm receiving only RT. Furthermore, almost 20% of the patients receiving TMZ with RT survived for over 2 years. The estimated adjusted hazard ratio from the SEER database showed that patients diagnosed in 2005–2006 (treated after the EORTC/NCIC 22981/26981 trial in 2004) had significantly improved survival rates compared to patients diagnosed in 2000–2001.[5] The MST and 2-year overall survival (OS) of 15 months and 26% in 2005–2006 (n = 2094) was similar to the MST and 2-year OS seen in the EORTC/NCIC phase III study. These results are encouraging and suggest that the current treatment of GB in the United States is now associated with improved survival compared to previous time cohorts. The SEER research database does not specify whether chemotherapy was administered, but the majority of patients diagnosed in 2005–2006 were presumably treated with TMZ plus RT, which led to the survival benefit when compared to earlier time periods. Widespread adoption of TMZ represents the most likely explanation for this survival improvement, although other treatment advances, such as increased extent of surgical resection, may also be important.[2] Analysis of 1,157 GB patients to investigate the effect of TMZ added to RT at population level, using the Cancer Registry of Norway, concluded that TMZ provided a 7.6-month OS benefit in the matched group analysis.[7]

Tohoku University Hospital is a flagship hospital in Sendai City, Miyagi Prefecture, in the middle of the Tohoku district. Patients are admitted from regional referring hospitals to our hospital. More than 90% of patients with GB in Miyagi Prefecture, with a population of about 2 million, are treated in our hospital. In addition, complicated cases including deep-seated or insulo-opercular tumors and tumors near/within eloquent areas are referred to our hospital from all parts of Tohoku district. The present study analyzed consecutive patients with newly diagnosed GB admitted since 1982 to assess trends in clinical characteristics over a 30-year period.

Materials and Methods

I. Data collection

Data was collected for the period 1982–2011 from the patient records and the electronic neurosurgical database. Only patients with histopathologically confirmed GB were included. Patient age, sex, performance status, date and type of surgery, adjuvant treatment, and length of survival were recorded. Recursive partitioning analysis (RPA) classification, proposed by the Radiation Therapy Oncology Group in 2011,[6] was utilized to evaluate the treatment results.

II. Historical changes of patient management and patient population

A total of 332 patients with newly diagnosed GB were treated consecutively in our department between 1982 and December 2011. All patients fundamentally underwent surgery to achieve the most extensive tumor resection possible. Two hundred and seventy patients underwent radical resection, and residual 62 underwent biopsy. RT was started within 2 weeks of surgery. Forty-six patients treated from 1982 to 1988 did not have preoperative evaluation by magnetic resonance (MR) imaging but by computed tomography (CT) (Group 1, pre MR era), 41 patients treated from 1989 to 1996 had preoperative MR imaging evaluation (Group 2, post MR era), and 38 patients treated from 1997 to 1999 underwent preoperative MR imaging with functional brain mapping and intraoperative navigation system monitoring (Group 3, post mapping era). Patients in these three groups received only extended local RT. The treatment volume for extended local RT was determined by the volume of the contrast-enhanced tumor on preoperative CT or MR imaging plus a 2-cm margin beyond the edema surrounding the tumor. In contrast, 96 patients aged below 70 years treated after 2000 underwent 30 Gy of whole brain RT followed by 30 Gy of extended local accelerated hyperfractionated (AHF) RT (Group 4, post whole brain radiation era). Patients aged 70 years and over were treated only with 60 Gy of extended

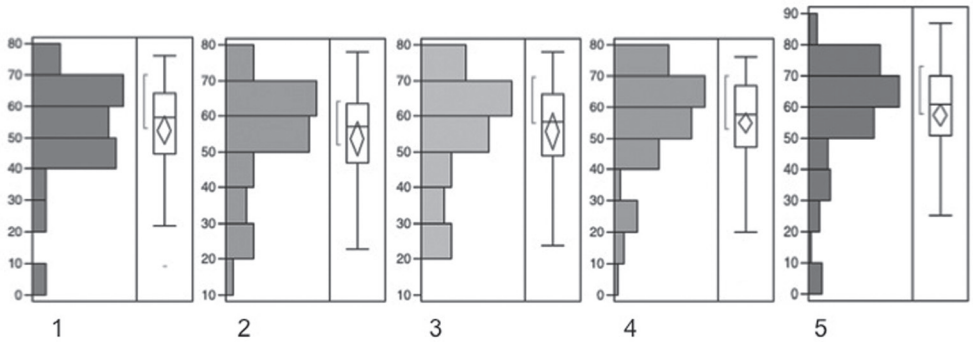

Fig. 1 Historical change of age distribution of patients with histologically proven glioblastoma in Tohoku University between 1982 and 2011. Numbers 1 through 5 correspond to Group 1 (1982–1988, pre magnetic resonance [MR] era), Group 2 (1989–1996, post MR era), Group 3 (1997–1999, post mapping era), Group 4 (2000–August 2006, post whole brain radiation era), and Group 5 (September 2006–2011, temozolomide era), respectively. Vertical axis indicates age.

