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Original Article

Gamma Knife Stereotactic Radiosurgery for Brain Metastases from Ovarian Cancer: A Case Series of 22 Patients

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Abstract

Background and objectives: Brain metastases from ovarian cancer (BMFOC) are rare but associated with poor prognosis. This study aimed to evaluate the efficacy and safety of Gamma Knife stereotactic radiosurgery (GKSRS) in managing patients with BMFOC.

Methods: A retrospective analysis was conducted on 22 patients with BMFOC who were treated with GKSRS between January 2015 and May 2019. The median age at the start of treatment was 57.7 years (range, 46–72 years). A total of 70 brain metastases were treated, with each patient having between one and nine metastatic tumors. The mean tumor volume was 3.6 cm^3 (range, 0.1–22.7 cm^3). The mean peripheral dose was 16 Gy (range, 7–20 Gy), and the mean isodose curve was 54.6% (range, 45–80%).

Results: At 12 months post-GKSRS, 68 metastatic tumors were assessed: 32 (47.1%) showed complete response, 20 (29.4%) had partial response, 14 (20.6%) remained stable, and two (2.9%) progressed, leading to a tumor control rate of 97.1%. No acute or chronic toxicity was observed.

Conclusions: GKSRS appears to be an effective and well-tolerated treatment for BMFOC, offering high tumor control rates and prolonged survival in selected patients.

Introduction

Ovarian cancer is one of the most common and aggressive gynecological malignancies, often diagnosed at an advanced stage due to its subtle or absent early symptoms.[1] Pectasides *et al*.[2] estimated that the incidence of brain metastases is approximately 1.01% among 22,240 patients with ovarian cancer. In recent years, there has been an increase in the incidence of brain metastases from ovarian cancer (BMFOC).[3] Platinum-based chemotherapy, targeted therapy, and immunotherapy have improved survival outcomes for patients with ovarian cancer, while advanced imaging techniques have enabled earlier detection of small brain metastases.[4]

Despite these advancements in systemic therapies such as platinum-based chemotherapy, targeted therapy, and immunotherapy, the prognosis remains poor, particularly when distant metastases occur.[5] BMFOC is rare, with an incidence ranging from approximately 0.49% to 6.1% among ovarian cancer patients.[5,6] However, recent studies suggest the incidence may be rising due to prolonged survival following systemic therapy and the widespread use of high-resolution neuroimaging (3.0T/7.0T magnetic resonance imaging (MRI)). Unlike brain metastases from lung or breast cancer, BMFOC tends to develop later in the disease course and typically exhibits relatively slow progression.[5] According to the latest NCCN (National Comprehensive Cancer Network) guidelines, there are no specific diagnostic or therapeutic recommendations for brain metastases from ovarian cancer.[7] Instead, treatment should follow the general principles established for brain metastases originating from other malignancies.

Gamma Knife stereotactic radiosurgery (GKSRS) is a minimally invasive treatment modality for brain metastases that offers high local tumor control rates while minimizing radiation exposure to surrounding healthy brain tissue. Compared to whole-brain radiation therapy (WBRT), GKSRS is associated with a lower risk of cognitive decline and may be a preferred option for selected BMFOC patients.[8] In the present study, we assessed the clinical characteristics of patients with BMFOC and evaluated the efficacy of GKSRS in improving survival outcomes in this population.

Keywords: Ovarian cancer; Brain metastases; Gamma Knife stereotactic radiosurgery; Tumor control; Survival; Radiotherapy; Prognosis; Minimally invasive treatment.

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Materials and methods

Patients

We retrospectively reviewed the medical records of patients treated with GKSRS for brain metastases from ovarian cancer (BMFOC) at The Sixth Medical Center of PLA General Hospital between January 2015 and May 2019. The inclusion criteria were: (1) histologically confirmed ovarian cancer; (2) radiologically confirmed brain metastases; and (3) treatment with single-session GKSRS. Patients lacking detailed follow-up data or those who had received prior stereotactic radiosurgery at other centers were excluded. Ultimately, 22 patients with BMFOC (2.1%) were included from a total of 1,008 patients treated for brain metastases at our Gamma Knife Surgical Center.

