

The efficacy of gamma knife radiosurgery for advanced gastric cancer with brain metastases

Young Seok Park · Jong Hee Chang ·
Jin Woo Chang · Yong Gou Park

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Abstract The aim of this study was to retrospectively investigate the efficacy of gamma knife radiosurgery for brain metastases from advanced gastric cancer (AGC) comparing whole brain radiotherapy (WBRT). Between January 1991 and May 2008, 56 patients with brain metastases from AGC, treated with GKR or WBRT, were reviewed to assess prognostic factors affecting survival. Most brain metastases were diagnosed based on MRI, both metachronous and synchronous brain metastases, adenocarcinoma and signet ring carcinoma were included, but excluded cases of gastric lymphoma. Fifteen patients with a median age of 54.0 years (range, 42–67 years) were treated with GKR: 11 were treated with GKR only, 2 with surgery plus GKR, 1 with repeated GKR, 1 with GKR plus WBRT, and the other 1 with WBRT plus GKR. Forty-one were treated with WBRT only. The median number of metastatic brain lesions was 3 (range, 1–15), and treatment involved 17.0 Gy (range 14–23.6 Gy), or 30 Gy with fractionated radiotherapy. The median survival after brain metastases for GKR treatment was 40.0 weeks [95% confidence interval (CI) 44.9–132.1 weeks] and WBRT was 9.0 weeks 95% CI, 8.8–21.9 weeks). The progression free survival of 15 GKR treated patients was 56.5 weeks (95% CI 33.4–79.5 weeks). The recursive partitioning analysis (RPA) (class 2 vs. class 3) and use of GKR were correlated with prolonged survival in univariate and multivariate analyses. Age, sex, pathology, leptomeningeal seeding, tumor size (≥ 3 cm), extracranial metastases, single metastasis, chemotherapy, and synchronous metastases were

not correlated with a good prognosis in both univariate and multivariate analysis. Based on our study, the use of GKR and RPA class 2 resulted in more favorable clinical outcomes in patients with brain metastases from AGC.

Keywords Gastric cancer · Metastasis · Radio surgery · Radiotherapy · Survival

Introduction

Gastric cancer is the fourth most common type of cancer in the world [1], the second most common cause of cancer-related death [2], and the most common cause of cancer-related death in Korea [3]. However, metastasis of gastric carcinomas to the brain is very rare, generally occurring in only 0.16–0.69% of gastric cancer patients, and resulting in a poor prognosis [4–6]. Patients with brain metastases from advanced gastric cancer (AGC) usually develop severe cachexia at the end stage of disease progression, and have a poor median survival time of only 1.3–2.4 months [2, 4, 5, 7].

Advances in surgery and chemotherapy have led to better clinical outcomes for gastric cancer patients, but these increased survival rates may lead to an increased incidence of metastases [6]. The treatments of brain metastases arising from other forms of gastrointestinal tumors have been described [4, 8–10]. These studies were typically presented as case reports, and with small study samples [11, 12]. Gamma knife radiosurgery (GKR) for these brain tumors has not been well described, and the role of whole-brain radiotherapy (WBRT) or GKR for brain metastases from AGC has not been thoroughly studied. The aim of this study was to retrospectively investigate the efficacy of gamma knife radiosurgery for brain metastases from AGC comparing WBRT.

Y. S. Park · J. H. Chang · J. W. Chang · Y. G. Park (✉)
Department of Neurosurgery, Gamma Knife Clinic, Severance Hospital, Brain Research Institute, Yonsei University College of Medicine, 134, Shinchon-dong, Seodaemun-gu, Seoul 120-752, Republic of Korea
e-mail: ygpark@yuhs.ac

Patients and methods

Patients

We retrospectively analyzed all patients who underwent GKR or WBRT for brain metastases from AGC between January 1991 and May 2008. A total of 56 patients with a mean age of 55.5 years (range, 30–77 years) were treated with WBRT or GKR at the same medical facility. We performed GKR in 15 patients. Of these 15 patients treated with GKR, 11 were treated with GKR only, 2 were treated with surgery plus GKR, 1 was treated with WBRT followed by GKR as a booster, and 1 was treated with GKR followed by WBRT for leptomeningeal seeding. GKR was performed repeatedly in 1 patient, and 41 patients (73.2%) with brain metastases underwent WBRT only. We reviewed the medical records, pathology reports, magnetic resonance imaging (MRI) and our GKR registry.