local AHF RT to reduce the treatment period and damage to the whole brain.

Until 1996, nimustine hydrochloride, 1-(4-amino-2-methyl-5-pyrimidinyl)methyl-3-(2-chloroethyl)-3-nitrosourea (ACNU), was administered to all patients, but ACNU treatment was stopped for patients aged 60 years and over (elderly GB) after 1997, because of the relatively high complication rate. TMZ became available in Japan after September 2006. All newly diagnosed patients aged 60 years and over and all recurrent cases received TMZ (Group 5, TMZ era, n = 111). All patients with newly diagnosed GB including those aged below 60 years (younger GB) were treated by TMZ after April 2009.

III. Surgical resection rate

Volumetric extent of resection was calculated based on the difference in preoperative and postoperative contrast-enhanced tumor volumes (expressed as a percentage) and the extent of resection for each patient was classified as gross total resection (disappearance of enhanced lesion on postoperative imaging), subtotal resection (over 75% resection), and partial resection (under 75% resection).

IV. Statistical analysis

The primary end point used for this study was OS, calculated as the time from the surgery to death from any cause. Statistical analysis was performed on July 31, 2012. At the time of the data analysis, 47 patients (14.2%) were known to be alive at recent clinical follow-up examination and were appropriately censored in the survival analysis. Another 13 patients (3.9%) were lost to follow up without available records of death. The Kaplan-Meier method was used to estimate OS for each group, and the logrank test was performed to determine statistically significant differences between groups. Factors with prognostic significance on univariate analysis were assessed by the Cox proportional hazards model for multivariate analysis. Significance was accepted at $p < 0.05$. All statistical tests were performed using JMP pro 9.0.2 (SAS Institute, Cary, North Carolina, USA).

Results

I. Treatment eras and age distribution

The historical change in age distribution during these 30 years is summarized in Fig. 1. Aging of the population was obvious, and both median and average ages increased by around 5 years. Median/average ages in Groups 1 to 5 were 56.5/52.3, 57.0/53.7, 58.5/55.5, 57.5/54.9, and 61.0/57.4 years.

II. Treatment eras and OS

The MST/2-year OS/5-year OS of Groups 1 to 5 were 322 days (10.7 months)/10.9%/0%, 520 days (17.3 months)/26.2%/6.9%, 476 days (15.9 months) /23.7%/5.3%, 603 days (20.1 months) /34.8%/15.5%, and 628 days (20.9 months) / 45.5%/19.7% (Fig. 2, Table 1). The prognosis for patients with GB was improved significantly only after the introduction of MR imaging ($p = 0.0004$). The survival curves demonstrated a trend toward improving, but the changes were modest and not statistically significant. However, the 2-year OS of all 111 patients in Group 5, treated since the introduction of TMZ, exceeded 45% and 5-year OS almost reached 20%.

III. Age, treatment eras, and OS

The OS of younger GB (n = 173) was significantly better than that of elderly GB (n = 159) ($p < 0.0001$) (Fig. 3A, Table 2). As mentioned above, the population of elderly GB was increasing, as more than half of the

patients were aged 60 years and over in Group 5 (Fig. 3B). Analysis of the OS according to age showed that introduction of MR imaging significantly improved the outcome in both groups (younger GB, p = 0.0065; elderly GB, p = 0.0014) (Fig. 3C, D, Tables 3 and 4). The OS of elderly GB was worse than that of younger GB, but the introduction of TMZ was significantly associated with improved OS (p = 0.0005) (Table 4). In younger GB, there was no significant difference between Groups 4 and 5. However, the 5-year OS of 49 patients aged below 60 years in Group 5 was 31.0% (Table 3).