GKSRS treatment

GKSRS was performed using a Leksell Gamma Knife Perfexion system (Elekta Instruments, Stockholm). The Leksell G stereotactic frame (Elekta Instruments) was attached to each patient's head under local anesthesia. Gadolinium-enhanced multiphasic thin-slice 3D MRI was conducted for all patients. Treatment planning was performed using GammaPlan version 10.1 (Elekta Instruments). A total of 70 metastatic lesions (range, one to nine lesions per patient) were treated. The mean tumor volume was 3.6 cm^3 (range, 0.1–22.7 cm^3). The mean prescription dose was 16 Gy (range, 7–20 Gy), and the mean isodose percentage was 54.6% (range, 45–80%). One patient was treated with single-fraction frame-based Gamma Knife radiosurgery. The rationale for this approach was twofold: (1) the patient had previously undergone whole-brain radiotherapy and had received four prior Gamma Knife treatments; and (2) the tumor was located in the medulla oblongata and was relatively large compared to the size of the medulla. All patients were discharged one to two days post-treatment and were followed clinically at two- to three-month intervals after GKSRS. Tumor size and radiation-induced injury were assessed using gadolinium-enhanced MRI. Tumor response was evaluated according to the Response Evaluation Criteria in Solid Tumors guidelines: Complete response (CR): Disappearance of all target lesions. Partial response (PR): At least a 30% decrease in the sum of the longest diameters of target lesions. Stable disease (SD): Neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for progressive disease (PD). PD: At least a 20% increase in the sum of the longest diameters of target lesions or the appearance of new lesions. The tumor control rate was calculated as the proportion of tumors classified as CR, PR, or SD. Survival outcomes were analyzed using Kaplan–Meier methods. Adverse events were evaluated according to the toxicity criteria of the Radiation Therapy Oncology Group.

Statistical analysis

The primary study endpoints included: (i) overall survival (OS) time from the first GKSRS, and (ii) overall survival time from the initial diagnosis of ovarian cancer. Kaplan–Meier survival curves were generated to estimate survival probabilities. All statistical analyses were performed using SPSS software (version 26.0).

Results

Clinical characteristics

A total of 22 BMFOC patients were included in this study. The median age at the start of GKSRS treatment was 57.7 years (range, 46–72 years). Twenty patients underwent surgery for the primary ovarian lesion, while the remaining two were diagnosed via biopsy. Two patients (12.5%) had abdominal cavity metastases, one patient (6.25%) had lung metastasis, and the remaining 18 patients (81.25%) had multiple systemic metastases. According to the RPA (Radiation Therapy Oncology Group Performance Status Assessment) classification, four patients (25%) were classified as Grade III, two patients (12.5%) as Grade II, and sixteen patients (62.5%) as Grade I. Regarding prior treatments, four patients (25%) had undergone WBRT, and all patients (100%) received chemotherapy. Among the 22 patients, two received GKSRS treatment twice, and four received it three times. The clinical characteristics of all patients are summarized in Table 1.

Follow-up and survival outcomes

The follow-up period ranged from one to forty-two months, with a median duration of 19 months. At the final follow-up, eight patients (36.4%) were alive, while 14 (63.6%) had died. Among the deceased patients, four (28.6%) died from progressive brain metastases, and eight (57.1%) died due to systemic disease progression, including one patient who died within one month of GKSRS. The cause of death in two patients (14.3%) could not be determined due to insufficient follow-up data (Table 1).

Treatment and patient characteristics

At the time of the first GKSRS treatment, Karnofsky Performance Status scores ranged from 60 to 100, with a median of 80. The median interval from the initial diagnosis of ovarian cancer to the occurrence of brain metastases was 21 months (range, 10–101 months) (Table 1).

OS rates

The median OS time from the first GKSRS was 19 months (range, one to forty-two months). The median OS time from the initial ovarian cancer diagnosis was 47 months (range, 21–123 months). The one-year, 1.5-year, and two-year OS rates after the first GKSRS were 90.9%, 63.6%, and 18.2%, respectively (Fig. 1).

Tumor response and control rate

At the 12-month follow-up, 68 metastatic lesions were assessed: 32 (47.1%) achieved CR, 20 (29.4%) showed PR, 14 (20.6%) remained SD, and two (2.9%) showed PD. The tumor control rate was 97.1%. No tumor hemorrhage was observed following GKSRS. Figure 2 illustrates a representative case in which a female patient experienced a significant reduction in tumor size following GKSRS treatment.

