Long-Term Outcome of Gamma Knife Radiosurgery for Vestibular Schwannoma

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Abstract

Objective We evaluated the long-term outcome of vestibular schwannoma (VS) treated with gamma knife radiosurgery (GKRS) as a primary treatment as well as an adjunct therapy.

Materials and Methods We performed a retrospective review (2000–2012) of 82 patients with VS who received GKRS. Of 82 patients, 20 patients with prior resection received GKRS treatment as an adjunct therapy. The remainder of the patients (62) received GKRS as a primary treatment.

Results GKRS for VS showed significant variations in tumor growth control (decreased in 44 patients [54%], arrested growth in 30 patients [36%], and increased tumor size in 8 patients [10%]). Progression-free survival rates after GKRS at 3, 5, and 10 years were 98%, 95%, and 95%, respectively. Hearing, facial nerve function, and Karnofsky performance scale were significantly improved after GKRS compared with pretreated status (79 versus 90). Two patients (2.5%) required resection again due to tumor progression and worsening of signs and symptoms.

Conclusion Long-term follow-up demonstrated 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 VS.

Keywords

- ▶ vestibular schwannoma
- ▶ gamma knife radiosurgery
- ▶ long-term outcome

Introduction

The incidence of vestibular schwannoma (VS) is rising because of the worldwide growth of the geriatric population, as well as the increased use and rapid improvement of magnetic resonance imaging (MRI).^{1,2} Common strategies for the treatment of VS include the wait and scan policy, microsurgical resection, and gamma knife radiosurgery (GKRS).³ Conventional microsurgical resection was practiced as a treatment of VS for a long time.^{3,4} However, stereotactic GKRS has emerged as an important alternative treatment option for brain tumors including VS.⁵ From the literature search, little information was found regarding long-term outcomes of GKRS or microsurgical treatment of VS. Most articles on GKRS or microsurgical treatment of VS reported only short-term outcomes.^{4,6,7} In addition, the treatment policy of VS is

still unclear because few patients benefit from radiosurgery or microsurgery alone. Some patients require microsurgical resection after radiosurgery, and others benefit from radiosurgery after microsurgical resections.³ Therefore, long-term outcomes from different treatment modalities would be informative to determine a future treatment policy for VS. We retrospectively evaluated our experience in the management of patients with new and recurrent or residual VS.

Materials and Methods

This study was done following approval by our institutional review board. Information related to clinical history, surgery, neuroimaging including MRI, and outcomes of patients with schwannomas between 2000 and 2012 was collected

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Table 1 Patient characteristics

Variables	Value
Age, y	
Median	62
Range	14–89
Gender (%)	
Male	31 (37.8)
Female	51 (62.2)
Ethnicity (%)	
Whites	71 (86.6)
African Americans	11 (13.4)
Tumor characteristics	
Side of tumor (%)	
Right	40 (49)
Left	42 (51)
Location (%)	
Intracanalicular	47 (57)
Cerebellopontine	22 (27)
Intracanalicular and cerebellopontine	13 (16)
Treatment policy (%)	
GKRS	62 (76)
Prior resection (Sx + GKRS)	20 (24)

GKRS, gamma knife radiosurgery; Sx, surgery.

retrospectively by reviewing patients' case notes and follow-up charts. All of the patients in the study were available for follow-up.

Patients and Tumor Characteristics

The median age of patients with VS was 62 years (range: 14–89 years). There were clear gender and ethnicity predilections, with 51 females (64%), 31 males (38%), 77 whites (87%), and 11 African Americans (13%). Twenty patients (24%) had a prior resection. Tumor distribution was 40 (49%) on the right side and 42 (51%) in the left side. Of 82 patients, VS was in an intracanalicular location in 47 patients (57%), the cerebellopontine angle in 22 patients (27%), and both intracanalicular and cerebellopontine angle in 13 patients (16%) (► **Table 1**).

Radiosurgical Techniques

GKRS was performed using the Leksell stereotactic unit model C with 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 MRI 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. Leksell Gamma Plan software v.5.34 was used to perform dose planning. The mean marginal dose to the tumor was 12 Gy (range: 12–13), maximum dose to the tumor was 27 Gy (range: 16–40), and mean isodose line was

Table 2 Marginal dose, maximum dose, isodose line, and radiation time during treatment of vestibular schwannoma

Parameter	Value
Mean marginal dose, Gy (range)	12 (12–13)
Mean maximum dose, Gy (range)	27 (16–40)
Mean isodose line, % (range)	50 (15–100)
Radiation time, min (range)	40 (4–98)

50% (range: 15–100). Mean radiation exposure time was 40 minutes (range: 4–98) (► **Table 2**).

Follow-up

Preoperative and follow-up data were collected from the patients in this study. If necessary, patients were contacted by telephone to update them on 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 months to 12 years).

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. A chi-square test was also used when applicable. A *p* value < 0.05 was considered significant.

