

CLINICAL INVESTIGATION

Benign Disease

SALVAGE GAMMA KNIFE STEREOTACTIC RADIOSURGERY FOR SURGICALLY REFRACTORY TRIGEMINAL NEURALGIA

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Purpose: To evaluate the clinical outcome of patients with surgically refractory trigeminal neuralgia (TN) treated with rescue gamma knife radiosurgery (GKRS).

Methods and Materials: Seventy-nine patients with typical TN received salvage GKRS between 1997 and 2002 at the Barrow Neurological Institute (BNI). All patients had recurrent pain following at least one prior surgical intervention. Prior surgical interventions included percutaneous destructive procedures, microvascular decompression (MVD), or GKRS. Thirty-one (39%) had undergone at least two prior procedures. The most common salvage dose was 80 Gy, although 40–50 Gy was typical in patients who had received prior radiosurgery. Pain outcome was assessed using the BNI Pain Intensity Score, and quality of life was assessed using the Brief Pain Inventory.

Results: Median follow-up after salvage GKRS was 5.3 years. Actuarial analysis demonstrated that at 5 years, 20% of patients were pain-free and 50% had pain relief. Pain recurred in patients who had an initial response to GKRS at a median of 1.1 years. Twenty-eight (41%) required a subsequent surgical procedure for recurrence. A multivariate Cox proportional hazards model suggested that the strongest predictor of GKRS failure was a history of prior MVD ($p=0.029$). There were no instances of serious morbidity or mortality. Ten percent of patients developed worsening facial numbness and 8% described their numbness as “very bothersome.”

Conclusions: GKRS salvage for refractory TN is well tolerated and results in long-term pain relief in approximately half the patients treated. Clinicians may reconsider using GKRS to salvage patients who have failed prior MVD. © 2009 Elsevier Inc.

Trigeminal neuralgia, Gamma knife radiosurgery, Microvascular decompression, Tic douloureux, Facial pain.

INTRODUCTION

Patients with idiopathic trigeminal neuralgia (TN) who have failed prior surgical or radiosurgical intervention represent a therapeutic challenge. Although primary surgical treatment is effective in most patients, pain recurs in a significant subset; patients who have persistent or recurrent symptoms despite intervention represent approximately 10% to 30% of patients who undergo microvascular decompression (MVD), 20% to 50% of those who undergo a percutaneous destructive procedure, and 30% to 40% of those who undergo gamma knife radiosurgery (GKRS) (1–9). Because it has a low incidence of adverse effects, is an outpatient procedure, and does not prevent the subsequent use of more invasive modalities should they be necessary, GKRS has been used as an alternative to MVD and percutaneous lesioning techniques in an attempt to salvage these patients. GKRS achieves its therapeutic effect by producing a lesion in the root entry zone of the trigeminal nerve that results in axonal

degeneration (10). Despite the use of GKRS as a salvage modality, the long-term outcomes and complications are not well studied. To learn more about the role of GKRS in this setting, we examined a cohort of patients who received salvage GKRS at the Barrow Neurological Institute (BNI; Phoenix, AZ) and were followed for 1–10 years.

METHODS AND MATERIALS

This study was approved by the St. Joseph's Hospital and Medical Center's Institutional Review Board. When possible, the guidelines proposed by Zakrzewska *et al.* (11) regarding the description of surgical series and trigeminal neuralgia were followed.

Patient population

Only patients with TN1 (typical trigeminal neuralgia) who had failed either surgery (*i.e.*, percutaneous rhizotomy with glycerol, heat, or balloon or MVD) or radiosurgical intervention were included in the study (12). The treatment indications were recurrent

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or persistent pain following surgical intervention, and subsequent failure of medical management. Patients were also offered GKRS if they experienced recurrent pain and were unable to tolerate medication. Between April 1997 and September 2003, 79 patients underwent GKRS salvage by the senior author (A.G.S.) at the BNI. Patient characteristics are noted in Table 1. The median patient age at treatment was 69. Forty-nine (62%) were women, and 50 (63%) suffered from right-sided pain. Thirty-eight (48%) had undergone at least one percutaneous lesioning procedure (*i.e.*, balloon compression, thermal rhizotomy, or glycerol rhizotomy). Twenty-four (30%) had undergone prior MVD and 21 (27%) prior GKRS. Thirty-one (39%) failed two or more prior procedures.