Toxicity and recurrence

No Grade 3 or higher toxicities, according to the Radiation Therapy Oncology Group criteria, were observed. Mild Grade 1–2 toxicities included transient headaches (18.2%) and mild nausea (9.1%), both of which resolved spontaneously. Six patients (27.3%) developed new brain metastases between six months and one year after initial treatment and subsequently received additional Gamma Knife sessions.

Discussion

BMFOC is a rare but life-threatening disease. GKSRS has been widely used in the treatment of brain metastases from primary tumors such as lung, breast, and melanoma.[9] However, its role in

Table 1. Patient characteristics of 22 patients with 70 brain metastases

Case no.	Age	KPS at first GKSRS	Number of brain metastases at first GKSRS	Total volume of brain metastases at the first GKSRS (cm^3)	Symptoms	Interval to brain metastases (months)	Prescribed dose (Gy)	Survival following diagnosis of brain metastases (months)
1	54	60	9	22.7	EW	21	12–15	19
2#	54	80	2	7.5	EW	67	14–20	42
3	46	70	2	14.2	Seizure	83	All are 16	14
4#	72	100	1	1.2	None[a]	19	15	15
5	64	100	1	2.3	EW[b]	21	7	32
6	57	60	5	7.5	Headache	15	All are 16	17
7	54	50	1	13.6	Headache	20	16	1
8	64	100	1	0.1	None[a]	25	18	22
9	55	100	1	1.6	None[a]	101	18	22*
10#	51	90	1	9.9	None[a]	10	15	21*
11	51	90	1	13.6	Headache	44	17	11*
12	55	70	1	9.5	EW	25	16	24*
13	53	80	2	8.5	Dysarthria	23	All are 16	12
14	48	60	1	5.8	EW	27	15	4
15#	69	60	2	12.6	Dizziness	28	All are 16	11
16	67	80	3	7.6	None[a]	84	All are 16	17
17	55	100	1	0.5	Headache	34	16	18
18	60	90	5	2.4	Seizure	9	16–20	23
19#	59	80	1	0.6	Aphasia	15	16	25
20#	56	70	2	2.6	None[a]	15	All are 16	10
21	49	90	1	1.8	EW	42	16	3
22	53	80	3	9.2	None[a]	40	All are 16	19

[a]Brain metastasis detected after MRI and/or CT; [b]Transient EW. #Patients received GKSRS treatment repeatedly; *Patients still survive at the end of the study. CT, computed tomography; EW, extremity weakness; GKSRS, Gamma Knife stereotactic radiosurgery; KPS, Karnofsky Performance Status; MRI, magnetic resonance imaging.

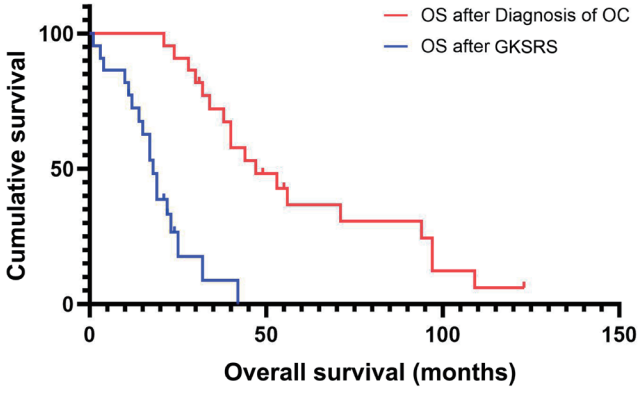

Fig. 1. Kaplan–Meier survival curves for overall survival from the start of GKSRS (blue line) and from the initial diagnosis of ovarian cancer (red line). The survival rates at one, 1.5, and two years after GKSRS were 90.9%, 63.6%, and 18.2%, respectively. The median survival time post-GKSRS was 19 months. GKSRS, Gamma Knife stereotactic radiosurgery; OC, ovarian cancer; OS, overall survival.

managing BMFOC remains less well-defined due to the rarity of the condition and the limited availability of large-scale data. While GKSRS offers high local tumor control and is less invasive than surgical resection, its impact on overall survival and disease progression in BMFOC requires further investigation.