Most brain metastases were diagnosed based on MRI, with the exception of 2 patients that were diagnosed based on biopsy. Both metachronous and synchronous brain metastases were also included in this study. All patients included in this study were diagnosed with AGC based upon pathology reports. We included adenocarcinomas and signet ring carcinomas, but excluded cases of gastric lymphoma. Fifty patients (89.3%) were diagnosed with adenocarcinoma and 6 patients (10.7%) were diagnosed with signet ring carcinomas. Thirty patients (53.6%) underwent subtotal or total gastrectomy, and 26 patients (46.4%) underwent a lymph node biopsy or open biopsy without surgical resection of the primary disease. Fifty patients (89.3%) were diagnosed with brain lesions after the primary diagnosis of metachronous carcinoma, and 6 patients (10.7%) were diagnosed simultaneously with synchronous carcinoma. Extracranial diseases were diagnosed through a systemic work up [13].

All but 6 of the patients were treated with various chemotherapy regimens. We could not analyze the impact of chemotherapy on survival because many different chemotherapy regimens with various cycles had been used. None of the patients in this study underwent intrathecal chemotherapy. We classified the causes of death as neurological or systemic.

Methods of GKR

GKR were performed using the Leksell Gamma Knife (Elekta, Stockholm, Sweden) model B or C. We obtained brain MRI image using image-compatible Leksell stereotactic coordinate frame (Elekta) in the morning of the day of operation with local anesthesia combined with or without intravenous sedation. MR image acquisition covered the entire brain with 2-mm-thick slices including T1, T2,

and double-dose gadolinium-enhanced MR images. Then, computerized imaging data were transferred to the Gammaplan Software (Elekta). After three-dimensional image reconstruction with a Gamma plan (Elekta), the neurosurgeon identified the tumor and its near critical structures. All patients underwent brain MRI before WBRT or GKR. The tumors eligible for GKR had a diameter of less than 3 cm and a number of metastasis less than 10 using preoperative contrast-enhanced MRI. Patients with multifocal over 10 brain metastasis and leptomeningeal metastases were treated with 10 fractions of WBRT at 30 Gy. We performed WBRT in several single brain metastases in our early experience. Two patients (patients #1 and #14 in Table 1) that had less than 10 lesions on the preoperative contrast-MRI, but found to have greater than 10 lesions on the planning MRI, were included in this study. Patients with single or multiple metastases were treated with a marginal dose of 17.0 Gy (range 14.0–23.6 Gy). The median number of parenchymal metastases was 3 (range, 1–18), and GKR treatment was carried out in one session, with the exception of one patient who was treated three times for new lesions.

Follow-up

The patients were followed-up for clinical and neurological exams 1 month after treatment, and every 3 months after the initial follow-up. An image follow-up was usually carried out at 2- or 3-month intervals after radiosurgery or WBRT using double-dose gadolinium-enhanced MRI. In the case of neurological aggravation, we performed additional brain imaging using brain computed tomography (CT) or contrast-enhanced brain MRI. We took at least one follow-up brain MRI or CT scan for 15 GKR patients, but only 14 patients were available in WBRT patients in this study. The recursive partitioning analysis (RPA) classification and Karnofsky performance status (KPS) were used to compare the prognosis. Patients were classified as RPA class 1 (KPS $\geq 70\%$, age < 65 years, controlled primary, no extracranial metastasis, RPA class 2 (KPS $\geq 70\%$, age ≥ 65 years, and/or uncontrolled primary, and/or extracranial metastases), or RPA class 3 (all patients with KPS $< 70\%$) [14]. All patients were assessed for KPS and RPA before radiotherapy or GKR. Local control was defined by as the reappearance of a metastasis as the original treated lesion and was detected using a brain CT image or MRI. Tumor progression was defined as more than a 25% increase in size of the tumor volume. We took at least one follow-up brain MRI or CT scan for all of patients with GKR, but only 14 patients were available to compare tumor progression in patients with WBRT in this study. It was probably caused by rapid systemic disease aggravation and retrospective data acquisition. This is a limitation in comparing PFS between WBRT and GKR in this study.