IV. Surgical resection rate, treatment eras, and OS

Total resection of the tumor (n = 175) was significantly associated with better prognosis (Fig. 4A, Table 5). Two-year, 5-year, and 10-year OS of the patients with total resection were 42.9%, 17.4%, and 7.3%, respectively. Around half of the enhanced lesions on CT/MR imaging could be resected totally. There were no significant differences in resection rate between the 5 groups (Fig. 4B). In the biopsy group, there was no significant difference during the 30 years of the study (Fig. 4C, Table 6). In contrast, in the total resection group, the introduction of MR imaging (p = 0.0002) and TMZ (p = 0.0194) were significantly correlated with better OS (Fig. 4D, Table 7). Five-year OS of patients of all ages with total resection in the TMZ era was 30.1%.

V. RPA classification, treatment eras, and OS

There were significant differences between the three RPA classes (Fig. 5A, Table 8). MST of PRA classes 3, 4, and 5 were 37.9, 20.5, and 15.8 months, respectively. Most patients were classified into PRA class 5. There were no significant differences in distribution of RPA classification during the treatment eras (Fig. 5B). Introduction of MR imaging was significantly associated with better prognosis in both classes 4 and 5 (class 4, p = 0.0026; class 5, p = 0.0217) (Fig. 5C–E, Tables 9–11). In class 5, adoption of TMZ was significantly correlated with improvement of OS (p = 0.0085) (Table 11). This outcome might be highly influenced by our treatment protocols for elderly patients.

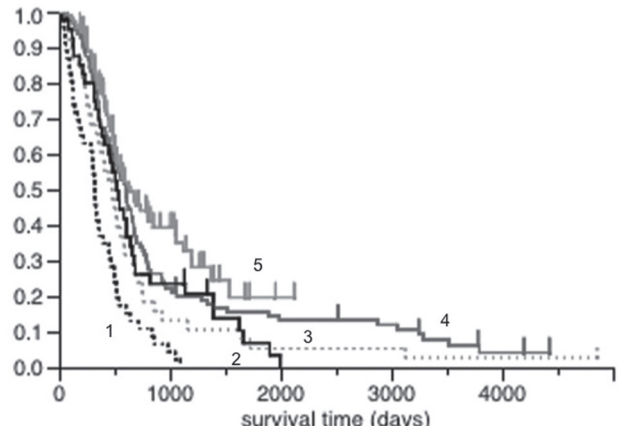

Fig. 2 Kaplan-Meier analysis of overall survival (OS) for histologically proven glioblastoma in Tohoku University between 1982 and 2011, stratified by the treatment eras. Numbers 1 through 5 correspond to Groups 1 (*black, dashed line*), 2 (*black, solid line*), 3 (*gray, dashed line*), 4 (*dark gray, solid line*), and 5 (*light gray, solid line*), respectively. Significantly increased OS was demonstrated between Groups 1 and 2 (p = 0.0004, logrank test).

VI. Prognostic factors

Multivariate analysis showed that all of the survival factors, introduction of MR imaging and TMZ, total resection of the tumor, age, and RPA classes previously identified by univariate analysis, were independent (Table 12). Introduction of MR imaging and total resection of the tumor were highly significant (p < 0.0001), followed by introduction of TMZ (p = 0.0004).

Table 1 Survival of patients with glioblastoma stratified by treatment era

Group (treatment era)	No. of patients	Median survival time (day)	Overall survival rate (%)			Probability			
			2-Year	5-Year	10-Year				
1	46	322	10.9	0.0	0.0	] p = 0.0004			
2	41	520	26.2	6.9	0.0		] NS		
3	38	476	23.7	5.3	2.6			] NS	
4	96	603	34.8	15.5	6.2				] NS
5	111	638	45.5	19.7	NR				

NR: not reached, NS: not significant.

