

Tumor control and hearing preservation after radiosurgery of intracanalicular vestibular schwannomas – systematic review

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Abstract

Intracanalicular vestibular schwannomas (IVS) account for 8% of all vestibular schwannomas and their detection is still increasing due to high availability of magnetic resonance (MRI). Radiosurgery is one of several commonly acceptable methods of IVS treatment, but some risk may still exist with that treatment. The aim of this study is to analyze the clinical outcomes in tumor control and hearing preservation after radiosurgery of IVS. The retrospective analysis included 14 scientific papers available in the PubMed database. Assessment of tumor volume was performed based on gadolinium-enhanced T1-weighted scans. Hearing preservation was assessed using the Gardner-Robertson classification (GR class). Statistical analysis was performed using IBM SPSS Statistics 27. It was revealed that tumor growth control in IVS treated with radiosurgery was higher than in the wait-and-see strategy. The hearing preservation was similar in patients after wait and see and the surgical group. Radiosurgery was associated with low risk of facial nerve dysfunction.

Key words: intracanalicular vestibular schwannoma, intracanalicular acoustic neuroma, hearing preservation, radiosurgery, tumor control, gamma knife.

Introduction

Intracanalicular vestibular schwannomas (IVS) constitute 8% of all vestibular schwannomas [1–4]. Due to high availability of high-resolution magnetic resonance (MR) imaging, the detection rate of IVS is still increasing. There are several treatment options for IVS including a conservative wait-and-see strategy, microsurgical resection, or radiosurgery. To date, no gold standard has been introduced concerning the best treatment option; therefore the discussion is still open, especially since IVS frequently produce only minor clinical symptoms or are asymptomatic. Regarding this issue morbidity has become an important factor driving therapeutic decisions [1–5].

Each of these options probably still has the same number of supporters and opponents despite a lot of papers published to date, especially regarding conservative and microsurgical treatment, whereas available literature concerning radiosurgery in IVS is still scarce in our opinion and there is no widely accepted consensus regarding if and when a patient with IVS should undergo radiosurgery.

Radiosurgery in contrast to microsurgery is still quite a new modality that does not require inpatient hospitalization or convalescence following treatment, although short-term and long-term risks also may exist with that type of treatment [6–8]. Of priority in the management of IVS are tumor control and hearing preservation, but it is commonly known that

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stereotactic radiosurgery may introduce radiation toxicity risks to adjacent neurologic structures and result in a functional threat to the adjacent delicate neural structures.

Moreover, being a high volume European radiosurgical center with more than 2000 irradiated vestibular schwannomas to date, including more than 150 of the intracanalicular type, we were interested in real efficacy concerning tumor control, hearing preservation and radiation toxicity risk. Therefore, we performed an extensive review of the English literature to analyze the results of patients with IVS treated with radiosurgery, including the paper from our center.

Aim

The aim of the study is to analyze the clinical outcomes in tumor control and hearing preservation after radiosurgery of intracanalicular vestibular schwannomas.

Material and methods

A literature search was performed via the PubMed database using the key words “radiosurgery”, “intracanalicular acoustic neuroma”, “intracanalicular vestibular schwannoma”, “hearing preservation” and “tumor growth control” alone and in all combinations. We identified 13 papers which met our above-mentioned search criteria. In 12 articles patients were treated with the Gamma Knife and in only one with the Cyber Knife.

Data from individual and aggregated cases were extracted from each paper. Tumor volume during follow-up was calculated on gadolinium-enhanced T1-weighted images according to the following formula: greatest length (cm) × greatest height (cm) × greatest width (cm) × 0.5. Enlargement or shrinkage of the neoplasm was defined as at least 10% change of its volume, compared to the baseline data determined at the time of radiosurgery. Deterioration of hearing was defined as downgrading of at least one Gardner-Robertson class (GR). Patients with GR I or II at their last follow-up visit were defined as having useful hearing preserved. Patients who had lost hearing prior to radiosurgery (GR class III, IV, or V) were excluded from the analysis. Patients with neurofibromatosis were excluded as well as all IVS patients treated with microsurgery. Data were analyzed for the

whole group of patients with intracanalicular vestibular schwannoma.

Statistical analysis

The IBM SPSS Statistic 27 program was used for statistical analysis. The Pearson test was performed to determine the coefficient correlation between marginal dose and useful hearing after SRS, tumor control, tumor regression and tumor stability. To establish the coefficient of determination of the correlation, the R^2 formula was used.

