Gamma Knife Radiosurgery for Vestibular Schwannomas and Quality of Life Evaluation

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Keywords

Acoustic neuroma · Outcomes · Short-Form 36-item Health Questionnaire · Stereotactic radiosurgery · Brain tumor

Abstract

Background: Further investigation is needed to look at the impact of vestibular schwannoma (VS) on the health-related quality of life (QOL) of participants who undergo Gamma Knife® radiosurgery (GKRS). **Objectives:** Investigators compared the QOL for VS participants to reported US population norms in order to evaluate disease burden and long-term QOL several years after GKRS. **Methods:** This cross-sectional study surveyed participants to assess hearing status, tinnitus, imbalance, vertigo, as well as the Short-Form 36-item Health Questionnaire (SF-36). The data were normalized, age adjusted, and functional status was correlated to determine clinically significant differences. **Results:** A total of 353 participants who underwent GKRS between 1997 and 2007 were included in this study with a median postoperative period of 5 years. SF-36 scores were very similar to population norms, and age-adjusted scores for participants followed the US population curve. Frequent vertigo and balance problems had the largest statistically and clinically significant effect on physical and mental component summary

scores followed by nonuseful hearing in the tumor ear. **Conclusions:** Participants reported a good long-term QOL that was very similar to the QOL of US population norms. Of the common VS symptoms, vertigo had the greatest impact on QOL followed by imbalance and then hearing loss.

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Introduction

Patients with vestibular schwannomas (VS) are presented with various management options that range from continued observation and microsurgical removal by one of several surgical approaches to stereotactic radiosurgery using one of several methodologies. Few published studies are available to describe the long-term health-related quality of life (QOL) of patients who undergo one or more management options for VS [1–3], and most studies have

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Table 1. Demographics and tumor descriptives

Vestibular schwannomas treated between 1997 and 2007	822
Participants invited to the study based on criteria	712
Participants included in the study	353 (49.6%)
Median tumor volume	0.5 cm ³ (range 0.012–17.3)
Median dose of radiation to tumor margin	13 Gy (range 7–30)
Gender female	178 (50.4%)
Mean current age (SD)	60 years (12)
Mean age at diagnosis (SD)	53 years (12)
Tumor location right side	175 (49.6%)
Previous craniotomy	30 (8.5%)
Previous radiation treatment	3 (0.9%)
Median time from diagnosis to treatment	3 months (0–265)
Median time from treatment to survey participation	63 months (18–141)
Surgery for tumor progression	
Repeat Gamma Knife	2
Microsurgery	1

compared various treatment modalities to each other. A different approach is to compare management outcomes to benchmarked population norms. QOL outcomes are increasingly important to VS patients given their choice of treatment options and the recognition of a tumor at earlier stages. Such QOL measures are also of increasing value from a public health standpoint as we try to understand the burden of this disease on society and on everyday functioning. At this institution, it has been noted that most (>80%) patients demonstrate clinical worsening and image-defined tumor growth within a period of 5–10 years without intervention. Previous studies have also confirmed that hearing preservation is better when patients undergo stereotactic radiosurgery earlier [4–6].

Early recognition of VS has been facilitated by the widespread use of magnetic resonance imaging (MRI) for patients with symptoms of imbalance or hearing dysfunction. The goal of this study was to take a look at the functional and QOL status of VS patients several years after they had undergone Gamma Knife[®] radiosurgery (GKRS), and it compares these results by age to normalized US population data.

Methods

This project was part of a comprehensive study of environmental risk factors for the development of VS. The details of that study have been previously described [7]. This study received the approval of the University of Pittsburgh Institutional Review Board for Human Research, and informed consent was obtained from all study participants.

Survey Design

An existing functional status questionnaire was used that has been reported in previous studies [8, 9]. The survey assessed the participants' perception of their current hearing status in both ears, tinnitus, balance disorder symptoms, and vertigo. The 36-item Short-Form Health Survey v2.0 (SF-36) was also administered in order to assess health-related QOL [10]. Participants were also queried about their overall satisfaction with the GKRS procedure and whether they would recommend the procedure to somebody else.

