Outcomes and Complications of Gamma Knife Radiosurgery for Skull Base Meningiomas

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J Neurol Surg B 2014;75:397–401.

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Abstract

Objective To review the outcomes and complications of meningiomas treated with gamma knife radiosurgery (GKRS) as a primary treatment as well as an adjunct therapy. **Materials and Methods** We performed a retrospective review (2000–2013) of 136 patients with meningiomas who received GKRS. Of 136 patients, 68 patients had recurrent or residual tumors after microsurgical resection, and the other 68 patients received GKRS alone. The study population was evaluated clinically and radiographically after GKRS treatment.

Results GKRS in meningiomas showed significant variations in tumor growth control (decreased in 69 patients [50.7%], arrested growth in 47 patients [34.6%], and increased tumor size in 20 patients [14.7%]). Progression-free survival rates after GKRS at 3, 5, and 10 years were 98%, 95% and 85%, respectively. Overall improvement of signs and symptoms after GKRS was 30% (71% versus 41%) compared with pretreated sign and symptoms ($p = 0.0001$). The Karnofsky performance scale was significantly improved after GKRS compared with the pretreated status (92 versus 80). Twenty patients (14.7%) required resection after initial GKRS.

Conclusion These study findings revealed that GKRS offers a high rate of tumor control, preservation of multiple nerve functions, and a good quality of life in both new and recurrent patients with meningiomas.

Keywords

- skull base meningiomas
- gamma knife
- outcomes and complications

Introduction

Although most meningiomas are benign, a large tumor can cause significant neurologic deficits including cranial nerve palsies, seizure, and hemiparesis from mass effect on adjacent brain tissue or cranial nerves.^{1,2} Conventionally, microsurgical resection has been practiced as a treatment of meningiomas for a long time, but resection of skull base is associated with perioperative and postoperative complications as well as a high recurrence rate.^{3–6} Moreover, previous reports suggested that complete resection may not be achieved in 20 to 30% of patients with meningiomas due to the close location to critical neurovascular structures.^{3,6} However, stereotactic gamma knife radiosurgery (GKRS) has emerged

as a safe, effective, and alternative to microsurgery for meningiomas.^{7–11} Little information is found from a literature review regarding long-term outcomes of GKRS on meningiomas, particularly on residual or recurrent meningiomas. In addition, the treatment policy of meningiomas is still unclear because few patients benefit from radiosurgery or microsurgery alone; some patients require microsurgical resection after radiosurgery, and other patients benefit from radiosurgery after microsurgical resections.^{2,12,13} Therefore, the outcomes from different treatment modalities may be informative to decide future treatment policies for meningiomas. In the present study, we retrospectively evaluated our experience in the management of patients with new and recurrent or residual meningiomas.

received
February 25, 2014
accepted
March 24, 2014
published online
May 27, 2014

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Stuttgart · New York

DOI <http://dx.doi.org/10.1055/s-0034-1376422>.
ISSN 2193-6331.

Materials and Methods

This study was done after approval by the institutional review board at our institution. Information related to clinical history, surgery, neuroimaging, and outcomes of the patients with meningiomas between 2000 and 2013 was collected retrospectively by a review of the patient's case notes, follow-up chart, and radiology reports. We had information on outcomes of GKRS in all the patients.

Patients and Tumor Characteristics

The median age of the patients in this study was 57 years (range: 27–101 years). There were clear gender and ethnicity predilection: 97 women (71%), 39 men (29%), 95 whites (70%), 40 African Americans (29%), and 1 Asian (< 1%). Sixty-eight patients (50%) had prior resection. Meningiomas were located in the following order including 58 cases (43%) in the anterior cranial fossa, 28 in the middle cranial fossa (20%), and 50 in the posterior cranial fossa (37%) (►Table 1).

Radiosurgical Techniques

GKRS was performed using the Leksell (Atlanta, Georgia, United States) stereotactic unit, model "C" with APS (automatic positioning system). The Leksell head frame was applied to the patient's head under intravenous sedation and local anesthesia. The patient was then transferred to the magnetic resonance imaging suite for imaging. High-resolution contrast-enhanced axial pictures of the brain were taken in the three-dimensional spoiled gradient recalled sequence. The imaging data were then transferred to the Gamma Knife planning computer via the Ethernet. The Leksell Gamma Plan software

Table 2 Summary of marginal dose, maximum dose, and isodose line and radiation times for treatment of meningiomas

Parameter	Value (range)
Mean marginal dose, Gy	14 (12–30)
Mean maximum dose, Gy	27 (10–44)
Mean isodose line, %	50 (50–80)
Radiation time, min	40 (4–94)

v.5.34 was used to perform the dose planning. The mean marginal doses to the tumor was 14 Gy (range: 12–30), the maximum dose to the tumor was 27 Gy (range: 16–44), and the mean isodose line was 50% (range: 50–80). Mean radiation exposure time was 42 minutes (range: 4–94) (►Table 2).