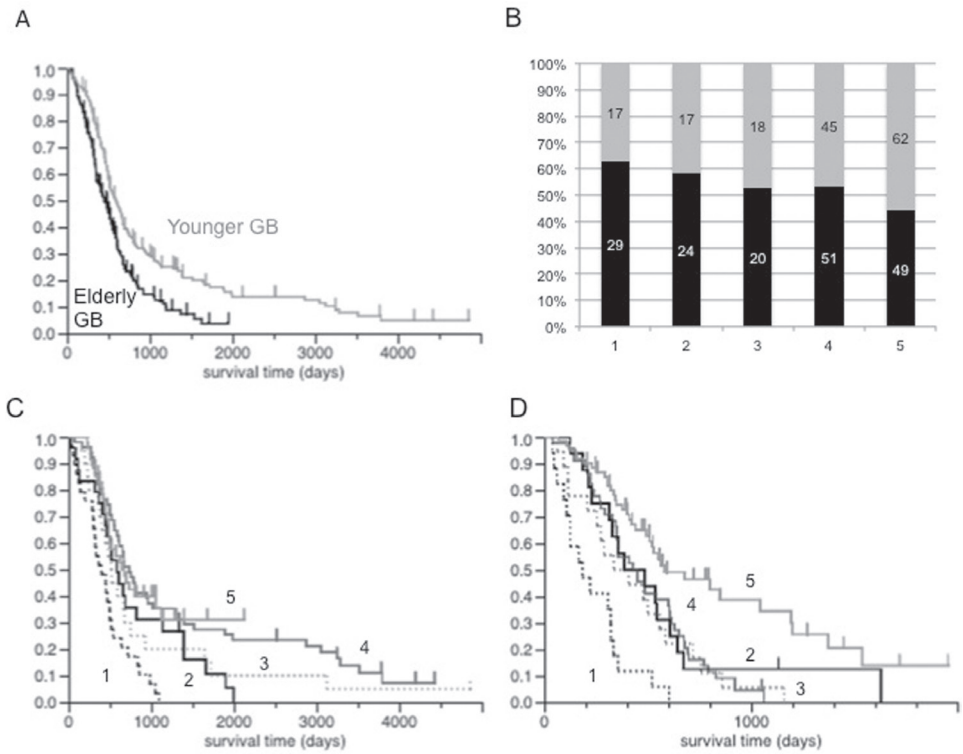

Fig. 3 A: Kaplan-Meier analysis of overall survival (OS) for histologically proven glioblastoma (GB) in Tohoku University between 1982 and 2011, stratified by the age groups. Younger and elderly GB were defined as patients aged below 60 years and those aged 60 years or over, respectively. There was a significant difference of OS between these two age groups ($p < 0.0001$, logrank test). B: Historical change of these two age groups stratified by the treatment eras. Numbers 1 through 5 correspond to Groups 1 through 5, respectively. In Group 5 (temozolomide era), more than half of the patients belong to the elderly GB. Younger and elderly GBs are indicated in gray and black, respectively. C: Kaplan-Meier analysis of OS for the younger GB, stratified by the treatment eras. Significantly increased OS was demonstrated between Groups 1 and 2 ($p = 0.0065$, logrank test). D: Kaplan-Meier analysis of OS for the elderly GB, stratified by the treatment eras. Significantly increased OS was demonstrated between Groups 1 and 2 ($p = 0.0014$, logrank test), and between Groups 4 and 5 ($p = 0.0005$, logrank test).

Table 2 Survival of patients with glioblastoma stratified by age group

Age group	No. of patients	Median survival time (day)	Overall survival rate (%)			Probability
			2-Year	5-Year	10-Year	
Younger	173	592	39	17.4	6.6	] $p < 0.0001$
Elderly	159	449	23.4	3.6	NR	

NR: not reached.

Table 3 Survival of younger patients with glioblastoma stratified by treatment era

Group (treatment era)	No. of patients	Median survival time (day)	Overall survival rate (%)			Probability			
			2-Year	5-Year	10-Year				
1	29	399	17.2	0.0	0.0	] $p = 0.0065$			
2	24	582	35.7	10.7	0.0		] NS		
3	20	518	30.0	10.0	5.0			] NS	
4	51	736	51.0	27.5	11.0				] NS
5	49	671	45.2	31.0	NR				

NR: not reached, NS: not significant.

Table 4 Survival of elderly patients with glioblastoma stratified by treatment era

Group (treatment era)	No. of patients	Median survival time (day)	Overall survival rate (%)			Probability			
			2-Year	5-Year	10-Year				
1	17	184	0.0	0.0	0.0	] p = 0.0014			
2	17	436	12.5	0.0	0.0		] NS		
3	18	373	16.7	0.0	0.0			] NS	
4	45	449	16.0	0.0	0.0				] p = 0.0005
5	62	581	46.4	13.8	NR				

NR: not reached, NS: not significant.

