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Risk Factors for Postoperative Recurrence of Acoustic Neuroma

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Abstract

Background: Acoustic neuroma (AN), also known as vestibular schwannoma, is a benign, generally slow-growing tumor which might result in hearing loss, tinnitus, and disequilibrium. There are currently studies showing that the mean duration from the original operation and the diagnosis of recurrence was 4.2 years and the main recurrent symptoms were intracranial hypertension and walking disorder.

Objectives: This study aimed to investigate the risk factors of postoperative recurrence of acoustic neuroma (AN) and provide a reference for its clinical prevention and treatment.

Methods: This retrospective study included a total of 30 patients with recurrent AN and 23 patients with non-recurrent AN who were admitted to the Department of Neurosurgery of the First Affiliated Hospital of Soochow University, Suzhou, Jiangsu, China from January 2013 to December 2018. The recurrence rate during the same periods was calculated and surgical treatment was decided according to the tumor size. The surgical effects of the recurrent patients further compared and investigated the way different treatments affected the preservation of the auditory nerve, facial nerve, and posterior group nerve and increased facial paralysis in AN patients.

Results: Univariate analysis of 30 recurrent AN cases showed that tumor size, internal auditory canal invasion, and tumor blood supply are linked to the recurrence of AN (P<0.05). In addition, the multi-factor analysis demonstrated that rich blood supply, medium texture, intratumoral canal invasion, incomplete resection, and large-diameter tumor were independent risk factors for recurrent AN. We observed a significant difference in the preservation of the auditory nerve, but not in the preservation of the facial nerve and posterior nerve, and between the recurrent and non-recurrent AN patients.

Conclusion: This study analyzed the risk factors of postoperative recurrence in patients with acoustic neuroma. The results showed that small size of tumor, tumor blood supply, tumor texture, tumor vascular invasion, and incomplete tumor resection were independent risk factors for recurrent AN patients. Therefore, these factors can be included in the reference indexes, and relevant prevention and treatment measures can also be taken during the operation to reduce the risk of postoperative recurrence.

Keywords: Acoustic neuroma, Correlation recurrence, Risk factors

1. Background

Acoustic neuroma (AN), also known as vestibular schwannoma, is a benign, generally slow-growing tumor that might result in hearing loss, tinnitus, and disequilibrium. Surgical treatment is the main treatment (1-2). Moreover, AN usually occurs in the acoustic nerve Schwann's sheath in the inner auditory canal or the vestibular segment of the auditory nerve in middle-aged people. It is worth mentioning that AN accounts for about 6-10% of all intracranial tumors and 80% of cerebellopontine angle tumors, with an incidence of 1-20 per 100,000 cases, annually(3). The female/male gender ratio for AN has been reported to be greater than 1, and the mean age at the time of tumor diagnosis was in the range of 50-55 years (4).

Due to the presence of proper diagnostic tools and an increased level of awareness of the disease, patients with AN can benefit from early diagnosis and better therapy using CT and MRI[5]. Although usually considered benign, AN with a large size can cause hydrocephalus, brain stem compression, brain hernia, other symptoms, and even death. Currently, there are three options for treating AN, including observation/ conservative treatment, surgical treatment, and radiosurgery treatment (6,7). Several studies have revealed some predisposing factors for the development of AN, such as ionizing radiation, electromagnetic radiofrequency fields, noise exposure, and allergic diseases. The study population included 53 patients with AN who received surgical treatment in the Department of Neurosurgery in the First Affiliated Hospital of Soochow University, Suzhou, Jiangsu, China from January 2013 to December 2018.

2. Objectives

This study aimed to investigate possible risk factors for the recurrence of AN and compare the effects of different treatment options and the effectiveness of non-surgical treatment and different surgical treatments on the recovery of auditory functions and recurrence of AN.

3. Methods

3.1. Clinical data

The clinical data of patients with non-recurrent AN (n=23) and recurrent AN (n=30) from January 2013 to December 2015 were analyzed, retrospectively. A total of 14 males and 39 females in the age range of 18-78 years (mean±SD ages of 52.1±14.2 years) participated in this study. All patients and related family members signed the informed consent form approved by the hospital's ethics committee.