Our study included 22 patients with BMFOC treated with GKSRS. Previous literature has reported that the median age at diagnosis for all ovarian cancers ranges from 51 to 59.5 years, the median age for brain metastases is 52.5 to 58 years, and the median time to brain metastasis occurrence is 14.5 to 46 months.[10] Our findings are consistent with these data. In this study, the average age at diagnosis of brain metastases was 57.7 years, and the median time from the diagnosis of ovarian cancer to intracranial metastasis was 21 months.

Brain metastasis from ovarian cancer represents late-stage manifestations. Once brain metastasis occurs, the survival is generally poor regardless of therapeutic modality.[10] Treatment options for BMFOC include corticosteroids, surgical resection, radiotherapy, chemotherapy, or a combination of these. Among these options, multimodal therapy tends to provide better survival outcomes and more effective responses.[11]

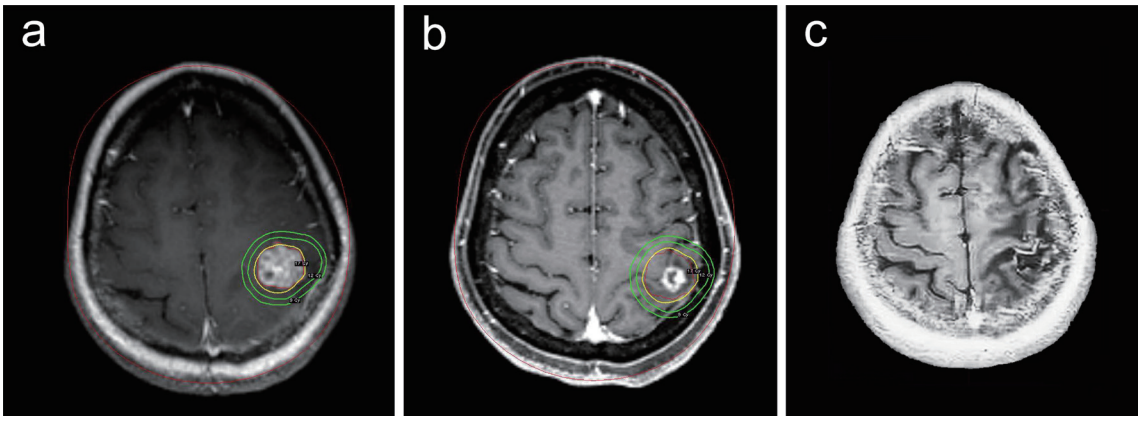

Fig. 2. Axial-loaded MRI of a 52-year-old female patient with right limb weakness. She underwent GKSRS for brain metastasis from ovarian cancer on May 14, 2019. The central and peripheral doses were 34 Gy and 17 Gy, respectively, with a 50% isodose line (a). A follow-up MRI on December 19, 2019, revealed a reduction in tumor size, and her right limb weakness gradually improved (b). A subsequent MRI on February 15, 2025, confirmed continued tumor shrinkage (c). GKSRS, Gamma Knife stereotactic radiosurgery; MRI, magnetic resonance imaging.

GKSRS for the treatment of BMFOC was first reported in 1997 by Kawana and co-workers.[12] Gamma Knife has been widely adopted for brain metastases because it is a non-invasive option that offers excellent local tumor control. Muacevic *et al*.[13] demonstrated that the one-year survival and local tumor control rates were not significantly different between patients treated with Gamma Knife alone and those treated with surgical resection plus WBRT. Corn and colleagues reported that compared to WBRT alone, radiosurgery resulted in a higher two-year survival rate (60% vs. 15%) and a higher CR rate (40% vs. 29%).[14] O'Neill *et al*.[15] found that the one-year survival rate was similar between patients treated with Gamma Knife and those who underwent tumor resection (62% vs. 56%, respectively). However, Gamma Knife significantly improved local control, with recurrence rates of 0% compared to 58% in the surgical group. Kim *et al*.[16] also reported that Gamma Knife treatment positively influences survival, suggesting it can improve outcomes in patients with brain metastases. Lee *et al*.[17] found that the median survival times for BMFOC patients treated with GKSRS and WBRT were 29 months and six months, respectively. Although current therapies may increase overall median survival to around 20 months, these findings are based on small sample sizes, and no prospective studies of Gamma Knife in BMFOC have yet been conducted.[18] Piura *et al*.[19] reported that the median survival time after the diagnosis of ovarian cancer and brain metastases was 33 months (range: 24–67 months) and six months (range: 1–28 months), respectively. Their data showed one-, 1.5-, and two-year OS rates of 90.9% (95% confidence interval (CI): 78.4–95.7%), 63.6% (95% CI: 50.2–75.1%), and 18.2% (95% CI: 9.8–30.3%), respectively. At 12 months post-GKSRS, the tumor control rate was 97.1%, with no reported tumor hemorrhage. These findings suggest that GKSRS is a promising modality for the treatment of BMFOC. A summary of the literature on stereotactic radiosurgery in BMFOC is presented in Table 2.[1,6,10,12,14,17]

