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Treatment Outcome of Hydrocephalus Associated with Vestibular Schwannoma

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Background and Purpose Managing hydrocephalus in patients with vestibular schwannoma (VS) is controversial. We evaluated the clinical factors associated with hydrocephalus.

Methods Between 2000 and 2019, 562 patients with VS were treated at our institute. We applied endoscopic third ventriculostomy (ETV), external ventricular drainage (EVD), and ventriculoperitoneal (VP) shunts to patients with hydrocephalus. The relationships of patient, tumor, and surgical variables with the hydrocephalus outcome were assessed.

Results Preoperative hydrocephalus (Evans ratio ≥0.3) was present in 128 patients. Six patients who received a preresectional VP shunt were excluded after analyzing the hydrocephalus outcome. Seven of the remaining 122 patients had severe hydrocephalus (Evans ratio ≥0.4). Primary tumor resection, VP shunting, ETV, and EVD were performed in 60, 6, 57, and 5 patients, respectively. The hydrocephalus treatment failure rate was highest in the EVD group. Persistent hydrocephalus was present in five (8%) and seven (12%) patients in the primary resection and ETV groups, respectively. Multivariate analysis revealed that severe hydrocephalus, the cystic tumor, and the extent of resection (subtotal resection or partial resection) were associated with hydrocephalus treatment failure.

Conclusions Larger ventricles and a higher cystic portion are predictive of persistent hydrocephalus. We recommend attempting near-total tumor resection in patients with VS.

Key Words hydrocephalus, neuroma, acoustic, ventriculostomy, schwannoma, endoscope.

INTRODUCTION

Hydrocephalus occurs in 3.7–42% of patients with vestibular schwannoma (VS).[1-4] This often complicates surgery due to the increased intracranial pressure, and requires additional management after tumor resection. Hydrocephalus in patients with VS can persist or even progress after tumor resection.[5] Classifying hydrocephalus as either communicating or obstructive is challenging. Obstructive hydrocephalus often does not improve after total tumor resection due to surgery-related arachnoid granule obstruction by protein components or hemorrhage.[2,6] It is therefore essential to establish individual plans for patients after tumor removal in order to avoid adjuvant management, such as external ventricular drainage (EVD), lumbar drainage, or ventriculoperitoneal (VP) shunting. Surgeons try to avoid VP shunts due to the possibility of catheter-associated infection, their invasiveness, and the need for valve adjustment. However, a few patients presenting with persistent hydrocephalus after tumor resection require a VP shunt. Previous studies have evaluated factors related to persistent hydrocephalus, and have revealed that a larger tumor, being older, a higher cystic portion, and greater severity of hydrocephalus are associated with a poor outcome.[1,2,4,7,8] Endoscopic third ventriculostomy (ETV) is an effective option to control hydro-

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cephalus before and after tumor resection. However, while some authors recommend preresectional ETV, others do not.[5,9,10]

This is the largest single-institution study that has aimed to determine the results of treating hydrocephalus in patients with VS.

METHODS

This was a retrospective, single-institution, case-series study. The approval granted by the AMC Institutional Review Board (number 2020-1761) waived the need to obtain informed consent.

Patient records, surgical reports, follow-up data, and neuroradiological findings for 562 consecutive patients with VS were collected and confidentially stored in a database. These patients had been treated using a standardized surgical technique at a single institution over a 20-year period (2000−2019). We included patients with hydrocephalus aged >18 years who underwent surgical removal of a newly diagnosed VS. To clarify the effectiveness of primary tumor removal or other cerebrospinal fluid (CSF) diversion procedures, data of patients who received VP shunts before tumor removal were included in the statistical analysis but excluded from the outcome analysis.

Basic patient characteristics, radiographic findings, EVD placement, ETV, CSF profiles, intraoperative findings, postoperative radiographic changes, and clinical improvements were recorded. Preoperative hydrocephalus was assessed by measuring the Evans ratio.[4,8] Fluid-attenuated inversion recovery (FLAIR) and T2-weighted MRI were used to evaluate the ventricle size. Mild and severe hydrocephalus were classified as 0.3−0.4 and ≥0.4 based on Evans ratio, respectively. The type of hydrocephalus was assessed according to the established radiological criteria. Obstructive hydrocephalus was defined as the fourth ventricle being disproportionally small compared with the lateral and third ventricles, whereas communicating hydrocephalus was defined as the fourth ventricle exhibiting a proportionate degree of dilation compared with that of the lateral and third ventricles.[11] Peritumoral edema was defined as any high-intensity signal in the cerebellum or brain stem on T2-weighted or FLAIR images. Periventricular capping was defined as a high-intensity signal adjacent to the frontal horn on T2-weighted or FLAIR images.