The inclusion criteria included 1) admission to the hospital for surgical treatment, 2) diagnosis of AN based on CT and MRI results before treatment, and 3) not having the same tumor for five years after surgery for patients with non-recurrent AN. However, patients with neurofibromatosis type II, those with other severe neurological or other systemic diseases, and patients without CT or MRI results were excluded from the study.

3.2. Clinical detection methods

All patients undertook preoperative audiological examination (including pure tone threshold audiometry, speech discrimination score, and auditory brainstem response), brain contrast-enhanced magnetic resonance imaging test, and computerized tomography (CT) scan of the temporal bone. Patients with AN were characterized by cone-shaped or funnel-shaped enlargement of the internal auditory canal with clear boundaries and smooth edges. Patients with pure tone threshold audiometry ≤50 dB and speech discrimination score ≥50% were defined as normal hearing. There were 2 cases of hearing loss in 20 cases.

Based on the House Brackmann scale, facial nerve function is classified as Grade I, normal; Grade II, mild functional abnormality, mild facial muscle weakness; Grade III, moderate dysfunction; Grade IV, moderate and severe functional abnormalities; Grade V, severe dysfunction; and Grade VI, complete paralysis, no movement. There were 22 cases of grade I facial paralysis, three cases of grade II facial paralysis, and one case of grade III facial paralysis in this study.

On contrast-enhanced images, the tumor size was recorded with the maximum diameter measured by the tumor pool. The cystic AN was confirmed when the cystic tumor volume accounted for more than 1/3 of the total tumor volume. Before the second treatment, all cases underwent MRI to confirm recurrence. Among the 30 recurrent patients, 4 were cystic AN and 4 were intratumoral acoustic invasion.

3.3. Follow-up analysis

Patients were followed up by outpatient service and telephone interviews. The endpoint was defined as recurrent or non-recurrent AN, and the recurrence was evaluated by follow-up imaging examination with recurrent tumor or even larger tumor tissues at the original surgical site. Recurrence Free Survival is the length of time from the day after surgery to the time of recurrence or the end of follow-up with non-recurrent AN.

3.4. Treatment after recurrence

A total of 30 recurrent AN patients were treated with different strategies based on their tumor size. In general, 15 patients with tumor diameter greater than 2cm had surgical treatment whereas the other 15 patients with tumor diameter less than 2cm had conservative treatment. The treatment outcomes were assessed by Glasgow Outcome Scale (GOS) scores (8). The ratio of internal auditory canal tumor diameter to total tumor diameter was compared between the recurrent and non-recurrent patients, and also between the first and second postoperative resection of recurrent patients. Specifically, preoperative condition, postoperative retention of the facial nerve, hindfoot nerve, and auditory nerve were set as 0 and postoperative resection of these nerves as 1. Therefore, nerve retention was compared through the calculation of the difference between preoperative and postoperative conditions.

3.5. Statistical analysis

Data were statistically analyzed using SPSS software (version 23.0). The measurement data subject to normal distribution were expressed as mean±standard deviation (SD). Two independent sample t-tests were used. The frequency description and the Chi-square test were adopted for the quantitative data. The GOS scores between different groups were compared using one-way ANOVA. The significant variables of univariate analysis were used in an unconditional logistic regression model and multivariate high-risk factor analysis. The differences were considered to be statistically significant at $P<0.05$.

4. Results

Of the 53 patients in this study, 30 had abundant tumor blood supply, 25 patients had medium tumor texture, 28 patients showed posterior cranial nerve adhesion, and 28 patients showed internal auditory canal invasion. The length and diameter of tumors in 34 patients were more than 2cm, among whom 30 patients with recurrence underwent the first operation and 11 patients underwent the second operation. As shown in Table 1, the recurrence of AN was significantly correlated with the tumor blood supply, medium tumor texture, tight posterior cranial nerve adhesion, acoustic canal invasion, and tumor diameter greater than 2 cm ($P<0.05$). The recurrence rate in patients with tumor diameter over 2cm (32.08%) was higher, compared to patients with normal tumor blood supply (13.21%), tough texture (20.75%), facial nerve adhesion (15.09%), no internal auditory canal invasion (15.09%), and tumor diameter less than 2cm (24.53%).

