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The assessment of state of hearing and audiometric configuration of patients with vestibular schwannoma before and after gamma knife radiosurgery

Оценка состояния слуха и аудиометрическая конфигурация пациентов с вестибулярными шванномами до и после лечения гамма ножом

Abstract

Vestibular schwannoma is benign tumor arising from myelin sheath of the vestibulocochlear nerve. As tumor growth it compresses structures and nerves in Internal Acoustic Canal (IAC) and may also prolapses into the cerebellopontine angle (CPA).
Conventional neurosurgery in many cases follows postsurgical complications as hearing loss. According to radiologists the Gamma Knife (GK) radiosurgery is a safe and complications after radiosurgery are minimal, however in our work based on comparative analyses of VS patients underwent to radiosurgery and conservative management (CM) we have revealed the significant hearing loss in GK radiosurgery group ($p<0.001$) in long term follow up reviews after radiosurgery.
Keyword: Vestibular schwannoma (VS), radiosurgery, complications, hearing loss.

Резюме

Вестибулярная Шваннома (ВШ) – это медленно растущая доброкачественная опухоль, образующаяся вследствие гиперпродукции Шванновских клеток миелиновой оболочки преддверно-улиткового нерва. По мере роста, ВШ часто сдавливает нервы, сосуды мостомозжечкового угла и может привести к компрессии мозга. Традиционная нейрохирургия и радиохирургия имеет ряд послеоперационных осложнений. В мировой литературе, радиологи утверждают, что осложнения от радиохирургии минимальны. Однако на основе длительного наблюдения и сравнительного анализа пациентов, получавших радиохирургию, и пациентов, находившихся в выжидательной тактике, установлено, что лица, подвергавшиеся радиохирургии, значительно ($p<0,001$) потеряют слух в более длительные сроки после лечения.
Ключеве слова: вестибулярная шваннома, радиохирургия, осложнение, потеря слуха.

■ INTRODUCTION

Vestibular schwannoma (VS) is an extra-axial brain tumor arising from overproduction of myelin forming Schwan cells of the vestibulocochlear nerve. It constitutes about 6% of all primary intracranial tumors [1–4]. The tumor is benign and usually grows quite slowly [1–10]. As VS grows, it compresses the vestibulocochlear or both vestibulocochlear and facial nerve in internal acoustic canal and affects the hearing, balance and facial function. Therefore, usually it causes unilateral or asymmetric hearing loss, tinnitus, and loss of balance from simple unsteadiness, up to serious vertigo. In some cases the tumor growth may interfere with the facial nerve causing facial numbness, or it may also affect the motor fibers of the facial nerve causing facial weakness or paralysis on the ipsilateral side. In case, if the tumor becomes larger and larger it may prolapse into CPA like an ice cream, and it will eventually compress against nearby the important brain structures like the brainstem and the cerebellum which makes the VS life-threatening [2]. Thus, the clinical presentation depends on location and size of the vestibular schwannoma. The majority of cases the presenting symptom of VS is a hearing loss. However, the complaint making the patient to come to the hospital could be different (Ergashev J. et all, 2014). Many patients, especially old patients do not pay attention to hard of hearing, but they concern either ringing in the ear or balance problems. At the diagnostic stage otolaryngologists perform audio-vestibular tests and usually reveal additional signs like hearing loss and symptoms of compression of other cranial nerves.

Although there are many conditions may cause hearing loss, tinnitus and balance problems, so the gold standard for the diagnosis of VS considered to be the Magnetic Resonance Imaging (MRI). In last decades the treatment modalities of VS developed and became less invasive [3, 8–10]. The outcomes of treatment for patients with VS have significantly improved. The