Results

Thirteen studies published between 1995 and 2020 were included in the analysis (Table I). There were 4 prospective and 4 retrospective studies, whereas in 5 cases no information concerning this issue was specified. The total number of patients meeting the study criteria was 621 (303 male and 318 female) [1–6, 9–15]. The gender information was specified in all but one paper including 25 people [9]. The number of patients varied from 1 to 136 (10.9). The average age of the patients was 52.7 years (the lowest was 19, the highest 89 years).

Tumor control results

Tumor volume ranged from 0.11 to 1.36 cm³ (average: 0.44 m³). Radiation dose to the periphery of the tumor was on average 12.9 Gy (it ranged from 12 Gy to 17 Gy) [12, 13]. The follow-up observation after radiosurgical treatment ranged from 14 to 89 months (with the average of 40.4 months). Within this observational time tumor growth control was achieved in 85.7% to 100% of patients (average: 96.8%) [2–6, 9–14]. Size of the tumor regressed in 0 to 93% (average: 45.3%) and was stable in 8 to 90% (average: 39.9%) [1, 2, 4, 5, 10, 12–15]. Size of the tumor increased in 0 to 76.6% (average: 21.9%) [2, 3, 5, 6], whereas pseudo progression of tumor volume was found in 5 to 52% of irradiated patients (average 24.2%) [2, 10, 13, 15]. Loss of contrast enhancement visible on follow-up MRI scans, indicative for good response to radiosurgery, was found in 45 to 51% of patients (average: 49%) [2, 4, 12] (Table II).

Hearing results

Serviceable hearing at the last follow-up was preserved in 41 to 88% of patients after radiosur-

Table I. Basic characteristics of data from studies included in the analysis

Author	Journal	Total no. of patients	Age average [years]	Tumor volume average [cm ³]	Average follow-up [months]	Marginal dose [Gy]	Hearing after SRS (%)	Tumor regression (%)	Tumor control (%)
Daniel Rueß (2017)	Radiation Oncology	49	54	0.24	54	12.6	78	10	100
Sebastian Dzierżęcki (2020)	Acta Neurologica	136	54	0.15	52	12	78.2	90.3	91.1
Amaol Raheja (2013)	Neurology India	1	37	0.9	21	12	n.d.	n.d.	n.d.
Ajay Niranjana (1999)	Neurosurgery	29	n.d.	0.5	33	14	65	43	99
Yoshiyasu Iwai (2008)	Journal of Clinical Neuroscience	25	25	0.27	89	12	63	88	96
Zachary N. Litvack (2003)	Neurosurgery Focus	47	54	n.d.	43	12	63.6	n.d.	n.d.
Nicolas Massager (2006)	International Journal of Radiation Oncology, Biology, Physics	82	57	1.36	24	12	63.4	n.d.	100
Ajay Niranjana (2008)	Neurosurgery	96	54	1.11	42	13	64.5	43	99
Young-Hoon Kim (2013)	International Journal of Radiation Oncology, Biology, Physics	60	50	0.34	61	12.2	57.3	64	97
Jean Régis (2008)	Progress in Neurological Surgery	47	54	n.d.	44	17	67.7	2.1	100
Olusola Ogunrinde (1995)	Stereotactic and Functional Neurosurgery	10	45	n.d.	25	16	0	0	100
Sandra Vermeulen (1988)	Stereotactic and Functional Neurosurgery	14	59	0.4	17	n.d.	n.d.	100	85.7
Rahul Chopra (2007)	International Journal of Radiation Oncology, Biology, Physics	25	n.d.	n.d.	36	n.d.	88	n.d.	n.d.

gery (average: 65.4%) [1, 5, 6, 9, 10]. Improvement of hearing was found in 0 to 100% (average: 16.4%) [1–5, 9–14], hearing was stable in 16% to 80% (average: 44.4%) [5, 9–14], whereas hearing deterioration was found in 5.8% to 100% (average: 40.3%) [9–15].

Neurological results

2.9% to 42.9% (average 8.6%) of patients developed facial nerve paresis which was found on a follow-up visit [9, 11–13, 15], while hemifacial spasm was found in 3.44% 2.04% to 28.57% (average:

3.44%) [11–13, 15]. None of the patients subjected to gamma knife surgery (GKS) showed trigeminal dysfunction, hydrocephalus, intratumoral bleeding or malignant transformation of the tumor after radiosurgical treatment.