Radiosurgery technique

The health care team consisted of a neurological surgeon, a radiation oncologist, neuroradiologist, radiation physicist, and a radiosurgery nurse. From 1997 to 2002, patients were treated with the Model B Leksell Gamma Knife unit (Elekta Instruments, Atlanta, GA) and with the Model C unit thereafter. Preprocedural stereotactic magnetic resonance imaging or computed tomography cisternography was obtained with the stereotactic frame rigidly affixed to the calvarium. A single 4-mm isocenter was positioned so that the 90% isodose line completely covered the nerve and the 50% isodose line abutted the surface of the brainstem. The most common maximum dose was 80 Gy used in 47% of patients. In patients who had undergone a previous radiosurgical procedure, we targeted the same portion of the proximal nerve root with maximum doses of 40–50 Gy with a single 4-mm isocenter as we have previously described (13).

Outcome assessment

Patients were evaluated in the clinic 1 month after treatment as part of routine follow-up. Long-term outcomes were established by standardized survey mailed to each patient by certified mail or by telephone interview and by review of medical records. As suggested by Zakrzewska *et al.*, the survey contained questions regarding the status of facial pain, subsequent surgical treatments, facial numbness, life enjoyment, and the impact of facial pain on daily activities (11). Pain questions were modified from the Brief Pain Inventory, short form, developed by Charles Cleland, Pain Research Group. Facial numbness and eye symptoms were assessed by asking patients how they affected everyday life activities. Fifty patients responded to the survey. Follow-up for the remaining patients was obtained by review of the medical record.

Pain outcome was assessed by the BNI Pain Scale, a self-reported index that has been used previously by several groups (Table 2) (14–16). Three categories of pain outcomes were defined. Pain relief was defined as maintaining Pain Score IIIb (comfortable and taking medication) or better without requiring further surgery. A pain-free outcome was defined as Pain Score I (no pain and no medication). Treatment failure was defined as a decline in pain score below the threshold level (Pain Score IV or V) or the need for further surgery. Only patients with at least 1 year of clinical follow-up were included in the outcome analysis.

Statistical analysis

Statistical analysis was completed using SPSS (version 14.0; SPSS, Chicago, IL) by a doctorally trained biostatistician. Categorical variables were analyzed by chi-square analysis, Fisher's exact test, and Mann-Whitney test as appropriate. Continuous variables were analyzed by a two-tailed *t* test. Variables that were either significant or approached significance by the above methodologies

Table 1. Characteristics of study cohort

Patient characteristic	n (%) (N=78)
Sex	
Male	29 (38)
Female	49 (62)
Age at treatment (years)	
Median	69
Range	34–79
Duration of symptoms pre-GKRS salvage (years)	
Median	11
Range	0.5–46
Right-sided pain	50 (63)
Nerve branches involved	
1	29 (38)
> 1	49 (62)
No. of prior procedures	
1	48 (61)
2	16 (20)
3	9 (11)
> 3	6 (8)
Prior procedures (no. of patients)	
Destructive procedures	
Thermal	18 (23)
Glycerol	30 (38)
Balloon	4 (5)
Peripheral alcohol	4 (5)
MVD	24 (30)
GKRS	21 (27)
Salvage treatment dose	
40–50 Gy*	18 (23)
70 Gy	12 (15)
80 Gy	37 (47)
90 Gy	11 (14)
Abnormal preoperative sensory exam	34 (43)
Interval between failed treatment and salvage GKRS (years)	
Median	3.7
Range	0.1–15.9

Abbreviations: GKRS = gamma knife radiosurgery; MVD = microvascular decompression.

* Dose used in patients with prior GKRS.

were included in a multivariate Cox proportional hazards model. A *p* value < .05 was considered significant.

RESULTS

Clinical follow-up is presented for the 68 patients with at least 1 year of data. Median follow-up from the date of salvage GKRS was 5.3 years (range, 1–10.5 years).

Table 2. The Barrow Neurological Institute Pain Score

Pain Score	Definition
I	No pain and taking no medication
II	Occasional pain but taking no medication
III	
a	No pain but taking medication
b	Pain present but adequately controlled with medication
IV	Pain improved but not adequately controlled with medication
V	No relief

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