Participant Recruitment

Participants were recruited from the University of Pittsburgh GKRS database [11]. In order to capture a long-term follow-up time in participants who underwent GKRS after the integration of MRI for treatment planning, participants were selected who underwent GKRS between the years 1997 and 2007. Participants with neurofibromatosis type 2 and those residing outside the North American continent were excluded. All participants were contacted by written letter via the United States postal service. Participants were given the option to fill out the questionnaire by hand or have it done over the telephone with a trained recruiter.

SF-36 Analysis

SF-36 questionnaire data were analyzed according to the SF-36 v2 user's manual [12] scoring criteria which included summary scores for physical (PCS) and mental health (MCS). The US population scores have been normalized to demonstrate a mean of 50 and a standard deviation of 10 for each of the 8 scales as well as the 2 summary scores [12]. Age groups were stratified and analyzed according to the SF-36 manual [12].

Effect Size Scoring

Cohen's formulation of effect size (ES) scoring [13] was used to benchmark clinically significant differences between SF-36 scores. This was done by dividing the difference in mean scores by the standard deviation of the participant score. The general accepted

Table 2. Self-reported current functionality

	<i>n</i> (%)
Hearing in tumor ear (usable: excellent/good/fair vs. nonusable: poor/deaf) for use in an everyday conversation	
Usable	104 (29.7)
Nonusable	246 (70.3)
Hearing in nontumor ear (usable: excellent/good/fair vs. nonusable: poor/deaf) for use in an everyday conversation	
Usable	334 (94.9)
Nonusable	18 (5.1)
Tinnitus in tumor ear	
Never/rarely	190 (53.8)
Often/continuous	163 (41.7)
Tinnitus in nontumor ear	
Never/rarely	334 (94.6)
Often/continuous	19 (5.4)
Tinnitus in both ears	
Never/rarely	314 (89)
Often/continuous	39 (11)
Balance problems	
Never/rarely	231 (65.6)
Often/continuous	121 (34.4)
Vertigo or dizziness	
Never/rarely	308 (88)
Often/continuous	42 (12)
Are you satisfied with your current overall functionality and activity level?	
Yes	318 (91.1)
No	31 (8.9)
Would you recommend the Gamma Knife radiosurgery procedure to a friend or family member with your type of tumor?	
Yes	337 (96.8)
No	11 (3.2)

Proportions are shown row-wise for each question. Some totals are <353 due to missing responses.

ranges are: 0.20–0.50 for a “small” effect size; 0.50–0.80 for a “medium” effect size; >0.80 for a “large” effect size. This usually translates to a mean score difference of around 2–5 points for a clinically significant difference [13–15].

Statistical Analysis

Descriptive statistics were used to display demographic data including median with range, means, standard deviations, and overall proportions when appropriate. The Student *t* test was used to explore relationships between univariate items. All data were analyzed using PASW Statistics 18, Release Version 18.0.0 (SPSS Inc., 2009, Chicago, IL, USA; www.spss.com).

Results

A total of 822 VS participants were treated with GKRS from 1997 to 2007, and 712 mailings were sent out based on our inclusion criteria. There were 420 (59%) participants who participated in the survey, and ultimately 353 (50%) had complete data. The mean age of the participants was 60 years (SD 12) at the time of the survey. The mean age at diagnosis of the VS was 53 years (SD 12). The median interval from date of diagnosis to GKRS was 3 months (range 0–265). The median time from GKRS to participation in this study was 63 months (range 18–141). The average tumor volume was 0.5 cm³ (range 0.012–17.3), and the median radiation dose to the tumor margins was 13 Gy (range 7–30) (Table 1).