Table 1 Clinical results of GKR after brain metastases

Patient no.	Age/sex	PATH	No. of metastases	Treatment modality	Median marginal dose (Gy)	Median tumor volume (cm ³)	Survival after brain metastasis (months)	Outcome ^a
1	53/F	A	6	Surgery + GKR	17.0 (9.8–21)	1.95 (0.17–6.24)	3	Systemic death
2 ^b	52/M	A	1,2,15	GKR + GKR + GKR	18.9 (15.1–28)	0.70 (0.11–12.70)	46	Alive
3	54/F	S	3	Surgery + GKR	16 (16–27)	0.41 (0.16–0.61)	3	Systemic death
4	51/M	S	2	GKR	18.1 (17–19.2)	7.38 (4.00–10.76)	16	Systemic death
5	45/M	A	1	GKR	14	1.10	7	Systemic death
6	66/M	A	3	GKR	18 (17–19.8)	12.39 (0.63–17.8)	7	Systemic death
7	54/M	A	1	GKR	16	14.90	25	Alive
8	67/M	S	2	GKR	16	0.39 (0.33–0.44)	11	Alive
9	42/F	A	7	GKR	14.3 (13.1–15.4)	0.24 (0.02–0.59)	12	Alive
10	63/M	A	8	GKR + WBRT ^c (30 Gy)	18.9 (15–19.5)	0.13 (0.01–10.3)	10	Neurogenic death
11	51/M	S	3	GKR	15.9 (15–17.99)	0.08 (0.03–3.30)	9	Systemic death
12	65/F	A	5	GKR	16 (15–28)	0.11 (0.01–0.42)	3	Alive
13	60/F	A	3	GKR	17 (17–19)	0.45 (0.41–3.40)	3	Alive
14	61/M	A	15	WBRT ^d (30 Gy) + GKR	23.6 (14.9–27.1)	0.26 (0.01–4.00)	31	Alive
15	57/M	A	1	GKR	18.0	3.00	4	Systemic death

A adenocarcinoma, GKR gamma knife radiosurgery, S signet ring carcinoma, WBRT whole brain radiotherapy

^a Survival data were updated to August 2008

^b The median marginal doses and median tumor volumes of the three GKR treatments were calculated for patient #2

^c The patient underwent WBRT 3 months after GKR due to leptomeningeal metastasis

^d The patient underwent WBRT over 10 lesions with 30 Gy, the tumors were decreasing but refractory after 6 months, GKR was performed as booster treatment

Statistical analysis

Independent sample *t* test and Fisher's exact test were used to compare the GKR and radiotherapy groups. Survival data were updated to August 2008. Comparative overall survival was calculated using the Kaplan–Meier method. Comparisons of overall survival according to clinical factors were calculated with a log-rank test. A Cox proportional hazard model with the forward stepwise method was used in multivariate analysis to determine the clinical factors affecting survival.

The mean \pm standard deviation, median and range of each clinical characteristic were calculated. We used SPSS 15.0 software for statistical analyses.

Results

Clinical characteristics

Patient characteristics are summarized in Tables 1 and 2. Patients with a mean age of 55.5 years (range, 30–77 years) were treated with GKR or radiotherapy. There were 12 female patients (21.4%) and 44 male patients (78.6%). The median interval from gastric cancer to brain metastasis was 6 months (0–78 months) in the GKR group and 11 months

(0–119 months) in the WBRT group. There was no difference in the time interval changes between the two groups. Nine patients in the radiotherapy group had leptomeningeal seeding.

Fifty-one patients (91.1%) had extracranial metastasis to the lung, liver, bone, distant lymph node, or adrenal gland. A systemic work-up had not uncovered a brain metastasis at the time of diagnosis in 5 of the patients (0.9%). The GKR and WBRT groups showed no differences in extracranial disease, and local control at 3 months was better in the GKR group.