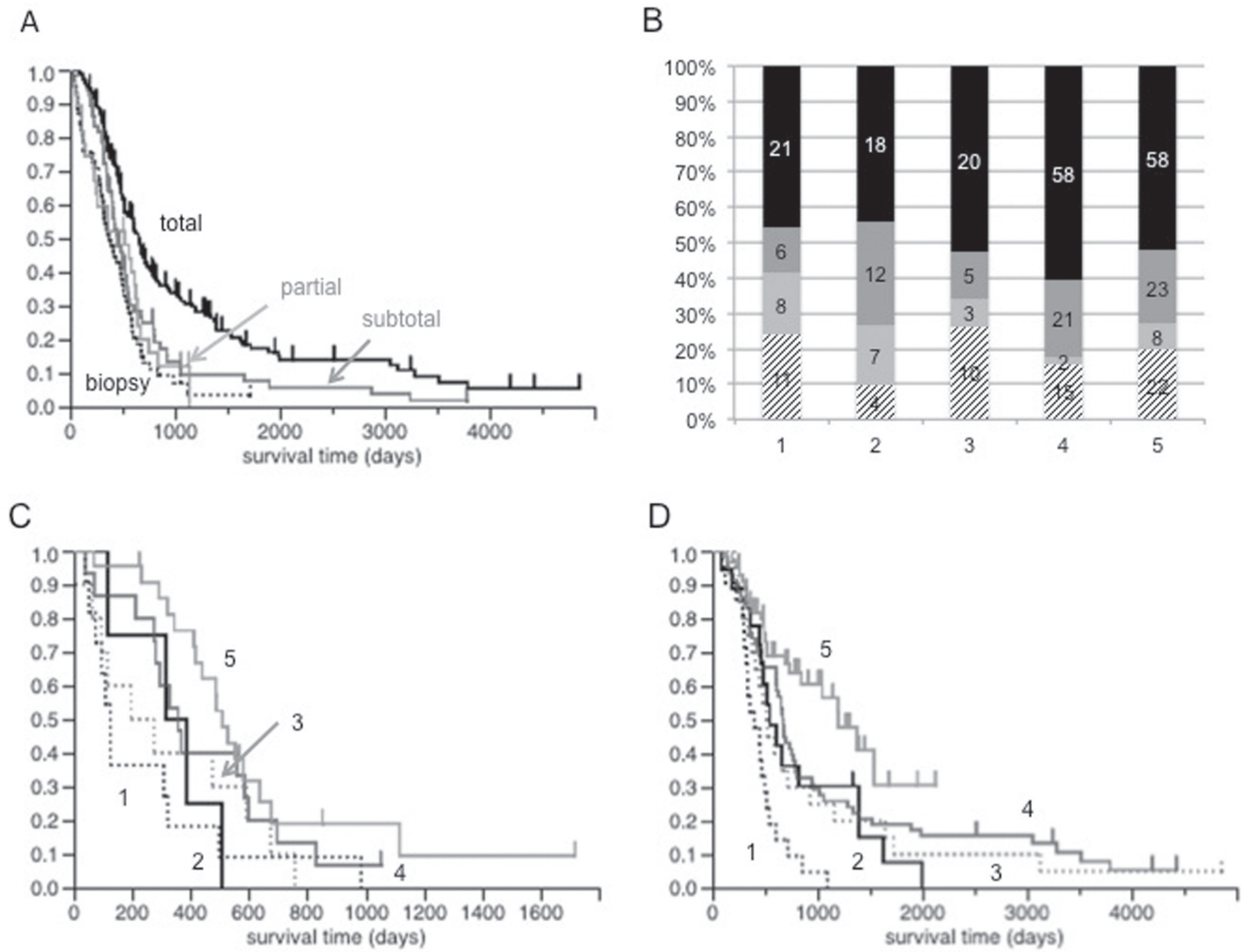

Fig. 4 A: Kaplan-Meier analysis of overall survival (OS) for histologically proven glioblastoma in Tohoku University between 1982 and 2011, stratified by the resection rate. Total, subtotal, and partial resection and biopsy are indicated in black, dark gray, light gray solid line, and black dashed line, respectively. There was a significant difference of OS between total and subtotal resection (p = 0.0011, logrank test). B: Historical change of resection rate stratified by the treatment eras. Total, subtotal, and partial resection and biopsy are indicated in black, dark gray, light gray, and black diagonal line, respectively. Numbers 1 through 5 correspond to Groups 1 through 5, respectively. C: Kaplan-Meier analysis of OS for the biopsied glioblastoma, stratified by the treatment eras. There was no significant difference. D: Kaplan-Meier analysis of OS for the totally resected glioblastoma, stratified by the treatment eras. Significantly increased OS was demonstrated between Groups 1 and 2 (p = 0.0002, logrank test), and between Groups 4 and 5 (p = 0.0194, logrank test).