Functional Outcomes

There were 104 (29.7%) participants who reported that they currently maintain useful hearing in the GKRS-treated tumor ear. For our questionnaire, useful hearing was defined as being able to use the ear at least fairly in an everyday conversation. Fifteen participants (4.2%) described their hearing as either poor or deaf in both ears.

Tinnitus was reported by 163 (41.7%) participants either often or continuously. Imbalance symptoms were noted by 121 (34.4%) participants either often or continuously. Vertigo symptoms were reported by 42 (12%) participants either often or continuously (Table 2).

Overall Satisfaction

There were 318 (91.1%) participants who reported that they were satisfied with their current overall level of functioning, and 337 (96.8%) noted that they would recommend the GKRS procedure for VS to a friend or relative (Table 2).

SF-36 Outcomes

The physical and mental health component scores were similar to the population normalized score of 50 (PCS = 50.45, MCS = 51.72). The PCS and MCS stratified by age groups also closely resembled the US population normalized scores and followed a similar curve that showed PCS lowering with age (PCS from 56 to 45) but no significant change in MCS with age (MCS from 52 to 53) (Table 3; Fig. 1, 2).

Each of the participants' 8 SF-36 scale scores were compared to the established US population normalized score of 50 with ES scoring. The vitality category for our participants was better with a small ES of 0.27. Our participants reported outcomes in the remaining categories

Fig. 1. Age-adjusted SF-36 PCS scores for GKRS cohort and US population.

Fig. 2. Age-adjusted SF-36 MCS scores for GKRS cohort and US population.

Table 3. Age-adjusted physical component score (PCS) and mental component score (MCS): means $\pm$ SD

Age	PCS		MCS	
	GKRS cohort	US population	GKRS cohort	US population
25–34 years	55.69 $\pm$ 5.89	53.57 $\pm$ 7.27	52.46 $\pm$ 4.18	49.20 $\pm$ 9.42
35–44 years	53.66 $\pm$ 7.68	52.26 $\pm$ 8.16	50.09 $\pm$ 7.23	49.08 $\pm$ 10.05
45–54 years	53.30 $\pm$ 9.09	49.62 $\pm$ 10.02	49.84 $\pm$ 9.80	50.54 $\pm$ 9.94
55–64 years	52.08 $\pm$ 7.29	47.44 $\pm$ 10.75	51.95 $\pm$ 9.01	51.71 $\pm$ 10.25
65–74 years	47.45 $\pm$ 11.5	44.70 $\pm$ 10.66	52.94 $\pm$ 10.86	53.17 $\pm$ 9.29
≥ 75 years	45.04 $\pm$ 9.51	40.00 $\pm$ 11.25	52.54 $\pm$ 10.8	50.37 $\pm$ 11

with effect sizes that were similar to the US population norms and did not exceed a clinically significant ES of at least 0.2 (Table 4).

The influences of functional status on PCS and MCS were evaluated by stratified analyses. Frequent vertigo and imbalance problems were associated with worst PCS

and MCS (vertigo PCS: ES -0.73 ; MCS: ES -0.71 , imbalance PCS: ES -0.56 ; MCS: ES -0.36 , $p < 0.001$). Nonuseful hearing in the tumor ear was associated with a worst PCS (ES = -0.27 , $p = 0.01$) but not MCS (ES = -0.02 , $p = 0.87$). No significant differences were found for tinnitus (Table 5).