Tumor size was defined as the largest diameter of the lesion in the cerebellopontine-angle cistern as evaluated on an axial MRI slice across the internal auditory canal. The cystic portion was grossly measured on a proton-density-weighted image when this was available, and otherwise a T2-weighted or FLAIR image was assessed. Hearing status was defined according to the American Academy of Otolaryngology-Head and Neck hearing classification guidelines.[12] Facial nerve function was assessed according to the House-Brackmann (HB) grading system.

All surgeries for VS were performed via the retrosigmoid approach with the patient in a semilateral position. The tumor removal technique was similar in all cases. Gross total resection (GTR) was defined as >99% tumor removal, near-total resection (NTR) was defined as 95−99% tumor removal (seen as focal enhancement at the internal acoustic meatus), subtotal resection (STR) was defined as 80−95% tumor removal, and partial resection (PR) was defined as <80% tumor removal.

Management of hydrocephalus

Patients who presented with acute hydrocephalus and signs of increased intracranial pressure (e.g., headache, vomiting, or diplopia) were treated before performing tumor resection. EVD, ETV, or VP shunting were considered according to the ventricle size, tumor size, and hydrocephalus type. CSF diversion procedures were applied before tumor resection. Follow-up computed tomography was performed on postoperative day (POD) 4 before discharge. The Evans ratio was measured at the initial presentation, before and after tumor removal, and on POD 4. If hydrocephalus persisted with the usual symptoms, adjuvant CSF diversion was recommended. Preresectional ETV was considered if the patient had hydrocephalus and symptoms along with delay of tumor resection due to the operation schedule. Tumor resection was subsequently performed as an elective procedure after controlling intracranial pressure and providing symptomatic relief.

Treatment failure

Treatment failure (or persistent hydrocephalus) was defined as radiographical and symptomatic hydrocephalus after tumor resection, regardless of the application of a preoperative CSF diversion procedure. The relationships of patient, tumor, and surgical variables with the hydrocephalus were assessed.

Statistical analysis

Data analysis was performed using IBM SPSS Statistics (version 23, IBM Corp., Armonk, NY, USA) and the R program (version 3.6.3, The R Foundation for Statistical Computing). We analyzed clinical, radiographical, and surgical variables to determine which factors were associated with persistent hydrocephalus after tumor resection. Basic characteristics, tumor characteristics, and radiographical, surgical, and clinical findings were evaluated in univariate analyses. The chi-square test was performed for nominal factor analyses, while Mann–Whitney U tests were applied to continuous parameters in each group. All tests were two sided, and p values <0.05 were considered statistically significant in both univariate and multivariate analyses. Multivariate analysis was performed using binary logistic regression analysis. The variables that were identified as statistically significant in logistic regression analyses were used to create a recursive decision-tree model, with the final nodes grouped according to the probability of failure to control hydrocephalus.

RESULTS

One hundred and twenty-eight patients (22.8%) presented with hydrocephalus at admission. The ratio between communicating and obstructive hydrocephalus was 1:1. The patients had a mean age of 53.1 years (range 19–80 years) and a male-to-female ratio of 49:79. The mean tumor diameter was 4.2 cm, and the mean Evans ratio was 0.32 (range: 0.30–0.46). Seven (5.5%) patients presented with an Evans ratio of ≥0.4. The mean cystic portion was 30%. Forty-nine (38%) patients initially showed peritumoral edema. Hearing disturbance was the most common symptom (81 patients, 63.2%), followed by facial numbness (34 patients, 26.6%). Nine (7%) patients had preoperative facial palsy (HB grades II and III in seven and two patients, respectively). Nine (7%) patients had long-tract signs (e.g., diplopia, ataxia, or nystagmus) and 25 (19.5%) patients presented with symptoms of hydrocephalus. Table 1 presents the detailed patient characteristics.