Table 5 Survival of patients with glioblastoma stratified by surgical resection rate

Resection rate	No. of patients	Median survival time (day)	Overall survival rate (%)			Probability		
			2-Year	5-Year	10-Year			
Biopsy	62	369	13.0	NR	NR	] NS		
Partial	28	520	20.0	0.0	0.0		] NS	
Subtotal	67	451	24.9	7.7	1.9			] p = 0.0011
Total	175	657	42.9	17.4	7.3			

NR: not reached, NS: not significant.

Table 6 Survival of patients with biopsied glioblastoma stratified by treatment era

Group (treatment era)	No. of patients	Median survival time (day)	Overall survival rate (%)			Probability			
			2-Year	5-Year	10-Year				
1	11	125	9.1	0.0	0.0	] NS			
2	4	352	0.0	0.0	0.0		] NS		
3	10	235	10.0	0.0	0.0			] NS	
4	15	357	13.3	NR	NR				] NS
5	22	510	19.1	NR	NR				

NR: not reached, NS: not significant.

Table 7 Survival of patients with totally resected glioblastoma stratified by treatment era

Group (treatment era)	No. of patients	Median survival time (day)	Overall survival rate (%)			Probability			
			2-Year	5-Year	10-Year				
1	21	399	9.5	0.0	0.0	] p = 0.0002			
2	18	545	36.4	7.6	0.0		] NS		
3	20	518	30.0	10.0	5.0			] NS	
4	58	670	41.4	19.0	8.0				] p = 0.0194
5	58	1198	66.5	30.1	NR				

NR: not reached, NS: not significant.

Discussion

Definitive conclusions are always difficult to establish based on retrospective analyses because of the heterogeneous clinical materials and treatments. But the present study strongly suggests improvement of outcomes for patients with GB in Tohoku University during the last 30 years. In particular, the MST has doubled, and the 5-year OS of patients aged below 60 years and with total tumor resection after introduction of TMZ exceeded 30%. In our department, 30 of 332 patients with GB lived for more than 5 years.

Heterogeneous populations of patients containing various prognostic factors can be adjusted using the RPA classification to some extent in comparison with the other institutional results of GB. However, many more factors are clearly involved with the prognosis of GB, for example, O^6-methylguanine deoxyribonucleic acid methyltransferase promoter methylation status.[8] In addition, race is a factor affecting the survival of patients with GB. A significant difference in survival was seen in the Asian population compared to white, black, and other populations. Racial differences in survival are known in patients diagnosed with GB, with the Asian race having increased survival when compared to other races.[13] The reason for this are