GKR

The characteristics and clinical demographics of the patients that underwent GKR are described in Table 1. The median number of lesions was three (range, 1–18), and they were treated with marginal doses of 17.0 Gy (range, 14–23.6 Gy). We decreased the radiation doses from the typical dose for patient #1 (brain stem lesion) and for patient #5 (cavernous sinus invading lesion near the optic nerve).

Patients #1 and #3 underwent GKR after tumor removal, while patient #2 underwent repeated GKR for new lesions. Patient #10 underwent GKR for a cerebella surface lesion (Fig. 1a). We initially diagnosed patient #10 with a

Table 2 Patient characteristics in the GKR only versus WBRT only groups

Patient characteristic	No. of patients		P value*
	GKR, n = 11	WBRT, n = 41	
Age	54 (42–67)	57 (30–77)	0.969 [†]
Sex			0.424
Female	3	7	
Male	8	34	
Pathology			0.283
Adenocarcinoma	9	38	
Signet ring carcinoma	2	3	
KPS at GKR			1.000
≥70	9	31	
<70	2	10	
RPA class			1.000
2	9	31	
3	2	10	
Pattern of metastasis			0.177
Parenchymal	11	32	
Leptomeningeal	0	9	
No. of metastases			0.503
1	4	21	
2–3	5	5	
4–6	1	1	
>6	1	14	
Tumor size			0.571
<3 cm	11	36	
≥3 cm	0	5	
Cause of death			0.566
Neurolocal	0	9	
Systemic	5	29	
Extracranial disease			1.000
Yes	10	37	
No	1	4	
Interval from gastric cancer to brain metastasis	6 months (0–78)	11 months (0–119)	0.769 [†]

GKR gamma knife radiosurgery, RPA recursive partitioning analysis, WBRT whole brain radiotherapy

* P value obtained using Fisher's exact test

[†] P value obtained using independent t test

parenchymal lesion, but the lesion progressed into a leptomeningeal metastasis after 3 months, and the patient underwent WBRT (Fig. 1b). Patient #14 also underwent WBRT for multiple lesions, but after 6 months, the metastatic lesions were refractory to WBRT and were subsequently treated using GKR as a booster. An MRI performed 12 months after the GKR treatment of patient #14 showed good local control for each of the multiple lesions (Fig. 2). Crude local control was 93.3% at

3 months for 15 GKR-treated patients. The progression-free survival of 15 GKR-treated patients was 56.5 weeks (95% CI, 33.4–79.5 weeks). The median survival after brain metastases for GKR was 40.0 weeks (95% confidence interval [CI] 44.9–132.1 weeks) and WBRT was 9.0 weeks (95% CI, 8.8–21.9 weeks).

GKR only versus WBRT only: univariate and multivariate analyses

The median age of the GKR only group ($n = 11$) was 54.0 years (range, 42–67 years), and the median age of the WBRT only group ($n = 41$) was 57.0 years (range, 30–77 years). There were no significant differences between the GKR only group and the WBRT only group with regard to age, sex, pathology, pattern of metastasis, RPA class, tumor size (≥ 3 cm), or the number of metastases. There was no difference in the number of neurological deaths between the two groups. Single metastasis was higher in the WBRT group with 21 patients (51.2%) compared to only 4 patients (36.3%) in the GKR only group; however, this difference was not significant. Multiple metastases (>6 lesions) were found in 1 patient in the GKR only group, but in 14 patients (34.1%) in the WBRT only group. The clinical characteristics of patients in the GKR only and WBRT only groups are shown in Table 2.

Univariate and multivariate analyses showed that survival outcome was not affected by age (<60), gender, pathology, metachronous lesions, tumor size (≥ 3 cm), single metastasis, extracranial metastases, or leptomeningeal metastases (Table 3). A tumor size greater than 3 cm in diameter did not affect survival in univariate and multivariate analyses. Patients with extracranial metastasis at the time of brain metastasis from AGC had a poor median survival, but the difference compared to that of patients without extracranial metastasis was not significant. Chemotherapy was used to treat 50 patients (89.3%) and was shown to have affected survival in univariate but not in multivariate analyses. However, these data may have been affected by selection bias since only patients with a good prognosis underwent chemotherapy. In addition, the use of a variety of chemotherapy regimens may also have affected these results.