Results

Tumor Growth Control

The average tumor volume was 3.24 cm³ (range: 0.2–16 cm³). The most recent follow-up showed that tumor size decreased

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

Follow-up	Value
Tumor size, cm³	
Before treatment (range)	3.24 (0.24–16)
After treatment	
Decreased	1.72
No change	2.93
Increased	4.29
Time to control, mo (range)	
Decreased	40 (4–76)
No change	34 (6–60)
Time to progression, mo (range)	29 (2–73)
No. of patients (%)	
Decreased	44 (54)
No change	30 (36)
Increased	8 (10)

Fig. 1 Kaplan-Meier progression-free survival rate in all patients with vestibular schwannoma after gamma knife radiosurgery.

in 44 patients (54%), displayed no change in 30 patients (36%), and increased in 8 patients (10%). GKRS reduced the tumor size to almost half of the average size of the pretreated tumor (3.24 cm^3 versus 1.72 cm^3). On average, it took 40 months to reduce tumor size, 34 months to arrest tumor growth, and 29 months for tumor progression after GKRS (►Table 3). A Kaplan-Meier statistical analysis revealed that progression-free survival after GKRS at 3, 5, and 10 years was 97%, 95%, and 95%, respectively (►Fig. 1).

Hearing Preservation

The follow-up results of hearing preservation after radiosurgery are depicted in ►Table 4 and in ►Fig. 2. Hearing loss before GKRS was found in 80 patients (98%). Hearing loss improved significantly in 64 patients (80%) when preoperative and postoperative testing were compared. The probability of progression-free hearing preservation in patients with VS after GKRS therapy at 3, 5, and 10 years was 90%, 83%, and 58%, respectively (►Fig. 2).

Facial Nerve

►Table 4 and ►Fig. 3 show the follow-up results of facial nerve function after radiosurgery. Facial nerve function was affected

Fig. 2 Possibility of progression-free hearing preservation in all patients with vestibular schwannoma after gamma knife radiosurgery.

in 16 patients (20%) before treatment. Facial nerve function improved in 11 patients (68%) with affected facial nerve after GKRS. The probability of progression-free preservation of facial nerve in patients with VS after GKRS therapy at 3, 5, and 10 years was 97%, 94%, and 90%, respectively (►Fig. 3).

Trigeminal Neuropathy

The follow-up results of trigeminal nerve after radiosurgery are listed in ►Table 4. There was no trigeminal neuropathy in any patients before treatment. Trigeminal neuropathy developed in 3 patients (4%) after GKRS.

Other Symptoms

►Table 4 lists the preoperative and postoperative findings of ataxia, tinnitus, vertigo, headache, and dizziness. Ataxia was significantly improved after GKRS (22 [27%] versus 6 [7%]) when preoperative status was compared with postoperative status. Similarly, headache and dizziness problems were significantly improved after GKRS (17 [21%] versus 7 [9%]; 17 [121%] versus 4 [7%], respectively, when preoperative status was compared with postoperative status. Although tinnitus and vertigo after GKRS tended to decrease, there was no significant improvement.

Table 4 Improvement of signs and symptoms after gamma knife radiosurgery in patients with vestibular schwannoma

Clinical features	Pre-GKRS	Post-GKRS	<i>p</i> value ^a
Hearing loss (%)	80 (98)	16 (20)	0.000
Facial nerve affection (%)	16 (20)	5 (6)	0.001
Trigeminal nerve affection (%)	0 (0)	3 (4)	NS
Ataxia (%)	22 (27)	6 (7)	0.000
Tinnitus (%)	12 (19)	9 (11)	NS
Vertigo (%)	5 (8)	1 (1)	NS
Headache (%)	17 (21)	7 (9)	0.019
Dizziness (%)	17 (21)	4 (7)	0.002

GKRS, gamma knife radiosurgery.

^a*p* < 0.05 was considered significant.

Fig. 3 Possibility of progression-free facial nerve function preservation in patients with vestibular schwannoma after gamma knife radiosurgery.

Functional Results

We used the Karnofsky performance status (KPS) scale in our study population and found it was 79 before GKRS. The KPS scale was significantly improved after GKRS (to 90) (►Table 5). Fifteen patients (18%) had no change in the KPS scale; the KPS scale of one patient (2%) deteriorated after GKRS.

Complications

The complications including hydrocephalus in patients after GKRS treatment are listed in ►Table 5. One patient (1%) developed hydrocephalus; one patient (1%) showed left-sided weakness. There was preexisting facial nerve affection in 6%, ataxia in 7%, and 4% of patients developed new trigeminal neuralgia after GKRS. Two patients (one new patient and one recurrent patient) required microsurgical resection after GKRS. The patients required microsurgical resection after

Table 5 Quality of life and Karnofsky performance scale before and after gamma knife radiosurgery (GKRS) and complications after GKRS

Clinical features	Pre-GKRS	Post-GKRS	<i>p</i> value ^a
KPS scale	79	90	0.01
Complications			
Hydrocephalus	0	1	
Left hemiparesis	0	2	
Facial palsy	16	5	
Ataxia	22	9	
Trigeminal neuropathy	0	3	
Resection required (% of patients)		2	

GKRS, gamma knife radiosurgery; KPS, Karnofsky performance scale.
^a*p* < 0.05 was considered significant.