The statistically significant indexes of univariate analysis were used as independent variables for multivariate logistic regression analysis. The results showed that abundant tumor blood supply, medium tumor texture, intratumoral canal invasion, incomplete resection, and tumor diameter greater than 2cm were the independent risk factors for

Table 1. Single-factor analysis of recurrent AN and clinicopathologic factors

Clinical factors		Case (n=53)	Recurrent cases (n=30)	Non-recurrent cases (n=23)	P-value
Gender	Male	14（26%）	6（43%）	8（57%）	0.348
	Female	39（74%）	24（62%）	15（38%）	
Age	≥50 Years	29（55%）	17（89%）	2（11%）	0.786
	＜50 Years	24（45%）	13（54%）	11（46%）	
Blood supply	Abundant	30（57%）	23（77%）	7（23%）	0.002
	Normal	23（43%）	7（30%）	16（70%）	
Texture	Medium	25（47%）	19（76%）	6（24%）	0.012
	Rough	28（53%）	11（39%）	17（61%）	
Developed or not?	Yes	18（34%）	10（56%）	8（44%）	0.570
Cystic change or not?	Yes	39（74%）	22（56%）	17（44%）	1.000
Tumor stroke or not?	Yes	4（7%）	3（75%）	1（25%）	0.642
Secondary surgery?	Yes	1（1%）	0（0）	1（100%）	0.434
Tumor location	Right side	28（53%）	14（50%）	14（50%）	0.278
	Left side	25（47%）	16（64%）	9（36%）	
Nerve adhesion	Facial nerve	25（47%）	8（32%）	17（68%）	0.001
	Posterior cranial nerve	28（53%）	22（79%）	6（21%）	
Internal auditory canal invasion	Yes	39 (74%)	22（56%）	17（44%）	0.002
Tumor size	≥2*2cm	34（64%）	17（50%）	17（50%）	0.049
	＜2*2cm	19（36%）	13（68%）	6（32%）	
Surgery angle	Retro-sigmoid approach	52（98%）	29（56%）	23（44%）	1.000
	Suboccipital approach	1（2%）	1（100%）	0（0）	
Complete resection or not?	Yes	18（34%）	3（17%）	15（83%）	0.000
Facial nerve retention or not?	Yes	50（94%）	28（56%）	22（44%）	1.000
Auditory nerve retention or not?	Yes	32（60%）	15（47%）	17（53%）	0.173

Table 2. Logistic multivariate regression analysis of acoustic schwannoma recurrence

Clinicopathologic parameter	Non-normalized coefficient		Normalized coefficient	P-value	Exp (B)	95% confidence interval of EXP (B)	
	B	SE	Beta			Lower bound	Higher bound
Blood supply	-3.463	1.983	3.050	0.031	0.031	0.001	0.528
Complete	3.636	2.256	2.598	0.007	7.957	0.456	9.266
Texture	2.796	1.684	2.758	0.047	6.382	0.604	7.102
Adhesion	2.001	1.464	1.868	0.172	7.396	0.420	10.342
Tumor size	0.186	0.188	0.979	0.022	7.830	0.574	10.200
Internal auditory canal invasion	6.786	4.504	2.270	0.032	5.598	0.130	5.991

Table 3. GOS scores of patients in different groups after treatment

Group（53）	GOS scores
Non-recurrent patients（n=23）	3.97±0.38
Frist surgery of recurrent patients（n=30）	4.03±0.47
Second surgery of recurrent patients（n=11）	3.85±0.36
***P*-value**	0.470

recurrent AN, with correlation risks of 0.031, 6.382, 5.598, 7.957, and 7.830, respectively (Table 2).

There was no significant difference in GOS scores between patients with recurrent and non-recurrent AN ($P>0.05$). As shown in Table 3, surgical treatment can present better results for patients with tumor diameter greater than 2cm, and there is no significant difference in the prognosis between the patients who had two consecutive operations and non-recurrent patients. In addition, there was no significant difference in the preservation of the facial nerve and posterior cranial nerve between recurrent and non-recurrent patients ($P>0.05$); however, the preservation of the auditory nerve in recurrent patients was significantly lower than that in non-recurrent patients ($P<0.05$) (Table 4).