Table 4. Effect size

SF-36	GKRS score mean $\pm$ SD	Effect size GKRS vs. US population
Physical component score	50.45 $\pm$ 9.73	0.05
Mental component score	51.72 $\pm$ 9.77	0.18
SF-36 individual scale items		
Vitality	52.87 $\pm$ 10.54	0.27
Body pain	51.84 $\pm$ 9.69	0.19
Social functioning	51.33 $\pm$ 9.43	0.14
Mental health	51.32 $\pm$ 9.35	0.14
General health	50.95 $\pm$ 9.95	0.10
Role emotional	50.58 $\pm$ 10.03	0.06
Role physical	49.53 $\pm$ 11.14	-0.04
Physical functioning	50.30 $\pm$ 10.07	0.03

Table 5. Functional status effect on summary scores

Functional status	PCS mean $\pm$ SD	PCS effect size	<i>p</i> value	MCS mean $\pm$ SD	MCS effect size	<i>p</i> value
Vertigo		-0.73	<0.001		-0.71	<0.001
Continuous/often	42.07 $\pm$ 13			45.04 $\pm$ 10.8		
Rarely/never	51.6 $\pm$ 8.63			52.69 $\pm$ 9.26		
Imbalance		-0.56	<0.001		-0.36	<0.001
Continuous/often	46.25 $\pm$ 11.38			49.06 $\pm$ 11.26		
Rarely/never	52.66 $\pm$ 7.91			53.12 $\pm$ 8.58		
Hearing in tumor ear		-0.27	0.01		-0.02	0.87
Nonuseful	49.64 $\pm$ 10.21			51.77 $\pm$ 9.87		
Useful	52.43 $\pm$ 8.2			51.95 $\pm$ 8.69		
Tinnitus in tumor ear		-0.19	0.1		-0.04	0.68
Continuous/often	49.74 $\pm$ 9.91			51.83 $\pm$ 10.74		
Rarely/never	51.6 $\pm$ 9.45			52.3 $\pm$ 8.47		

Discussion

This study found that its participants who were treated with GKRS for VS maintained a good, long-term QOL that was comparable to the age-adjusted general US population, overall. More than 90% of participants were satisfied with their current overall functionality and activity level. Three items demonstrated a negative impact on QOL: vertigo, imbalance, and nonuseful hearing. These items were associated with small to moderate ES changes.

Several published studies have evaluated the outcomes of GKRS and indicate that this management strategy is associated with long-term improvement, especially in comparison to outcomes reported after microsurgical management (Table 6) [8, 9, 16–25]. Our study compares

QOL after GKRS for VS to age-matched US population norms. There are two other studies from the Netherlands and Norway that also compare their GKRS participants with population norms and they found similar results to this study [19, 24]. Two additional studies looked at QOL compared with population norms but without surgical intervention. In 2010, Lloyd et al. [26] evaluated QOL in the UK for VS participants who underwent continued observation without intervention and compared them with UK SF-36 population norms, and they did significantly worse than the UK population. In 2008, Vogel et al. [27] did a cross-sectional study to look at baseline SF-36 scores upon initial diagnosis of VS and found that they scored lower than the Dutch population norms prior to intervention. In 2015, Carlson et al. [16] compared several

Table 6. Literature review of Gamma Knife radiosurgery quality of life outcomes

Author	Follow-up, years	Quality of life measurement tool	<i>n</i>	Results
Carlson et al. [16], 2015	7.7	SF-36, PROMIS-10, GBI, PANQOL	642	Small differences were found between GK, MS, and conservative management but the authors noted that none of them were clinically significant differences QOL scores were also similar to nontumor controls
Kim et al. [17], 2015	1.6	SF-36	108	QOL scores did not differ significantly in 4 of the 8 questionnaire domains, but the MS group had a significantly higher score in general health perception, and GK scored lowest overall
McLaughlin et al. [18], 2015	2.6	PANQOL	186	PANQOL scores were reported for GK, MS, and conservative management but statistical comparisons were not performed due to intrinsic differences between groups Overall, scores were not very different, and conservative management scores were highest followed by GK and then MS
Myrseth et al. [19], 2005	1.5–13	GBI, SF-36	168	GK fared better than MS on both measures Combined GK/MS SF-36 scores were similar to slightly lower than Norwegian population norms Stratified GK scores were not reported independently when compared to population
Myrseth et al. [20], 2009	2	SF-36, GBI	88	Prospective look at GK improved from baseline on GBI
Pollock et al. [8], 1995	2–4	Functional outcome rating scale	87	GK resumed regular activities sooner than MS postoperatively GK did better than MS on functional scale but did not reach significance
Pollock et al. [21], 2006	1–5	HSQ	82	GK had no prospective decline MS had significant prospective decline
Régis et al. [22], 2002	3	Functional evaluative questionnaire	210	GK had better functional outcomes compared to MS
Van Roijen et al. [9], 1997	2	“Health and Labor Questionnaire” (employment productivity), SF-36, EuroQol	145	GK had better outcomes than MS; GK was more cost-effective than MS
Sandooram et al. [23], 2004	2–5	GBI	165	GK and MS did worse than successful observation but observed tumors were about half the size of treated ones GK results did not reach significance
Timmer et al. [24], 2010	0.17–4.6	SF-36, GBI	97	GK SF-36 results were similar to Dutch population norms GBI did not have significant difference
Wangerid et al. [25], 2014	8.7	EQ-5D	128	High QOL and low morbidity at long-term follow-up for VS patients treated with GK No comparison group was measured