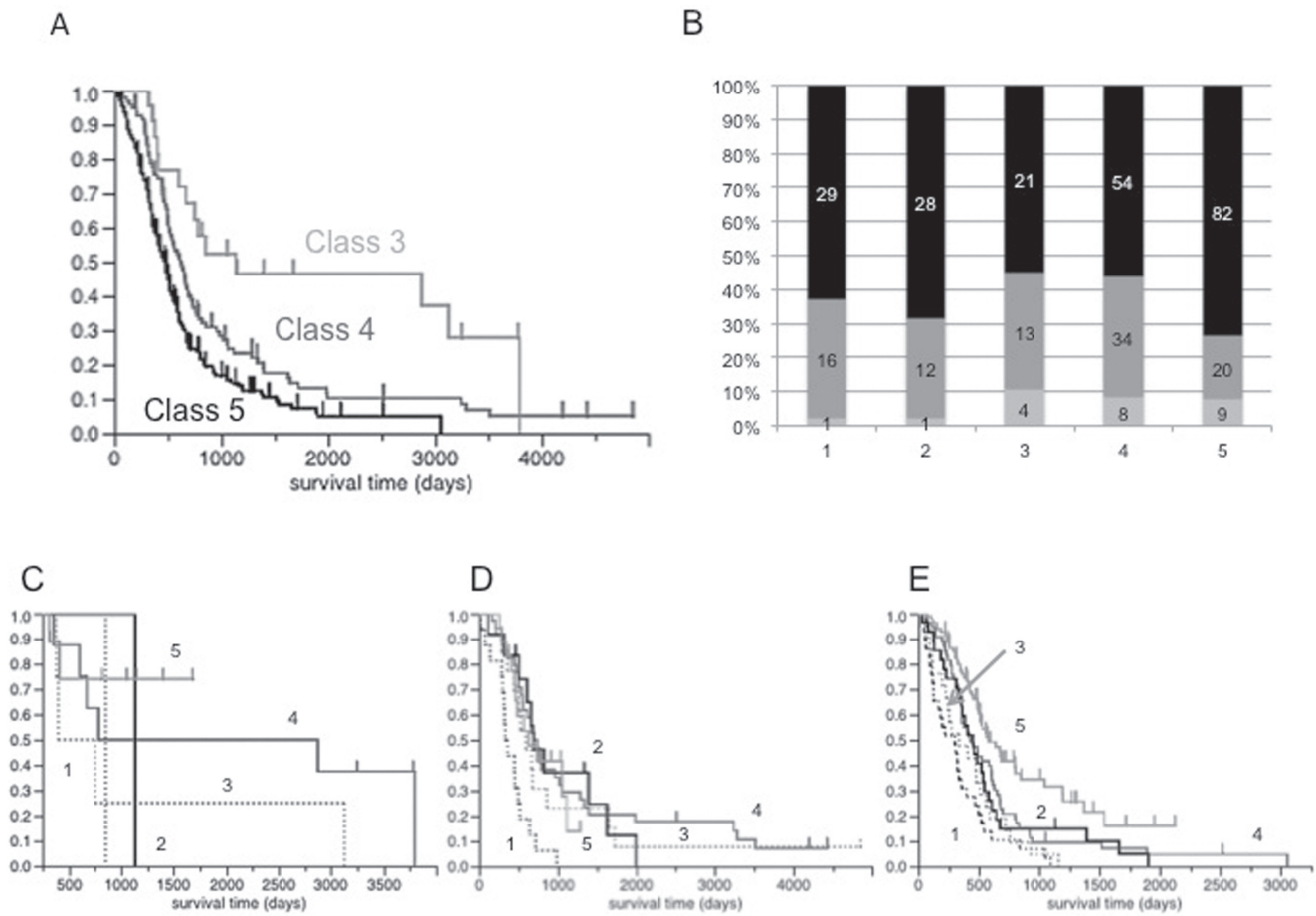

Fig. 5 A: Kaplan-Meier analysis of overall survival (OS) for histologically proven glioblastoma in Tohoku University between 1982 and 2011, stratified by the recursive partitioning analysis (RPA) classification. RPA classes 3, 4, and 5 are indicated in light gray, dark gray, and black, respectively. There was a significant difference of OS between RPA classes 3 and 4 (p = 0.0144, logrank test), and between classes 4 and 5 (p = 0.0024, logrank test). B: Historical change of resection rate stratified by the RPA classification. Numbers 1 through 5 correspond to Groups 1 through 5, respectively. C: Kaplan-Meier analysis of OS for the RPA class 3 glioblastoma, stratified by the treatment eras. There was no significant difference. D: Kaplan-Meier analysis of OS for the RPA class 4 glioblastoma, stratified by the treatment eras. Significantly increased OS was demonstrated between Groups 1 and 2 (p = 0.0026, logrank test). E: Kaplan-Meier analysis of OS for the RPA class 5 glioblastoma, stratified by the treatment eras. Significantly increased OS was demonstrated between Groups 1 and 2 (p = 0.0217, logrank test), and between Groups 4 and 5 (p = 0.0085, logrank test).

Table 8 Survival of patients with glioblastoma stratified by RPA classification

RPA class	No. of patients	Median survival time (day)	Overall survival rate (%)			Probability	
			2-Year	5-Year	10-Year		
3	23	1136	67.1	46.5	27.9	] p = 0.0144	
4	95	615	38.9	13.2	5.1		] p = 0.0024
5	214	474	24.7	7.3	0		

RPA: recursive partitioning analysis.

Table 9 Survival of patients with RPA class 3 glioblastoma stratified by treatment era

Group (treatment era)	No. of patients	Median survival time (day)	Overall survival rate (%)			Probability			
			2-Year	5-Year	10-Year				
1	1	853	100.0	0.0	0.0	] NS			
2	1	1136	100.0	0.0	0.0		] NS		
3	4	577	50.0	25.0	0.0			] NS	
4	8	1829	62.5	50.0	37.5				] NS
5	9	NR	74.1	NR	NR				

NR: not reached, NS: not significant, RPA: recursive partitioning analysis.