GKR was the only form of treatment for 11 of the patients (19.6%), and WBRT was used to treat 41 patients (73.2%). Patients in the GKR only group had better overall survival than those in the WBRT group (Fig. 3a). Due to the small patient population, we could not compare the surgery and GKR combination treatment with the WBRT only treatment. RPA class 2, as opposed to RPA class 3 (cox, $P < 0.001$), and GKR (cox, $P < 0.001$) showed better prognoses in univariate and multivariate analyses (Table 3; Fig. 3a, b).

Fig. 1 Gamma knife stereotactic radiosurgery was performed on a 64-year-old male patient (patient #10 in Table 1) for cerebellar metastases. **a** A T1 gadolinium-enhanced magnetic resonance image (MRI) shows cerebellar surface metastasis prior to GKR. **b** This tumor showed leptomeningeal metastasis after 3 months, at which time WBRT was performed

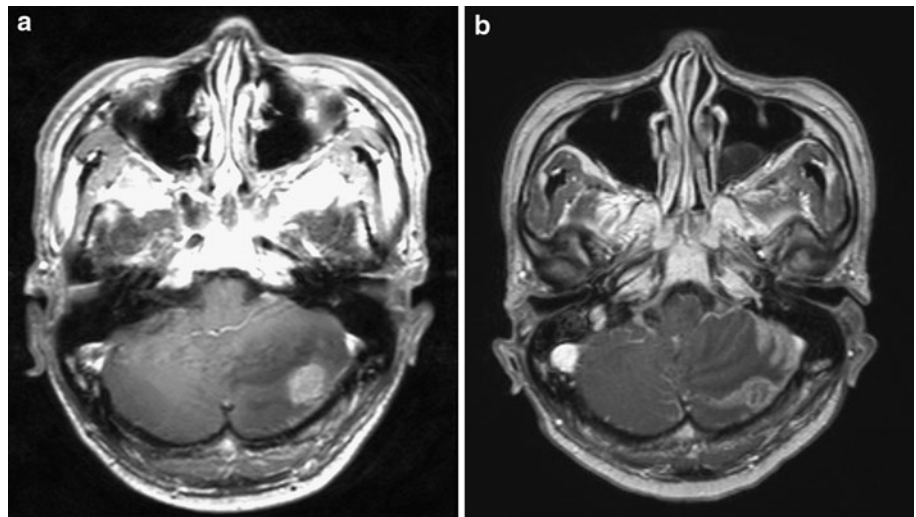
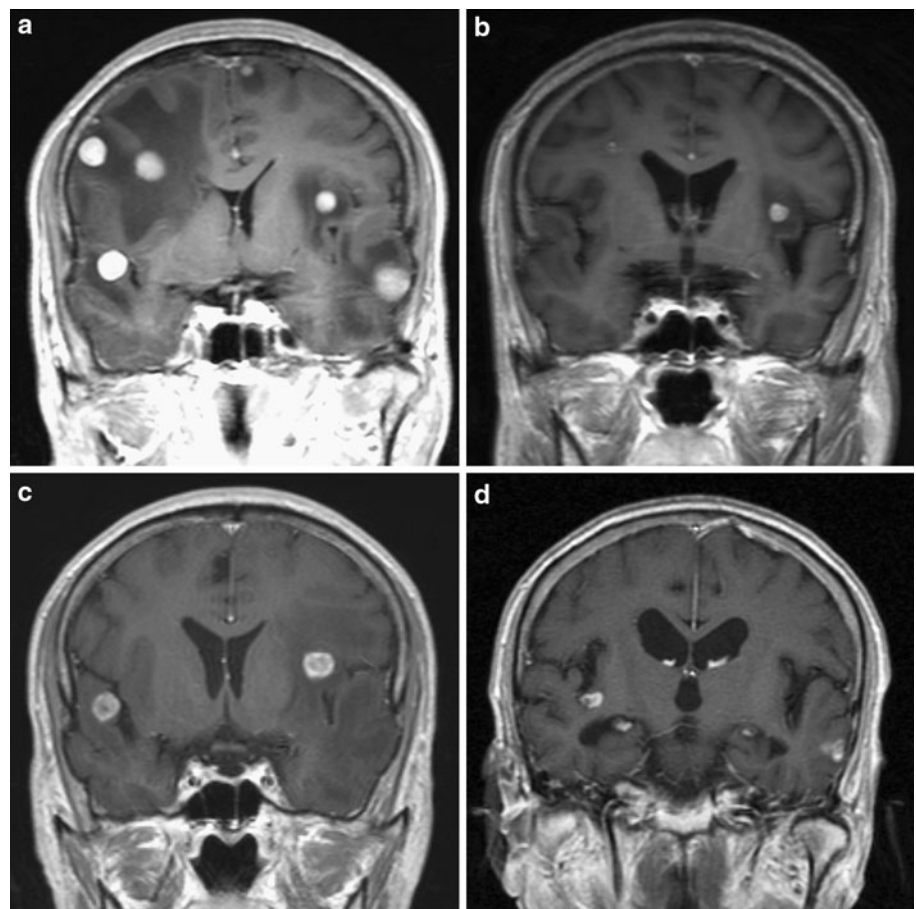