Follow-up

Preoperative and follow-up data were collected from the study population. If necessary, patients were contacted by telephone to update their outcome status. Neuroimaging studies were performed at 3-month intervals in the first year of the GKRS treatment, at 6-month intervals for the following 2 years, and annually thereafter. The median duration of follow-up was 5 years (6–156 months).

Statistical Analysis

Commercially available software, SPSS v.21.0 (SPSS, Inc, Chicago, Illinois, United States) was used for statistical analysis. Progression-free survival was analyzed using the Kaplan-Meier test. When necessary a chi-square test was also used. A *p* value < 0.05 was considered significant.

Results

Tumor Growth Control

►Table 3 lists tumor growth control after GKRS. The average tumor volume before GKRS was 5.4 cm³ (range: 0.4–18 cm³). The most recent follow-up showed decreased tumor size in 69 (50.7%) of the patients, arrested tumor growth in 47 (34.6%), and increased tumor size in 20 (14.7%). Tumor size after GKRS was reduced > 50% (5.40 cm³ versus 2.05 cm³) of the pretreated tumor size. There was no significant difference in tumor size in growth-arrested tumors (5.40 cm³ versus 5.73 cm³) after GKRS. There was considerable increase in tumor size in the progressive tumors (5.40 cm³ versus 11.80 cm³) after GKRS. On average, it took 38 months to reduce the tumor size and 22 months for tumor progression after GKRS (►Table 3). Kaplan-Meier statistical analysis revealed that overall survival rates after GKRS at 3, 5, and 10 years were 98%, 95%, and 85%, respectively (►Fig. 1).

Neurologic Deficits

With the GKRS, the total number of sign and symptoms was significantly improved when compared with the amount of pretreated sign and symptoms (pre-GKRS: 96 [71%] versus post-GKRS: 56 [41%]). The visual problem was improved significantly after GKRS (pre-GKRS: 37 [27%] versus

Table 1 Characteristics of patients and meningiomas

Variables	Value (%)
Age, y	
Median	57
Range	27–101
Gender	
Male	39 (28.7)
Female	97 (71.3)
Ethnicity	
White	95 (69.9)
African American	40 (29.4)
Asian	1 (0.7)
Tumor location	
Anterior cranial fossa	58 (43)
Middle cranial fossa	28 (20)
Posterior cranial fossa	50 (37)
Treatment policy	
GKRS	68 (50)
Prior resection (Sx + GKRS)	68 (50)

Abbreviations: GKRS, gamma knife radiosurgery; Sx, surgery.

Table 3 Tumor size, percentage of patients with tumor control, and progression after gamma knife radiosurgery

Follow-up	Value
Tumor size, cm3	
Before treatment (range)	5.40 (0.4–18)
After treatment, %	
Decreased	2.05
No change	5.73
Increased	11.80
Time to control, mo	
Decreased tumor size (range)	38 (4–51)
Time to progression, mo (range)	22 (5–72)
No. of patients (%)	
Decreased	69 (50.7)
No change	47 (34.6)
Increased	20 (14.7)

Fig. 1 Kaplan-Meier survival rate in all patients with meningiomas after gamma knife radiosurgery treatment.

Table 4 Improvement of sign and symptoms after gamma knife radiosurgery therapy in the patients with vestibular schwannoma meningiomas^a

Clinical features	Pre-GKRS (%)	Post-GKRS (%)	p value
Headache	37 (27)	22 (16)	0.000
Imbalance	6 (4)	5 (3)	NS
Visual impairment	25 (18)	7 (5)	0.009
Trigeminal nerve dysfunction	4 (3)	3 (2)	NS
Facial nerve dysfunction	8 (6)	4 (3)	NS
Hearing deficit	9 (7)	7 (5)	NS
Tinnitus	2 (1.5)	2 (1.5)	NS
Dizziness	4 (3)	6 (4)	NS
Vertigo	1 (0.7)	0 (0)	NS
Total symptoms	96 (71)	56 (41)	0.000

Abbreviations: GKRS, gamma knife radiosurgery; NS, not significant.

^ap < 0.05 is considered significant.

post-GKRS: 22 [16%]). Although the imbalance (4% versus 3%), trigeminal nerve dysfunction (3% versus 2%), facial nerve dysfunction (6% versus 3%), and hearing deficits (7% versus 5%) were reduced after GKRS, there was no significance difference (→ **Table 4**).

Other Symptoms

Significant improvement of headache after GKRS was noted compared with pre-GKRS (37 [27%] versus 22 [16%], respectively). There was no improvement of dizziness, but rather dizziness developed in two new patients after GKRS. There was no significance difference in tinnitus and vertigo after GKRS (→ **Table 4**).

Results of Functional Status

We have demonstrated the Karnofsky performance score (KPS) in our study population and found a significant difference in the KPS after GKRS compared with pre-GKRS (92 versus 80). Twenty-seven patients (19.9%) had no change in the KPS scale; 1 patient (0.73%) showed a deteriorated KPS after GKRS. The patients with meningiomas in the anterior cranial fossa had significantly higher KPS than meningiomas in other locations (→ **Table 5**).