SF-36, Short-Form 36-item Health Questionnaire; PROMIS-10, 10-item Patient-Reported Outcomes Measurement Information System; GBI, Glasgow Benefit Inventory; PANQOL, Penn Acoustic Neuroma Quality-of-Life Scale; GK, Gamma Knife; MS, microsurgery; QOL, quality of life; HSQ, Health Status Questionnaire; EQ-5D, European Quality of Life 5 Dimensions; VS, vestibular schwannoma.

QOL measures with a nontumor control group and found small but clinically insignificant differences between GKRS, microsurgery, conservative management, and even the nontumor controls (Table 6).

Tinnitus is a commonly reported symptom of participants with VS but the impact of tinnitus is variable among participants, and its presence does not easily correlate with a participant's level of discomfort [28–30]. This study did not find any significant association between tin-

nitus and SF-36 summary score changes. These findings agree with previous studies that also failed to find a significant correlation between summary scores and the tinnitus handicap index [26, 31]. Other tinnitus studies have shown that approximately 80% of participants who suffer from chronic tinnitus did not seek treatment for it [28].

Limitations

There is no specific VS QOL questionnaire that has been widely used, and so there is some heterogeneity in the measurement tools of existing research. A publication by Schaffer et al. [32] validated a VS-specific QOL measurement tool named PANQOL, and that may be something researchers begin to use more moving forward. This study used a functional questionnaire that is very similar to one that was developed by the VS Association and one that has been used in previous research [8, 33]. This study looked at QOL with a widely validated tool (SF-36) that is generic across many disease processes, has been used in several VS studies, and allows comparisons with age-matched population norms. There were no pretreatment QOL survey data available in this study and therefore we could not compare changes over time. The cross-sectional survey method we used limits our ability to draw conclusions regarding improvement after treatment. Retrospective questioning of QOL status was avoided due to the possibility of poor recollection, misclassification, and recall bias.

This study was performed with data from a single institution with a survey response rate of 59% and completed data from 50% of surveyed patients, which might

raise questions of generalizability and respondent bias. The patient survey was not incentivized, which lowers the expected response rate, and ultimately the respondents in this study were similar to typical patients with VS who are treated with GKRS in the USA based on age, gender, tumor volume, and radiation dose. The overall sample size of this study's cohort is also much larger than that of similar studies done on QOL (Table 6).

Conclusion

Overall, after undergoing GKRS for VS, participants reported a good long-term QOL that was very similar to the QOL of US population norms. Of the common symptoms, vertigo had the greatest impact on QOL followed by imbalance and then hearing loss. Tinnitus did not have a significant impact on QOL. Participants reported that they are satisfied with their current level of functioning and activity.

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Disclosure Statement

Dr. L. Dade Lunsford is a stockholder of Elekta.

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