Table 10 Survival of patients with RPA class 4 glioblastoma stratified by treatment era

Group (treatment era)	No. of patients	Median survival time (day)	Overall survival rate (%)			Probability			
			2-Year	5-Year	10-Year				
1	16	348	6.3	0.0	0.0	] p = 0.0026			
2	12	687	46.3	12.4	0.0		] NS		
3	13	592	30.8	7.7	7.7			] NS	
4	34	715	50.0	20.6	7.1				] NS
5	20	628	47.6	NR	NR				

NR: not reached, NS: not significant, RPA: recursive partitioning analysis.

Table 11 Survival of patients with RPA class 5 glioblastoma stratified by treatment era

Group (treatment era)	No. of patients	Median survival time (day)	Overall survival rate (%)			Probability			
			2-Year	5-Year	10-Year				
1	29	301	10.3	0.0	0.0	] p = 0.0217			
2	28	449	14.8	5.0	0.0		] NS		
3	21	336	14.3	0.0	0.0			] NS	
4	54	427	20.8	7.1	0.0				] p = 0.0085
5	82	581	41.6	16.1	NR				

NR: not reached, NS: not significant, RPA: recursive partitioning analysis.

Table 12 Multivariate hazard ratios, confidence intervals, and p values for survival of patients with glioblastoma

Factor	Hazard ratio	95% Confidence intervals	p Value
MR imaging	0.426	0.302–0.602	< 0.0001
Total resection	0.587	0.458–0.751	< 0.0001
Temozolomide	0.590	0.434–0.793	0.0004
Age (below 60 years)	0.636	0.475–0.851	0.0022
RPA class 5	1.460	1.082–1.973	0.0132

MR: magnetic resonance, RPA: recursive partitioning analysis.

not clearly defined.

Previously, our retrospective study investigated the outcome in elderly patients aged 60 years or over with malignant astrocytic tumor treated in Tohoku University before (1982–1988) and after (1989–1999) the adoption of routine clinical use of MR imaging.[3] This study demonstrated that preoperative MR imaging contributed to longer survival time by providing earlier diagnosis in patients with better performance status, by allowing more thorough surgical resection, and resulting in better performance status after the treatment.

In the present study, the outcome of both younger and elderly GB was significantly improved after the introduction of MR imaging. Elderly GB, RPA class 5, and totally resected GB were associated with significantly improved prognosis after the introduction of TMZ, as follows: MST/2-year OS/5-year OS in Group 4 (n = 45, 449 days (15.0 months)/16.0/0) vs Group 5 (n = 62, 581 days (19.4 months)/46.4%/13.8%) for elderly GB (p = 0.0005), Group 4 (n = 54, 427 days (14.2 months)/20.8%/7.1%) vs Group 5 (n = 82, 581 days (19.4 months)/41.6%/16.1%) for RPA class 5 (p = 0.0085), and Group 4 (n = 58, 670 days (22.3 months)/41.4%/19.0%) vs Group 5 (n = 58, 1198 days (39.9 months)/66.5%/30.1%) for totally resected GB (p = 0.0194). Multivariate analysis showed that introduction of MR imaging and TMZ, and total resection of the tumor were highly significant as survival factors.

No chemotherapeutic agents were used for elderly GB in Group 4, so the improvement in outcome of elderly GB after the introduction of TMZ might represent the difference in therapeutic effectiveness between only RT and RT plus TMZ. In contrast, patients aged below 60 years showed no difference in prognosis between management by ACNU and after the introduction of TMZ. In the present study, TMZ was much more effective in totally resected GB, as already been demonstrated.[9,10]

The prognosis for patients with GB has improved during the last 30 years in Tohoku University, even with the aging population. This retrospective analysis showed that the introduction of MR imaging and TMZ, and total resection of the tumor have had significant impacts on improving the outcomes of GB treatment. The MST has doubled during these 30 years, and the 5-year OS of patients aged below 60 years and with total tumor resection has exceeded 30% after the introduction of TMZ.

Conflicts of Interest Disclosure

The authors have no personal, financial, or institutional interest in any of the drugs, materials, or devices in the article. T. Kumabe, R. Saito, M. Kanamori, M. Chonan, Y. Mano, I. Shibahara, T. Kawaguchi, H. Kato, Y. Yamashita, Y. Sonoda, J. Kawagishi, R. Katakura, T. Kayama, and T. Tominaga have registered online Self-reported COI Disclosure Statement Forms through the website for JNS members.

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