Fig. 2 Whole-brain radiotherapy (WBRT) was performed on a 61-year-old male patient (patient #14 in Table 1) with multiple metastases. **a** A T1-weighted gadolinium-enhanced coronal image shows multiple lesions prior to WBRT. **b** Three months after WBRT, there was decrease in the enhanced lesions. **c** Six months after WBRT, MRI showed an increased size and number on the right temporal and left insular areas, prior to GKR. **d** The post-GKR 12-month follow-up MRI showed a decreased size and number of tumors



Complications

In the GKR group, one patient had severe brain swelling due to radionecrosis which was controlled with intravenous corticosteroids medication. One patient had cavernous sinus invasion with diplopia, her diplopia aggravated temporarily and improved after GKR. One had developed uncontrolled seizure at 3 months after GKR. It might be

related with peritumoral edema. It improved after intravenous corticosteroid medication and anticonvulsant medication. There were no intracranial tumor bleeding after GKR or radiotherapy. One patient presented with intracranial tumor bleeding; she underwent GKR for the previous tumor bleeding area and the other lesion after craniotomy. There were no mortalities related to radionecrosis. As of August 2008, 43 patients (76.8%) had died, including 9

Table 3 Univariate and multivariate analyses for survival in 56 patients with brain metastases from advanced gastric cancer

Variable	No. of patients	MST ± SE weeks (95% CI)	Univariate Analysis ^a	Multivariate analysis ^b	Hazard ratio (95% CI)
Age (years)			0.694	0.969	
<60	33	14 ± 2.2 (9.6–18.4)			1
≥60	23	13 ± 7.1 (0.0–27.0)			0.98 (0.43–2.26)
Sex			0.881	0.209	
Male	44	14 ± 2.7 (8.6–19.4)			1
Female	12	13 ± 2.6 (8.0–18.1)			0.56 (0.23–1.39)
Pathology			0.866	0.023	
Adenocarcinoma	50	14 ± 1.6 (10.8–17.2)			1
Signet ring carcinoma	6	9 ± 15.3 (0.0–39.0)			3.40 (1.18–9.81)
Pattern of metastasis			0.615	0.104	
Leptomeningeal	9	9 ± 1.5 (5.9–12.1)			1
Parenchymal	47	14 ± 1.0 (12.0–16.0)			0.34 (0.09–1.25)
Synchronous			0.698	0.762	
Metachronous	50	13 ± 1.5 (10.0–16.0)			1
Synchronous	6	11 ± 2.4 (6.2–15.8)			1.24 (0.31–4.89)
RPA class			<0.001	<0.001	
2	43	14 ± 1.5 (11.0–17.0)			1
3	13	5 ± 0.3 (4.5–5.5)			15.8 (4.58–54.80)
Single metastases			0.139	0.146	
1	25	13 ± 2.0 (9.1–16.9)			1
>1	31	14 ± 2.5 (9.0–19.0)			0.46 (0.16–1.31)
Tumor size (cm)			0.145	0.464	
<3	51	14 ± 2.7 (8.6–19.4)			1
≥3	5	12 ± 4.3 (3.4–20.6)			1.70 (0.41–7.00)
Extracranial metastasis			0.152	0.065	
None	5	14 ± 2.0 (10.0–17.9)			1
Yes	51	13 ± 2.0 (9.2–16.8)			9.03 (0.88–93.25)
Chemotherapy			0.009	0.165	
None	6	8 ± 2.7 (2.6–13.4)			1
Yes	50	14 ± 1.1 (11.8–16.1)			0.37 (0.09–1.50)
Treatment			<0.001	<0.001	
GKR	15	40.0 ± 19.3 (44.9–132.1)			1
WBRT	41	9.0 ± 0.4 (8.8–21.9)			7.96 (3.10–20.41)