Surgical outcome

GTR or NTR was achieved in 94 (73.4%) patients, while STR or PR was achieved in 34 (26.6%). Facial nerves were intraoperatively preserved in 90.6% of the patients, whereas lower cranial nerves were preserved in 88.3%. The immediate postoperative HB grades were I, II, III, IV, V, and VI in 16.4%, 17.2%, 35.2%, 21.1%, 0.8%, and 0.8% of the patients, respectively. The incidence of surgery-related morbidity was 14.8%, which included meningitis, CSF leakage, arterial injury, pseudomeningocele, and cranial nerve palsy. The mastoid air cavity was exposed in 89 (69.5%) patients; it was usually covered with autologous muscle grafts and fibrin glue.[13] CSF leakage occurred in 8 (6.3%) patients, of which five required surgical repair.

Comparison of treatment modalities (primary tumor resection vs. ETV vs. VP shunting vs. EVD)

Table 2 presents the detailed clinical characteristics in each group. Sixty (46.9%) patients underwent primary tumor resection, and 57 (46.7%) underwent ETV before tumor resection. Six (4.7%) patients underwent VP shunting before tumor resection, and five received EVD before tumor resection. Five of the 128 patients underwent a combined procedure to control intracranial pressure before tumor resection. Primary

Table 1. Clinical characteristics of 128 patients with vestibular schwannoma and hydrocephalus

Basic characteristics	
Age, years	53.1 (19–80)
Sex, male:female	49:79
Preoperative EVD	9 (7)
Primary ETV	61 (47.8)
Adjuvant GKRS	22 (17.2)
Tumor component	
Mean tumor size	4.2 cm
Cystic portion	30
Initial Evans ratio	0.32 (0.30–0.46)
Peritumoral edema	49 (38)
Obstructive/communicating HCP ratio	1:1
Symptoms	
Symptom duration	33.7 months
Preoperative hearing status	
A	12 (9.4)
B	5 (3.9)
C	3 (2.3)
D	96 (75)
Preoperative facial nerve palsy	12 (9.4)
I	117 (91.4)
II	7 (5.5)
III	2 (1.6)
Preoperative trigeminal nerve symptoms	35 (27.3)
Preoperative hydrocephalus symptoms	25 (19.5)
Preoperative long-tract sign	9 (7)
Surgical outcome	
Extent of resection	
GTR or NTR	94 (73.4)
STR or PR	34 (26.6)
Anatomical facial nerve preservation	116 (90.6)
Lower cranial nerve preservation	113 (88.3)
Immediate postoperative HB grade	
I	21 (16.4)
II	22 (17.2)
III	45 (35.2)
IV	27 (21.1)
V	1 (0.8)
VI	1 (0.8)
Surgery-related morbidity	19 (15)
Mastoid air cavity exposure	89 (69.5)
CSF leakage	8 (6.3)
CSF repair operation	5 (3.9)

Data are *n* (%) or mean (range) values.
CSF: cerebrospinal fluid, EVD: external ventricular drainage, ETV: endoscopic third ventriculostomy, GKRS: Gamma Knife radiosurgery, GTR: gross total resection, HB: House-Brackmann, HCP: hydrocephalus, NTR: near-total resection, PR: partial resection, STR: subtotal resection.

Table 2. Comparison of treatment strategies for HCP

	Primary resection	VP shunting	ETV	EVD	Total	*p**
Number of patients	60	6[†]	57[‡]	5	128	
Age, years	58.4±11.1	45.2±14.5	48.5±13.0	52.0±11.9	53.1	<0.001
Tumor size, mm	38.0±8.60	37.8±8.0	45.1±7.9	51.2±8.2	41.7	<0.001
Cystic portion	32.0±34.6	0	30.4±32.7	42.0±44.4	30.2	0.133
Evans ratio	0.32±0.02	0.35±0.04	0.34±0.04	0.32±0.02	0.33	<0.001
Communicating vs obstructive	19 vs. 41	6 vs. 0	34 vs. 23	5 vs. 0		<0.001
Treatment failure rate	5 (8)	-	7 (12)	2 (40)		0.159

Data are *n*, *n* (%), or mean±two-standard-deviation values.
*One-way analysis of variance, [†]One patient underwent ETV, EVD, and VP shunting, and one patient underwent ETV before VP shunting, [‡]Three patients underwent additional EVD before tumor resection.
EVD: external ventricular drainage, ETV: endoscopic third ventriculostomy, HCP: hydrocephalus, VP: ventriculo-peritoneal.