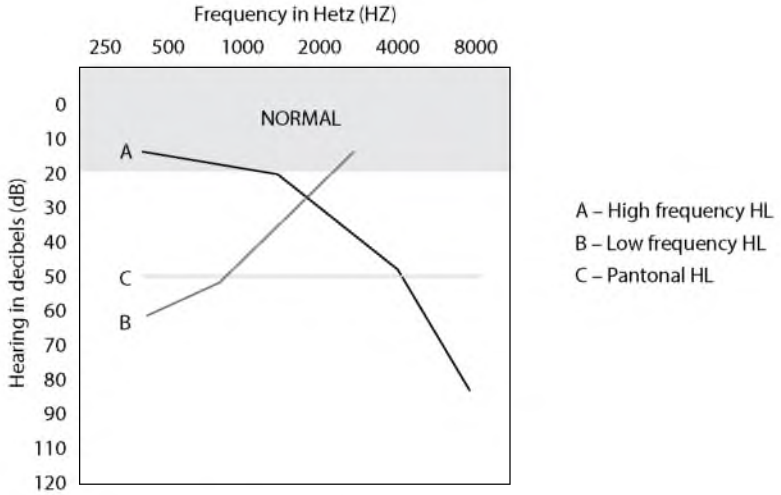

Fig. 1. Common types of Audiometric Configuration

goal of the treatment in the early 20th century was to remove the VS without perioperative mortality. However, with the improvement of diagnostic tools, advances in anesthetic care, introduction of microsurgical techniques, and intraoperative monitoring, mortality and neurologic morbidity have been significantly reduced without compromising the radicality of tumor resection. The goal of the treatment in 21th century become to excise the tumor with preservation of normal function of cranial nerves, while causing minimal injury to the cerebellum and brainstem.

Traditionally, there are two treatment modalities for VS: the conventional neurosurgery and radiosurgery. However, by virtue of the fact that the vestibular schwannoma growth very slowly there is one more management option going to be popular among otolaryngologists. This popular modality based on watchful waiting Conservative Management (CM) [2].

The first option is conventional neurosurgery that unifies three different approaches such as translabyrinthine, retro-sigmoid and middle cranial fossa approaches. The radiosurgery is a type of targeted radiotherapy that aims the radiotherapy beams very precisely at the VS [7].

Present day, the hearing preservation is an important goal for majority of patients. It has recently been recognized that the radiation dose to the cochlea plays a significant role in hearing outcomes for patients receiving GK. Techniques that reduce the cochlear dose below 4 Gy appear to have higher rates of serviceable hearing preservation [1, 3, 5, 7]. However, low-dose may lead to tumor reoccurrence [2].

While no surgery is without risk, the conventional neurosurgery always leads to more or less early and postsurgical complications. Complications after any surgery include bleeding, infection, blood clots, and reactions to anesthesia. However, there are some specific complications related to a craniotomy, which may include stroke, seizures, venous sinus occlusion, swelling of the brain, and CSF leakage. In some occasions VS surgery may even lead to eye problems tue to loss of muscle control on one side of the face caused by facial nerve swelling or damage [4].

The Middle Cranial Fossa (MCF) and retrosigmoid approaches are more difficult with a worse angle of dissection and with greater risk to the facial nerve due to its location during the procedure and a greater risk of incomplete tumor removal in the lateral IAC for the retrosigmoid approach [3]. These two approaches considered hearing sparing with better hearing preservation reported in the middle cranial fossa approach for small sized (< 1 cm) VS that do not extend to the fundus. In case of large VS, the retrosigmoid approach is advocated when hearing preservation is a possibility. However, in medium to large tumors in retrosigmoid approach is 44% and 18%, respectively [3].

According to general viewpoints and observations, the radiosurgery, in its turn also may lead to some side effects during and after treatment but in many studies, especially studies performed by radiologists it considered to be not significant [8–10]. Nevertheless, in many of above mentioned studies the sample size included to the study are small [2]. One of most frequent complications leading both treatment modality is hearing loss [2, 5, 8].

In current article, we will describe our observations of VS patients before and after Gamma Knife Radiosurgery (GKR). Usually, older patients are more vulnerable to hearing deteriorating effect of radiosurgery. As long

as the tumor not grows, patient benefits from conservative management. Therefore, accepting the conservative management as a screening tool for the newly diagnosed VS, especially VS diagnosed in old patients is promising [2]. In its turn, in order to prevent complications in some cases radiologists try to reduce the percentage of the cochlear volume exposed to radiation doses greater than 5.3 Gy [5].

Large tumors are overrepresented in surgical series compared to their prevalence. Postoperative facial nerve function correlates to tumor volume and hearing preservation in these tumors is rare. Intraoperative electrophysiological techniques are valuable for attempted preservation of cranial nerve function. Persistent facial palsies can be remedied by dynamic and static interventions for facial rehabilitation.

■ OBJECTIVES

Based on recent trends our goal was to analyze the side effect of GKR to hearing function in a series of 48 VS patients underwent to GKR over the last 7 years. We also reviewed the international literature on the side effects of VS GKR to hearing function.

■ MATERIALS AND METHODS

In our database, we have found one hundred seven patients with diagnosis of VS and managed by the Santiago de Compostela University Hospital from the period between February 21, 1992 and May 05, 2012. According to our inclusion criteria, we have included only 42 patients diagnosed by gadolinium enhanced MRI and underwent to Gamma Knife Radiosurgery.