RPA recursive partitioning analysis, MST median survival time, SE standard error, WBRT whole brain radiotherapy, CI confidence interval

^a Log-rank test for univariate analysis dependent variables

^b Forward stepwise cox proportional hazard model for multivariate analyses

neurological deaths (20.9%) and 34 (79.1%) systemic deaths. There was no difference in the number of neurological deaths between the GKR and WBRT groups.

Discussion

In this study, we found that RPA class 2 as opposed to RPA class 3 and GKR were good prognostic factors in patients diagnosed with brain metastases from AGC. Although WBRT is the most common type of treatment for multiple metastases, surgical resection of metastases and stereotactic radiosurgery (SRS) are important options

if the patient has a limited number of metastases [15, 16]. The prognosis for patients with one to three brain metastases appears to be better than that for patients who have more than three lesions [17, 18]. Although WBRT is effective for brain metastasis, SRS could be as effective as WBRT. Patients can undergo WBRT multiple times to combat disease progression, but this may increase the patients' risks for the delayed effects of radiation [19–23]. IF SRS delivered in higher doses at a single fraction, it increases the risk of radionecrosis as high-dose irradiation. Therefore, both WBRT and SRS have its optimum radiation dose and limitation due to radiation adverse effect.

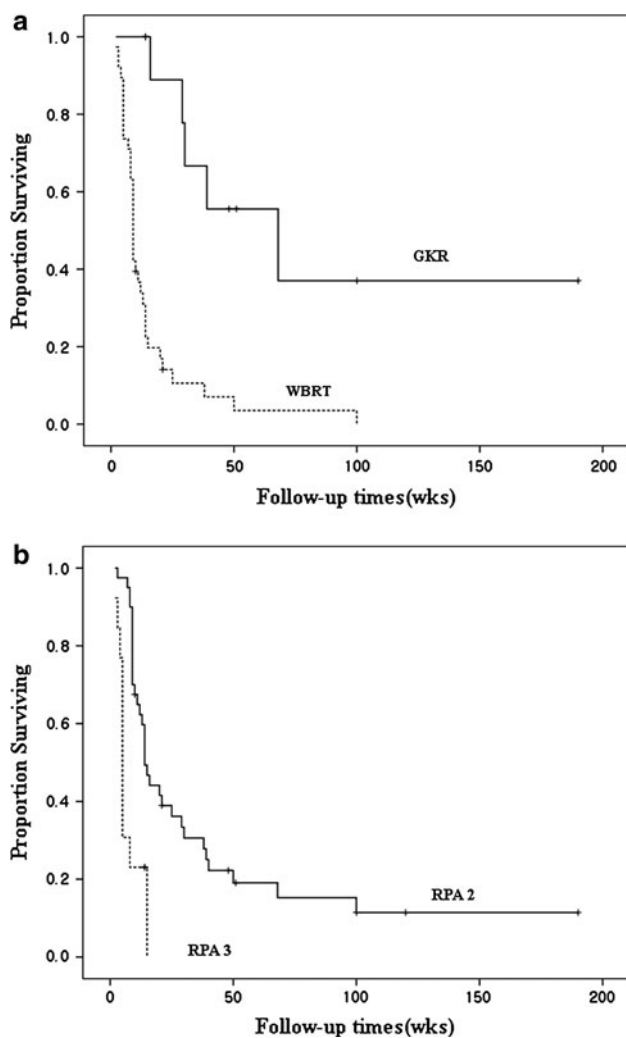


Fig. 3 **a** A Kaplan–Meier curve illustrating the overall survivals of patients who had undergone GKR ($n = 11$) as opposed to those who had undergone WBRT ($n = 41$). Patients who underwent GKR had better overall survival (log rank, $P < 0.001$). **b** Patients with RPA class 2 had a better prognosis in Kaplan–Meier curve analysis (log rank, $P < 0.001$)