Statistical results

A Pearson’s data analysis revealed a moderate negative correlation, $r = -0.689$, between marginal dose and functional hearing after SRS. The coefficient of determination of the correlation is 47.4% (Table III). Statistical significance was not observed for the correlation of marginal dose and regression as well as tumor stability. Based on that analysis we found that an increased dose is related to lower hearing usefulness. The coefficient of determination indicates that 47.4% of the applied dose may be related to the usefulness of hearing after SRS.

Discussion

To our knowledge this is the first review strictly concerning treatment with radiosurgery of solely intracranial vestibular schwannomas. There are many publications presenting radiosurgical treatment results of all sizes of vestibular schwannomas together – Koos from 1 to 4 – but only a few focusing primarily on the intracranial type – Koos 1. Therefore, we found and included only 13 articles that meet the criteria for that review. The first available article was published more than twenty years ago by Ogunrinde *et al.* and presented results based on only 10 patients [13]. The last article was published 2 years ago by Dzierżęcki *et al.* and included, in comparison to the abovementioned article, a large (the largest to date) group of 136 patients [1].

Nowadays, three reasonable IVS management options exist: the “wait-and-see” strategy, surgical treatment, and radiosurgery/fractionated radiation therapy. There are a number of studies that have analyzed the outcomes of the “wait-and-see” strategy in the management of IVS. The largest series of patients with IVS demonstrated that 17% of conservatively treated intracranial schwannomas continued to grow and, interestingly, the growth rate of these tumors was higher than those rising into the cerebellopontine angle [16]. The same observations were published by Régis *et al.* and by Thomsen *et al.*, and they observed continued growth of IVS during the “wait-and-see” strategy in

Table II. Tumor control and hearing results

Total no. of articles	Total no. of patients	Age average [years]	Tumor volume average [cm ³]	Radiation dose average [Gy]	Average follow-up [months]	Tumor grow control average (%)	Tumor regression average (%)	Tumor stability average (%)	Tumor increasing average (%)	Tumor progression average (%)	Loss of contrast average (%)	Maintained serviceable hearing (%)	Improved hearing (%)	Stable hearing (%)	Deteriorated hearing (%)
13	621	52.7	0.44	12.9	40.4	96.8	45.3	39.9	21.9	24.2	49.0	65.4	16.4	44.4	40.3

Table III. Correlation between marginal dose and functional hearing after SRS

		Marginal dose [Gy]	Useful hearing after SRS LFU (%)
Marginal dose [Gy]	Pearson's correlation	1	-0.689*
	Significant (one-sided)		0.014
	N	12	10
Useful hearing after SRS LFU (%)	Pearson's correlation	-0.689*	1
	Significant (one-sided)	0.014	
	N	10	12

* Correlation significant at the level of 0.05 (one-sided).

74% and 67.5% of cases, respectively [14, 17]. On the other hand, Raut *et al.* followed up 18 patients with IVS and documented only 1 case of tumor growth [18]. Hearing preservation rates with the “wait-and-see” strategy varied depending on the publication and ranged from 41% to 74% during 5 years of observations [2, 14, 19]. Another option is surgical treatment, in which continuous progress in diagnostic technology and operational techniques has a profound effect on surgical outcomes in patients with schwannomas. While surgical mortality reached up to 86% at the beginning of the 20th century, it declined to 1% after the introduction of microsurgical instruments, operational microscopes, and the development of microsurgical techniques [20, 21]. However, preservation of the facial and vestibulocochlear nerve function still constitutes an important issue during the selection of a surgical approach [21]. Hearing preservation and facial nerve function sparing rates vary from study to study, but it needs to be stressed that most of the examined study populations were relatively small, 14–26 patients at most [14, 22, 23]. According to Samii *et al.* [23], the hearing preservation rate in a group of 16 patients with intracanalicular acoustic neurinomas was 40%, whereas the facial nerve function remained intact in all the study subjects. Haines *et al.* [24] achieved a markedly larger proportion of patients with serviceable hearing (82%), but a substantially lower facial nerve function preservation rate at 62%. According to Hillman *et al.* [25], hearing preservation depends on the type of surgical approach used. The only independent predictor of hearing preservation turned out to be the middle fossa approach, the use of which was associated with significantly greater odds of maintaining hearing at preoperative levels [26].