Table 4. Comparison of auditory nerve preservation before and after operation in different groups

Groups（n=53）	Auditory nerve retention	P-value
Patients who had conservative treatment after the first surgery（n=19）	0.53±0.51	0.151
Non-recurrent patients（n=23）	0.30±0.47	
Patients who had surgical treatment after the first surgery（n=11）	1.00±0	<0.001
Non-recurrent patients（n=23）	0.30±0.47	
First surgery of recurrent patients（n=30）	1.00±0	-
Second surgery of recurrent patients（n=11）	1.00±0	

As shown in Table 5, there was a significant difference in the preservation of the auditory nerve between the recurrent and non-recurrent patients after the first operation ($P<0.05$).

As shown in Table 6, the ratio of internal auditory canal tumor size to the total tumor size was significantly higher in the recurrent patients, compared to the non-recurrent patients ($P<0.05$). Moreover, the ratio of tumor recurrence in recurrent patients was higher than that in primary disease, indicating that a higher ratio of internal auditory canal tumor size to the total tumor size was more likely to result in recurrence of AN.

As presented in Table 7, no significant difference was observed among different groups in terms of an increase in facial paralysis ($P>0.05$).

Table 5. Comparison of facial nerve retention before and after operation in different groups

Groups（n=53）	Facial nerve retention	*P*-value
Patients who had conservative treatment after the first surgery（n=19）	0.014±0.21	0.172
Non-recurrent patients（n=23）	0.018±0.39	
Patients who had surgical treatment after the first surgery（n=11）	0.1±0.32	0.556
Non-recurrent patients（n=23）	0.018±0.39	
First surgery of recurrent patients（n=30）	0.1±0.32	0.131
Second surgery of recurrent patients（n=11）	0.43±0.53	

Table 6. Ratio of internal auditory canal tumor diameter to total tumor diameter in different Groups of patients

Groups（n=53）	Ratio of internal auditory canal tumor diameter to total tumor diameter
Non-recurrent group（n=23）	0.015±0.018
First surgery of recurrent group（n=30）	0.125±0.143*
Second surgery of recurrent group（n=11）	0.648±0.397*

* denotes $P<0.01$

Table 7. Comparison of facial paralysis before and after operation in different groups

Groups（n=53）	Increased value of facial paralysis	*P*-value
Patients who had conservative treatment after the first surgery（n=19）	2.58±1.39	0.591
Non-recurrent patients（n=23）	2.39±0.84	
Patients who had surgical treatment after the first surgery（n=11）	2.38±1.41	0.973
Non-recurrent patients（n=23）	2.39±0.84	
First surgery of recurrent patients（n=30）	2.58±1.39	0.124
Second surgery of recurrent patients（n=11）	1.29±1.11	

5. Discussion

Acoustic Neuroma is a slow-growing benign tumor, accounting for about 10% of intracranial tumors (9). The main clinical manifestations include the compression of the cerebellum and brainstem caused by the impairment of cerebral nerve function and the increase of posterior fossa pressure (10). Microsurgery is the main treatment for AN. However, due to the complexity of its anatomical structure, minimizing the incidence of postoperative complications based on total tumor resection has become one of the challenges faced by modern neurosurgeons (11).

Most AN tumors originate from the vestibular part of the auditory nerve, the superior vestibular nerve, and the cochlea (in a few cases). The vestibular nerve is enclosed by the arachnoid membrane, which is pushed up by the tumor to form a layer of arachnoid membrane on the surface of the tumor. During the tumor growth, the arachnoid membrane, which belongs to the Pontine Cistern, is pushed to the inside of the tumor, and then folded over the tumor surface to form the parietal arachnoid membrane of the tumor. With the growth of the tumor, the cisternal space of the cerebellopontine angle narrows gradually, and the blood vessels and nerves in the cerebellopontine angle slowly deform and shift, but still lie in the visceral and parietal arachnoid membranes of the tumor, which is the anatomical basis of the total tumor resection (12-13). It should be noted that adequate knowledge of the anatomic location of AN is essential even with facial nerve monitoring (14).

The study results showed that the recurrence rate of total resection is relatively low. The early relapsed clinical symptoms of recurrent AN are extremely hard to be recognized and diagnosed. Therefore, postoperative dynamic MRI follow-up examination should be recommended for AN patients due to its important role in the early diagnosis of tumor recurrence (15). Other than removing the tumor, AN surgery aims to preserve facial and cochlear nerves since the preserved size of acoustic schwannoma is important for auditory functions (16-18). The symptoms of an will last for several months to more than ten years from the beginning of discovery. The tumor often causes vestibular function change, leading to cochlear nerve stimulation. At the same time, patients often feel sick in the foramen magnum area. In this study, it was demonstrated that total tumor resection is the most effective solution in preventing the recurrence of AN; therefore, complete resection should be performed for AN patients as soon as possible. Fortunately, with the recent developments in neuroimaging, microsurgery, and intraoperative monitoring, the complete AN resection rate has increased dramatically. In addition, the best results of AN resection are the total removal of the tumor, complete preservation of the facial nerve function, and preoperative residual hearing.