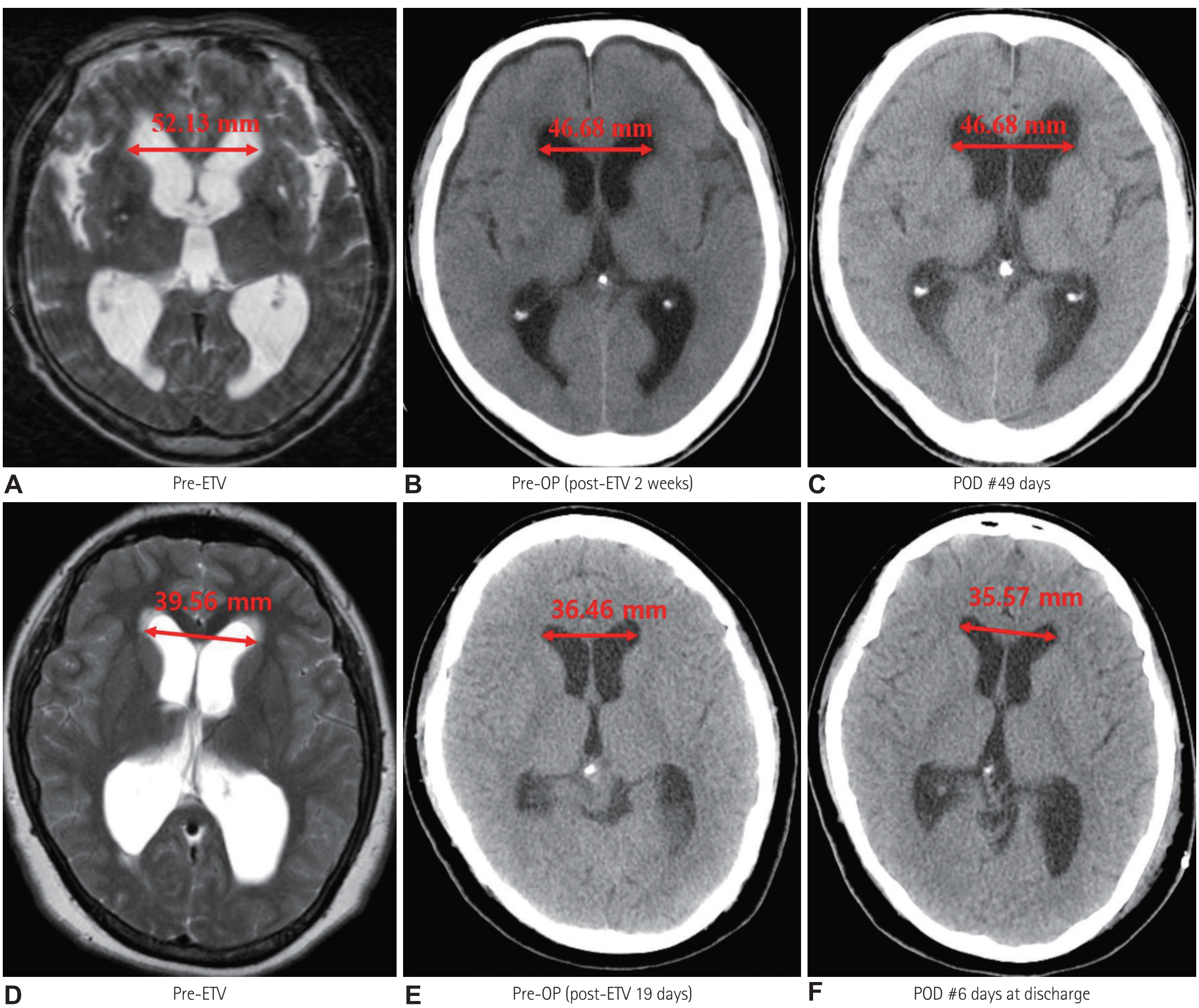

Fig. 1. Representative cases demonstrating improvement of HCP after ETV before tumor resection (A-F). A: 56-year-old male had 50 mm VS at left CPA. Initial T2-weighted MRI of the brain. B: Improvement of HCP 2 weeks after ETV before tumor resection. C: Maintenance of ventricle size at POD 49. D: 28-year-old woman had 58 mm VS at left CPA. Initial T2-weighted MRI of the brain. E: Nineteen days after ETV, and before tumor resection. F: Computed tomography image of the brain at discharge (on POD 6). CPA: cerebellopontine angle, ETV: endoscopic third ventriculosomy, HCP: hydrocephalus, POD: postoperative day, VS: vestibular schwannoma.

tumor resection was usually performed in elderly group with relatively smaller tumor and ventricle sizes than other groups. VP shunting was usually performed in patients with large ventricles and communicating hydrocephalus. Patients who received preresectional ETV were carefully selected. If patients presented with hydrocephalus or symptoms, ETV was performed prior to tumor removal. CSF opening pressures were high in most patients in the ETV group. The mean CSF protein and glucose levels were 25.5 mg/dL and 74.5 mg/dL, respectively. There was no complication associated with ETV. Fig. 1 shows illustrative images of two patients who underwent preresectional ETV. Hydrocephalus persisted after tumor resection in two (40%), five (8%), and seven (12%) patients in the EVD, primary tumor resection, and ETV groups, respectively.