Currently, there are no available treatments for brain metastases from AGC that are likely to produce long-term survival, and the use of WBRT, regardless of steroid use, has not been shown to increase survival [4]. York et al. reported 24 brain metastases patients from AGC and they showed better survival with surgical resection plus WBRT relative to the other groups among the steroid use only, WBRT, and surgical resection plus WBRT group [4]. Several reports have dealt with the radiosurgery for brain metastasis from AGC as a case report or mixed with other gastrointestinal cancers [10, 24, 25]. Han et al. report 11 cases with radiosurgery for brain metastases from AGC and they advocated that radiosurgery plus WBRT seem to be a good alternative to surgical resection for these patients [8].

Leptomeningeal seeding is a relatively common and devastating neurological complication of cancer [2, 6]. Occurring in 3–8% of all cancer patients, it is associated with major neurologic disability and high mortality rates [2, 26, 27]. Although leptomeningeal metastases may occur with virtually any malignancy, leptomeningeal seeding is most commonly seen in patients with leukemia, breast cancer, lymphoma, and lung cancer [28]. Although leptomeningeal metastasis is relatively rare in patients with gastric cancer, intracranial metastases in AGC patients usually occur in the form of leptomeningeal or parenchymal lesions [6, 27]. Our study shows that there is no significant difference in the survival rates for patients with leptomeningeal metastases.

Non-small cell lung cancer (NSCLC) and breast cancer are considered to be chemo-responsive tumors. Although several chemotherapy regimens have been used to treat brain metastases from AGC, no standard chemotherapy regimen has been developed. For example, paclitaxel or irinotecan, cisplatin along with irradiation, and 5-fluorouracil and cisplatin have been used for brain metastases from AGC [29, 30].

There was no significant difference in the number of neurological or systemic deaths between the GKR and WBRT groups. We investigated the local control rate at the 3-month follow-up only because a brain metastasis from AGC is usually accompanied by cancer cachexia and a dismal survival outcome.

To our knowledge, no large-scale study on the prognosis of patients with brain metastases from gastric cancer has been conducted. One study showed that KPS and the number of metastases were independent prognostic factors in brain metastases from gastrointestinal tumors in 10 patients (17.5%) with gastrointestinal tumors [9]. They used 50 or 30 Gy in their study, with fractions, but no significance for overall survival [9].

RPA class is one of the most predictive factors for patients with brain metastases arising from other tumors [14, 18, 31]. We confirmed that those patients with RPA class 2 rather than RPA class 3 have a better prognosis for brain metastases from AGC.

Our study was limited by its retrospective design and small sample size. The patient population was heterogeneous, including both primary surgery and a non-surgical group. Not all brain metastases were confirmed by pathologic diagnosis, since some were diagnosed on MRI. In addition, we used various chemotherapy regimens and frequencies. The two treatments were not independent rather used in complementary [32, 33]; however, we could not assess and compare combined treatment such as WBRT plus GKR or GKR plus WBRT because of the limitation of our cases.

However, our study is valuable despite this retrospective design and the small number of cases because brain metastasis from AGC is very rare and large clinical studies have not been reported. Further investigation is needed in a large-scale study with a prospective controlled design.

Conclusion

We found that GKR treatment and RPA class 2 rather than class 3 are favorable clinical outcomes for patients with brain metastases from AGC. Age, sex, pathology, leptomeningeal seeding, tumor size (≥ 3 cm), extracranial metastases, single metastasis, chemotherapy, and synchronous metastases were not correlated with a good prognosis in either univariate or multivariate analysis.

Despite its retrospective design and the small number of cases, our study is meaningful because brain metastasis from AGC is very rare and large clinical studies have not been reported. Further investigation is required in a large scale study with a prospective controlled design. Even though the prognosis was very poor in brain metastases from AGC rather than other metastatic brain tumors, this study highlights the efficacy of GKR for optimum brain metastases from AGC in RPA 1 or RPA 2.

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