The survival rate for brain metastases may improve with multimodal treatment involving surgical resection or stereotactic radiosurgery. Several factors—including age, histologic subtype, Karnofsky Performance Status, and the number of metastases—should be considered when selecting the optimal treatment strategy for BMFOC patients.[11] Notably, the age at brain metastasis diagnosis, the time interval to brain metastasis, the number of brain metastases, and the specific treatments used were not significantly associated with survival. However, patients with solitary brain metastasis tend to have better outcomes than those with multiple metastases.[20]

Given the rarity of BMFOC, only a limited number of patients have undergone GKSRS, and prospective clinical data remain lacking. While current findings suggest that GKSRS offers favorable tumor control and potential survival benefits, larger multicenter studies are necessary to validate these observations. Moreover,

Table 2. Literature review of brain metastases from ovarian cancer: treated with stereotactic radiosurgery

Authors	Study period	Number of patients	The median age at first treatment	Median interval to brain metastases (Months)	Median prescribed dose (Gy)	Radiographic tumor control (%)	Median survival after GKSRS (Months)
Kawana *et al*.[12]	1997[a]	1	50	36	20	100	21
Corn *et al*.[14]	1999[a]	5	57	27	15	80	–
Shepard *et al*.[10]	2014[a]	8	61	49.5	–	–	18[b]
Lee *et al*.[17]	1983–2005	7	56	28	–	–	29
Ogino *et al*.[1]	2006–2010	16	56.5	27.5	20	86.4	12.5[b]
Ordoñez *et al*.[6]	1993–2018	9	57	37	16	95	10.6
Our series	2015–2019	11	57.7	21	16	97.1	19

[a]year of publication; [b]the median survival following diagnosis of brain metastases. GKSRS, Gamma Knife stereotactic radiosurgery.

GKSRS is generally well tolerated, minimally invasive, and provides excellent local control. Combination therapies may further improve prognosis, and Gamma Knife can be effectively integrated with other cancer treatments. At present, there are no standardized treatment guidelines for BMFOC. The rarity of the disease presents a challenge for conducting large-scale studies. Therefore, it is necessary to establish multicenter collaborative research efforts to develop standardized management protocols.

Limitations

This study has several inherent limitations. Firstly, the retrospective nature of the study and the limited sample size may introduce selection bias and reduce the ability to establish causal relationships. The small sample size also limits statistical power and may not capture the full variability of clinical presentations and treatment responses. Additionally, the absence of a control group further restricts the strength of the conclusions drawn. These limitations should be considered when interpreting the findings.

Conclusions

The findings of this study indicate that GKSRS may serve as an effective treatment modality for selected BMFOC patients, offering high intracranial tumor control rates. The data indicate that GKSRS is generally well tolerated, with no significant adverse effects observed in this study. While GKSRS may be a valuable option for managing BMFOC, treatment decisions should be individualized, taking into account factors such as tumor burden, extracranial disease status, performance status, and patient preferences.

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Conflict of interest

All authors declare that they have no conflicts of interest.

Author contributions

Study conception, study design, statistical analysis, data interpretation (CH, JS), drafting of the manuscript, revision (CH, JS, WL), and study and analysis of follow-up clinical data (HW, SW, GC, HZ). All authors have contributed significantly to the study, read and approved the final version of the manuscript for publication.

Ethical statement

This study protocol was developed in accordance with the ethical standards of the 1964 Declaration of Helsinki and its subsequent amendments. The protocol was approved by the Ethical Committee of the Chinese People's Liberation Army General Hospital (Approval No. HZXJY-PJ-2025-26). Written informed consent for publication of the images was obtained from the patient or their legal representative.

Data sharing statement

The datasets used and analyzed during the current study are available from the corresponding author upon reasonable request.

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