Based on a meta-analysis of 34 cases of acoustic neuroma, Zanoletti *et al*. proposed that the retention rate of the facial nerve function was negatively correlated with tumor size (19). In this study, 17 out of 34 patients with tumor diameter greater than 2cm had a postoperative recurrence, which was consistent with what was reported in the literature. The tumor extrusion causes the deformation and thinning of the facial nerve, and even the tumor wraps the facial nerve, which increases the difficulty to protect the function of the facial nerve. Large tumors have a rich blood supply. When bipolar electrocoagulation is frequently used for hemostasis, the function of the facial nerve will be damaged due to heat conduction (20). In addition, it was shown that tumor blood supply, medium tumor texture, tight posterior cranial nerve adhesion, acoustic canal invasion, and tumor diameter greater than 2cm were independent risk factors for AN recurrence. It was revealed that the ratio of internal auditory canal tumor size to the total tumor size was significantly higher in the recurrent patients than that in the non-recurrent patients. This was in line with the study conducted by Tanakala *et al*. (21), who adopted the maximal length of the cerebellopontine angle as the tumor diameter, which was defined as the maximal length parallel to the long axis of the petrous bone. The results of this study showed that larger the recurrent AN was correlated to larger tumor size and a higher degree of internal auditory canal invasion. The tumor diameter increased significantly after recurrence, which made the treatment more difficult. Therefore, patients should be observed regularly after the surgery. The suboccipital retrosigmoid approach is often used in patients, which can fully expose the structure of the cerebellopontine angle and provide a good visual image for the separation and resection of the brain stem.

Further comparison of surgical treatment effectiveness showed that the group who had conservative treatment after the first surgery preserved more auditory nerves than the non-surgical treatment group, whereas no significant differences in facial and posterior cranial nerve retention were observed in this study. Similarly, a meta-analysis performed by Noudel *et al*.(22) showed that the suboccipital sigmoid sinus approach is superior to the facial and auditory neuroprotection. Since the suboccipital retrosigmoid approach can not directly expose the internal auditory canal, the posterior wall of the internal auditory canal should be removed to expose the base of the internal auditory canal to the tumors invading the internal auditory canal, which can easily damage the posterior semicircular canal and facial nerve. This study also found that patients receiving a suboccipital sigmoid sinus approach had a lower incidence of suboccipital median approach facial paralysis.

5.1. Limitations

In this study, two conditions in association with recruited patients should be taken into consideration: 1) the auditory canal is not incised, and 2) whether the internal auditory canal is cut or not, since they may also influence the prognosis of the patients. In addition, this study was designed as a single-center retrospective study, which may be affected by geographical and other factors. The surgical treatment of AN has proved its effectiveness in this study. Due to the small sample size of this study, it is suggested to carry out multicenter, large samples, and double-blind randomized controlled trials in the future.

6. Conclusion

This study analyzed the risk factors of postoperative recurrence in patients with acoustic neuroma. The results showed that small tumor size, tumor blood supply, tumor texture, tumor vascular invasion, and incomplete tumor resection were independent risk factors for recurrent AN. Therefore, these factors can be included in the reference indexes, and relevant prevention and treatment measures can be taken during the operation to reduce the risk of postoperative recurrence. Eventually, a personalized surgical treatment plan should be formulated, according to the patient's condition before the operation, to obtain the best treatment effect.

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Not applicable.

Footnotes

Conflicts of Interest: The authors declare that they have no personal, financial, commercial, or academic conflicts of interest regarding the publication of this study.

List of Abbreviations: AN: Acoustic Neuroma
RFS: Recurrence Free Survival

Declarations

Ethics approval and consent to participate: This study was approved by the Ethics Committee of The First Affiliated Hospital of Soochow University in Suzhou, Jiangsu, China and conducted in accordance with the Declaration of Helsinki.

Consent for publication: Not applicable.

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