6.5 and 8 years of GKRS as secondary and tertiary treatment in new and recurrent patients, respectively (►Table 3).

Discussion

In the last 100 years, several treatment options were established for the treatment of VS. Patients and surgeons today may find it difficult to choose the appropriate treatment options including conventional microsurgical resection, radiosurgery, and observation.⁸ A growing body of evidence suggests that GKRS is one of the most effective treatment modalities for VS and is a reasonable alternative option to microsurgical resection, especially for small to medium size tumors, older patients, and patients with comorbidities.^{5,8–13} However, for the larger VS, it is more difficult to choose treatment options because several treatment strategies are available including GKRS, gross total resection, near total resection, subtotal resection (STR), STR with planned secondary GKRS, STR with observation, and repeat GKRS or STR for regrowth with a deteriorating condition.^{3,10} Therefore, variables including characteristics of tumor, individual patients, and comorbidities, as well as patient preference, should be considered before deciding on any treatment modality.¹⁰ In our series of VS, we have reported the long-term outcome (> 10 years) of GKRS as a primary treatment for new patients with VS and as a secondary treatment for patients with a prior resection.

In the present study, the overall long-term tumor control was 90% after GKRS treatment, which is consistent with other previous reports.^{14–16} Although one report¹⁷ showed a correlation between tumor size and growth control rate, our findings did not show any correlation between tumor size and growth control rate and are consistent with another previous report.⁸ GKRS required ~ 3 years to control tumor growth, which is also consistent with a previous report. In our study, although 2.5% of patients required revision surgery, 97.5% of patients did not require any further treatment after GKRS. Therefore, complications of revision surgery including CSF leakage, ataxia, and multiple cranial nerve deficits can be avoided with GKRS in 97.5% of patients with VS.¹⁸

Another target of the VS treatment is the preservation of hearing. This study demonstrated that the probability of hearing preservation progressively decreased over the years. Long-term preservation of hearing after GKRS was 80%. Supporting our results, variations (38–94%) in the preservation of hearing after the GKRS treatment were reported in different articles.^{3,8,19–21} Similarly, consistent with another report,¹⁶ our study showed a significantly lower rate of facial nerve affection in overall patients (6%). GKRS in the patients with prior resection showed a significantly higher rate of facial nerve affection compared with primary treatment (20% versus 3%), which could be due to the effect of prior microsurgery.⁸ Unfortunately, the long-term effects of treatment with GKRS alone in our findings showed that 4% of patients developed trigeminal neuropathy, consistent with previous reports.^{22,23} Our study did not show trigeminal neuropathy in any patient when GKRS was used as an adjuvant therapy; other reports suggested that microsurgery causes significant

trigeminal neuropathy.^{8,24} Although there was no significant improvement of tinnitus and vertigo after GKRS treatment compared with pretreatment, there was a tendency for those symptoms to reduce. Unfortunately, two new patients developed tinnitus in a prior resection group. Importantly, consistent with other observations, other symptoms including headache and dizziness were significantly reduced in all patients with VS.⁵

Another component of radiosurgery is to identify the progression-free survival rate in treated patients. This study revealed that the progression-free survival rate was 90% 10 years after GKRS. There was a higher survival rate in the patients with a prior resection. Supporting our study, other reports also showed a similar survival rate with GKRS treatment in the patients with VS.¹⁶ Likewise, our study also demonstrated that overall activity was improved after GKRS, which could be due to an improvement in signs and symptoms of the disease including balance problems, hearing, facial nerve function, headache, and dizziness.^{25,26}

This study did not show any major complications including hydrocephalus and edema after GKRS in new patients. However, from the prior resection group, one patient showed hydrocephalus and another patient experienced right-sided weakness. A similar risk was seen in resection or conservative management.^{4,27}

Study Limitations

This study has a few limitations including its retrospective nature, lack of a control group to assess the full benefit and complications of GKRS, and the small number of patients.

Taken together, given the good control of tumor growth, possible hearing preservation, preservation of facial nerve function, a good overall survival rate, no or a lesser number of complications, and improvement of the long-term quality of life, GKRS can be an ideal treatment option for VS. In addition, GKRS can also be a good treatment option for recurrent or residual VS after resection to avoid repeated resections and craniotomy-related complications. Further study in a large volume of patients with recurrent or residual tumors and a randomized controlled trial are required to accomplish a good comparison of treatment modalities.

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