We achieved in this review an average 96.8% tumor growth control after assessing 13 articles available to date concerning results of treatment of only IVS with radiosurgery. It should be highlighted that observational time was relatively long, with a mean of 40.4 months. In our opinion the number of analyzed articles and the follow-up are sufficient to state that the treatment result was good, especially in comparison to the “wait-and-see” strategy, where the tumor growth control was only 26–83% [14, 16, 17]. In our systematic review we did not find a significant correlation between the size of the marginal dose (≤ 12 Gy vs. > 12 Gy) and tumor growth control ($p > 0.05$). The same results were obtained by Yang *et al.* in their review, but for the treatment of all sizes of vestibular schwannomas (Koo 1–4) [27]. The authors concluded that despite the fact that in the earlier radiosurgery treatments higher rates of radiation were used, in opposition to more modern treatments with the use of lower dose radiosurgery, the rate of tumor control was similar. They confirmed the safety of using a lower radiation dose of 12.5 Gy with good tumor control (average: $94 \pm 3\%$) at an average follow-up of 41.2 months [27].

Hearing preservation continues to be an essential concern of patients undergoing radiosurgery especially for IVS. Only a few authors have combined the published research to achieve the statistical power needed to accurately characterize hearing preservation outcome in radiosurgery treatment for IVS. In our review, 12 out of 13 available articles refer to that important issue. Our results of serviceable hearing preservation after radiosurgery of IVS were not as spectacular as tumor growth control and ranged from 41% to 88%. However, similar distributions were also obtained by the “wait-and-see” strategy and surgical treatment for the treatment of IVS (41–74% and 40–

75%, respectively) [4, 14, 28]. In our study, contrary to Yang *et al.*, we did not find any significant correlation between the value of marginal dose (≤ 12 Gy vs. > 12 Gy) and the rate of hearing preservation ($p > 0.05$). However we would like to highlight that our group consisted of only 13 articles versus 74 of Yang *et al.* [8]; therefore we may expect that the lack of correlation may be related to the relatively small size of our group. We may only conclude that more data are needed to confirm our suppositions. Although no correlation was found, our experience with the rate of prescribed dose is that the recommended dose should be lowered to 12 Gy, which provides adequate preservation of the vital structures located in close proximity of the tumor and allows one to achieve high rates of hearing preservation and at the same time tumor control [1]. A similar approach was proposed by Régis *et al.*, where the prescribed dose depends on the patient's actual hearing status; a lowered dose even to 11 Gy was selected for a patient with serviceable hearing [29].

It may be interesting that we found a moderate relationship between prescribed dose applied and hearing usefulness after SRS. This relationship is manifested by a decrease in the usefulness of hearing with an increased dose. Based on the above review, this direct correlation was present in 47.4% of patients. It is worth noting that among many dosimetric features of the hearing system the mean dose to the cochlea was the most significant factor of hearing preservation after SRS. In order to obtain in-depth statistical analysis, more publications are required.

It is important to highlight that morbidity rates after GKS for intracanalicular vestibular schwannomas may exist and vary from study to study. Potential complications include hydrocephalus, facial spasm or palsy, trigeminal neuralgia, intratumoral bleeding or malignant transformation of the tumor [5, 30, 31]. We observed a low morbidity rate in our group – only 8.63% of patients developed a transient facial nerve paresis and 3.44% developed hemifacial spasm at the follow-up visit. In our opinion, the low morbidity rate may be primarily associated with dynamic optimization of radiosurgical planning focused on lowering the doses to critical structures around the tumor [8]. Interestingly, we indicated no cases of carcinogenesis in patients who had undergone gamma knife radiosurgery for IVS. The potential risk of that transformation is extremely low but possible, as there is documented malignant transformation after

microsurgical resections without any radiation use [14, 32, 33].

A potential disadvantage of radiosurgical treatment, but only concerning those cases in which tumor control could not be achieved and when there is a need for open surgery, is post-operative preservation of facial nerve function, which was lower than in the group treated only microsurgically [34]. The preservation of good facial function (HB grade 1 or 2) was lower in the previously irradiated group (37% vs. 70%). Moreover, the rate of less-than-complete resection was usually higher in the post-GKS group [34].

Conclusions

To our knowledge this is the first review of the literature exclusively concerning only intracanalicular schwannomas. There is still scarce available literature concerning this issue; therefore only 14 articles could be included in the study. We achieved very high rates of tumor control and hearing preservation, 96.8% and 65.4%, respectively. Tumor growth control in our study was superior to the “wait-and-see” group, whereas hearing preservation was similar to the wait-and-see and surgically treated group. The rate of facial nerve dysfunction was low at 8.6%, and this rate is lower than in the surgically treated group. The present results may allow us to conclude that radiosurgery for IVS is an efficient and safe tool which constitutes a good alternative to the wait-and-see and surgical strategy.

Conflict of interest

The authors declare no conflict of interest.

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