In agreement with our exclusion criteria, we have excluded cases of CPA tumors other than VS or cases of CPA/IAC tumors of unknown origin including VS due to Neurofibromatosis Type II (we had one bilateral VS case related with NF2).

The Audiometric testing was performed mainly by the clinical audiometer labeled "Audiotest 340" (Interacoustic Incidencia, Barcelona) with the background noise less than 5dB.

In order to establish average Pure Tone Audiometry (PTA) we have calculated the arithmetic mean of speech frequencies at 500, 1000, 2000 and 300 hertz.

Our groups of patients were under follow up over the years, therefore in each revision in the otolaryngology department; they were directed to the Radiology Department to perform an MRI scan for comparing the size of the VS with the previous MRI. All MRI scans of the VS patients were performed with gadolinium contrast. For the data collection, we have used Microsoft Excel 2010 and for the data analysis we have used IBM Statistical Package for the Social Sciences (SPSS) version 19, for Windows.

■ RESULTS AND DISCUSSION

Among the patients included to the study there were 19 (45.2%) males with the mean age of 55.23 years and 23 (54.7%) females with the mean age of 56.15 years. As a control group, we have selected 48 patients under conservative (watch-and-wait) management with mean age of

61.17 years (Range 24–85). Among them there were 27 (57.1%) females and 21 (42.8%) males.

During the data collection, we also registered the initial shape of audiometric configuration of VS patients with hearing loss. The audiometric configurations that comprised the average thresholds used to define each category were described as sloping, rising or flat (e.g. see fig. 1). The audiometric configuration was considered sloping when the thresholds occurred at equal or successively higher levels from 250 and 8000 Hz >20 dB. We determined that the configurations were rising when thresholds occurred at equal or successively lower levels from 250 to 8000 Hz. The difference between thresholds at 250 and 8000 Hz was always >20 dB and the configurations were flat when thresholds across the frequencies did not vary more than 20 dB from each other.

As we can see from above table 1 the initial average PTA in males (48.95 dB) is smaller than females (56.15dB) this difference actually statistically significant (p=0.03), however the sample size (number of patients) of two groups are too small to be statistically reliable.

In order to catch the hearing deterioration we compared GKR group with "wait-and-watch" group. The patient date of "wait-and-watch" group is presented in table 2.

As we see and compare above presented tables 1 and 2, the overall average initial PTA for the radiosurgery group was 55.23±26.08 dB. After each year, the hearing loss gradually increased. At the diagnostic stage, there are 20 out of 42 patients presented PTA ≤50 dB which considered to be useful hearing. Also, at the initial stage there are 30.9% (13/42) of patients presented pantonal audiometric configuration, but at the last follow-up year 50.0% (21/42) patients presented pantonal audiometric configurations. Above mentioned difference was statistically significant p<0.0001 (t-test). The results of comparative analyses presented in tables 3 and 4.

We found that the PTA, at the initial point in both groups, does not differ significantly (p=0.21). However, if we compare both groups in each of the

Table 1
Distribution of patients in GKR group before the radiosurgery

Gender	n	Age (yrs)	PTA (dB)			
			Mean	Minimum	Maximum	Std. Dev
Male	19	55.23	48.95	3.75	81.75	21.21
Female	23	56.15	61.10	16.25	120	28.27
Total	42	55.73	55.60	3.75	120	26.08

Table 2
Distribution of patients in wait-and-watch group with the initial PTA

Gender	n	Age (yrs)	PTA (dB)			
			Mean	Minimum	Maximum	Std. Dev
Male	21	62.58	57.40	18.75	111.25	27.4491
Female	27	60.07	57.61	16.25	120.00	28.41
Total	48	61.17	57.52	16.25	120.00	27.70

Table 3
Distribution of patients in wait-and-watch group with the initial PTA

Follow up time	Average PTA ±	95% CI	
		Lower Bound	Upper Bound
Initial	57.30±28.53	50.34	64.26
6 months	59.17±28.21	52.29	66.06
1 year	61.91±28.50	54.96	68.86
3 year	68.41±31.19	60.80	76.02
5 year	71.38±30.31	62.45	77.98
p-value	p=0.0013	p=0.0013	p=0.0013

Table 4
Distribution of patients in GK group with the initial PTA

Follow up time	Average PTA ±	95% CI	
		Lower Bound	Upper Bound
Initial	55.23±26.08	49.18	70.43
6 months	69.18±26.28	58.78	79.58
1 year	74.71±24.42	86.04	84.37
3 year	78.96±24.95	69.09	88.83
5 year	81.58±23.66	72.22	90.94
p-value	p<0.0001	p<0.0001	p<0.0001

follow-up levels, we can see minimal differences between the mean PTA of two groups. Therefore we have analyzed the results of audiometric test and revealed that, at the initial stage and at the six months points the difference between two groups is clear and is statistically and significant p=0.005 (Repeated Measures ANOVA). Following difference between the initial point and one year is also statistically and significantly different p=0.002. Over the years, we have observed the difference between two groups going to