Complications

→ **Table 5** lists the complications including hydrocephalus and seizure in the patients after GKRS treatment. Two patients (1.5%) developed hydrocephalus, and 5 patients (3.7%) experienced seizure. There was preexisting ataxia in 5 patients (3.7%), visual problems in 7 (5.1%), trigeminal nerve affection in 3 (2.2%), facial nerve dysfunction in 4 (2.9%), and hearing problems in 7 (5.1%) after GKRS. In addition, 20 patients (14.7%) required microsurgical resection after GKRS. Five patients (3.7%) required another GKRS after the initial GKRS. The patients required microsurgical resection after 3.5 and 4.2 years of initial GKRS treatment as secondary and tertiary treatment for new and recurrent patients, respectively (→ **Table 5**).

Table 5 Quality of life or Karnofsky performance scale before and after gamma knife radiosurgery (GKRS) treatment and complications post GKRS^a

Clinical features	Pre-GKRS	Post-GKRS	p value
KPS scale	80	92	0.01
Predictive factors for KPS			
Tumor location			
Anterior cranial fossa	80	94	0.02
Middle cranial fossa	77	88	
Posterior cranial fossa	80	91	
Complications			
Hydrocephalus	0	2	
Seizure	0	5	
Ataxia		5	
Facial palsy		4	
Visual problem		7	
Trigeminal neuropathy		3	
Resection required, n (%)		20 (14.7)	

Abbreviations: GKRS, gamma knife radiosurgery; KPS, Karnofsky performance scale.

^ap < 0.05 is considered significant.

Discussion

Although several treatment options have been established for the treatment of meningiomas, patients and surgeons still face difficulties in choosing appropriate treatment options including conventional microsurgical resection, radiosurgery, and observation.^{2,12} Moreover, patients with recurrent and residual meningiomas have a less favorable prognosis and require further resection.^{14–16} Therefore, variables including characteristics of tumor, individual patients, and comorbidities, as well as patient preference, should be considered before deciding any treatment modality for meningiomas.¹⁷ In our series of meningiomas, we have reported the long-term (> 10 years) outcome of GKRS treatment as primary and adjuvant therapy for the patients with new, recurrent, and residual meningiomas.

In this study, the overall long-term tumor control was 86% after GKRS treatment in new and recurrent patients, which is consistent with other previous reports (75–100% of tumor growth control).^{12,18–22} Our result showed 91% control of tumor growth by GKRS as a primary treatment of meningiomas, and 81% as an adjuvant therapy; therefore GKRS would be the best option for long-term management of patients with new and recurrent meningiomas as previously reported.^{12,22–26} GKRS required almost 3 years to control tumor growth, which is also consistent with previous reports.

This study also demonstrated that compared with new patients, recurrence rate (10% versus 19%) and further resection (12% versus 19%) were required more for recurrent and residual tumors. These less favorable outcomes of GKRS on recurrent and residual meningiomas usually depend on the characteristics (aggressive or not) and Simpson grades of resection of those tumors.^{14–16} In this, the additional resections were required in those patients with recurrent meningiomas due to the tumor progression and related complications. However, complications of repeated surgery including cerebrospinal fluid leakage, hydrocephalus, and multiple cranial nerve deficits still can be avoided using GKRS therapy in 81% of patients with recurrent meningiomas.^{25,27}

Another target of the meningioma treatment is preservation of neurologic function and other systemic symptoms in affected patients. Our findings revealed that GKRS therapy improved 30% of total signs and symptoms. This study also demonstrated that neurologic problems including visual impairment, facial nerve dysfunction, and trigeminal nerve dysfunction were markedly improved after GKRS therapy, which is consistent with a previous report.²⁶ Systemic symptoms such as headache and dizziness were improved after GKRS therapy in the patients with new and recurrent meningiomas.²⁶

Another component of radiosurgery is to identify the progression-free survival rate in the study population. Consistent with a previous finding, this study demonstrated that the progression-free survival rates were 98%, 95%, and 85% at 3, 5, and 10 years, respectively, after GKRS.²⁸ There was a higher survival rate in patients with prior resections. Our study also demonstrated that overall activity was improved after GKRS, which could be due to improvement in signs and symptoms of the disease including visual problems, headache, and dizziness.²⁹ This study did show some complications including hydrocephalus, seizure, preexisting visual problems, and ataxia after GKRS as reported in previous reports.^{28,29}

Limitations

The limitations of this study include its retrospective nature and the lack of a control group, restricting us from assessing the full benefit and complications of GKRS. Taken together, given the good tumor growth control, possible preservation of neurologic defects, good overall survival rate, lesser number of complications, and improvement of performance in the patients, GKRS can be an important treatment option for patients with skull base meningiomas. In addition, GKRS can be also a good treatment option for recurrent or residual meningioma patients to avoid repeated resections along with craniotomy-related complications. Further studies with a large volume of patients with skull base meningiomas and a randomized controlled trial are required to accomplish a good comparison of treatment modalities.

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