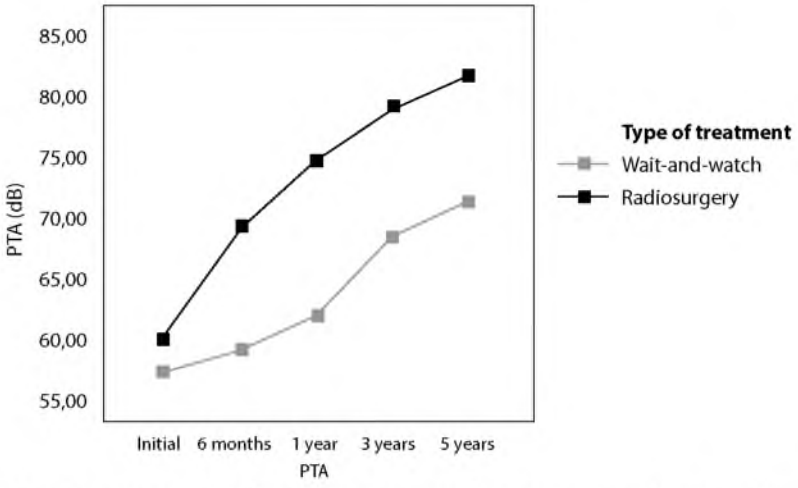

Fig. 2. Hearing deterioration over the follow-up years between the patients under the wait-and-watch and radiosurgery groups

be more significant. According to multivariate test (Repeated Measures ANOVA), the PTA is statistically and significantly different between the subjects in the two groups (Sphericity Assumed) p=0.028.

The plotted graph above shows the two groups after the initial diagnosis and shows the lines being directed far apart. The test indicated that there is a significant time effect. In other words, the wait-and-watch and radiosurgery groups do certainly change over time. Both groups changes over time, but the radiosurgery group shows a greater increase in the mean PTA over time. Moreover, the interaction of time and group is significant, because the groups do not have parallel lines that increase over the time periods. At the diagnostic stage the both groups showed sloping audiometric configuration losing the hearing mainly in high frequencies, however GK group unlike CM group, over the years after the radiosurgery gradually passed into the flat or pantonal hearing loss.

Kondziolka and his colleagues studied 5 to 10 year outcomes in 162 patients with VS who had undergone radiosurgery. In this study, a long-term 98.0% tumor control rate was reported. In another study performed by the same authors in 157 patients, there was a decrease in tumor size in 114 patients (73.0%), no change in 40 patients (25.5%), and an increase in 3 patients who later underwent resection (1.9%). In their series, only 2.0% of patients required tumor resection after radiosurgery [7].

Kim and his colleagues (2007, Korea) 8 observed 59 post-radio surgery patients with the duration of at least 5 years, and in their series, the tumor control rate was 97.0%. They classified the patterns of change in tumor volume into three categories. Transient increases in tumor volume were detected in 29.0% of the patients, and the maximum transient increase in tumor volume was identified at 6 to 30 months after GK Radiosurgery. The report stated that the hearing was preserved in 4 of the 12 patients who had serviceable hearing prior to treatment. They concluded that the tumor control after GK Radiosurgery depends on the dosage of radiation, and they believe that with an average of 12 Gy, the tumor control would be between 86.0% and 98.0% [8].

■ CONCLUSION

In spite of GK Radiosurgery has often been cited as a safe and effective treatment for small and medium sized VSs, but sometimes this safety and effectiveness may be questioned due to the lack of comparison with the natural course of other studies.

The side effects of radiosurgery to hearing are obvious and it surely affects the hearing, nevertheless, in some cases, its direct necrotizing effect to the tumor tissue could be more important. The side effect of GK to the hearing could be due to its direct effect to cochlea. But pantonal hearing loss after GK radiosurgery appears to be interesting for us.

However we believe the reason for the hearing deterioration after GK radiosurgery in patients with VS could be different, including its direct effect of the brainstem, which is believed to be a significant prognostic factor for hearing deterioration after GK.

Also, the cochlear nucleus may be one of the other sensitive structures to be damaged by radiotherapy. In order to reveal such effects very large trials would be required for interaction tests to reach significance.

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