Hydrocephalus and predictive factors

Age, sex, tumor size, tumor surface regularity, peritumoral edema, preoperative symptoms, and functional outcome were not significantly associated with hydrocephalus. Univariate analysis revealed that solid mass, low Evans ratio, and GTR or NTR were related to a favorable outcome. Multivariate analysis revealed that Evans ratio [<0.4 vs. ≥0.4, p=0.003, odds ratio (OR)=16.14], the cystic portion (<80% vs ≥80%, p=0.007, OR=8.10), and the extent of resection (GTR or NTR vs. STR or PR, p=0.006, OR=7.71) were statistically significant factors (Table 3).

Fig. 2 shows the rate of failure to control hydrocephalus based on clinical factors. The predictive factors associated with hydrocephalus outcome were used to construct the recursive decision-tree model. Four terminal nodes were created based on the severity of hydrocephalus, extent of resection, and the cystic portion. Patients with a high Evans ratio (≥0.4) can expect a worse hydrocephalus outcome, independent of the extent of resection and the cystic portion. None of the VS patients with relatively low Evans ratios (<0.4), GTR or NTR, and a cystic portion of <80% presented with failure of hydrocephalus control after the surgical resection of VS.

DISCUSSION

Hydrocephalus in patients with VS has been well documented, but optimal treatment strategies remain controversial. It is difficult to simply classify hydrocephalus as either communicating or obstructive due to the diversity of characteristics exhibited by patients with tumors.[1,14] Gerganov et al.[4] reported that hydrocephalus improved spontaneously after primary tumor resection in 87.5% of patients with VS, while the other six (12.5%) patients required additional treatment for hydrocephalus. Those authors also found that irregular

Table 3. Results from univariate and multivariate analyses for HCP treatment failure

	Univariate analysis			Multivariate analysis		
	p	Odds ratio	95% CI	*p*	Odds ratio	95% CI
Patient factors						
Sex	0.343	0.583	0.19–1.78	-	-	-
Age, <55 years vs. ≥55 years	0.079	2.981	0.88–10.06	0.489	1.646	0.40–6.76
Symptom duration, <6 months vs. ≥6 months	0.907	1.167	0.09–15.46	-	-	-
Preoperative hearing disturbance	0.521	2.000	0.24–16.58	-	-	-
Preoperative facial nerve palsy	0.762	0.720	0.09–6.04	-	-	-
Preoperative trigeminal symptom	0.600	0.699	0.18–2.67	-	-	-
Preoperative HCP-related symptom	0.850	1.140	0.29–4.44	-	-	-
Tumor factors						
Tumor size, <40 mm vs. ≥40 mm	0.308	1.885	0.56–6.37	-	-	-
Cystic portion, <80% vs. ≥80%	0.004*	5.827	1.75–19.46	0.007*	8.101	1.77–36.99
Shape of tumor surface, smooth vs. irregular	0.602	0.659	0.14–3.16	-	-	-
Peritumoral edema	0.323	0.587	0.20–1.69	-	-	-
Periventricular capping	0.838	1.250	0.15–10.57	-	-	-
Evans ratio, <0.4 vs. ≥0.4	0.002*	11.000	2.38–50.78	0.003*	16.135	2.56–101.57
Communicating HCP, vs. obstructive HCP	0.263	1.931	0.61–6.12	-	-	-
Treatment factors				-	-	-
Primary ETV	0.852	1.111	0.37–3.37	-	-	-
Extent of resection, GTR or NTR vs. STR or PR	0.012*	4.296	1.37–13.48	0.006*	7.708	1.81–32.76

*p<0.05.
CI: confidence interval, ETV: endoscopic third ventriculostomy, EVD: external ventricular drainage, GTR: gross total resection, HCP: hydrocephalus, NTR: near-total resection, PR: partial resection, STR: subtotal resection.

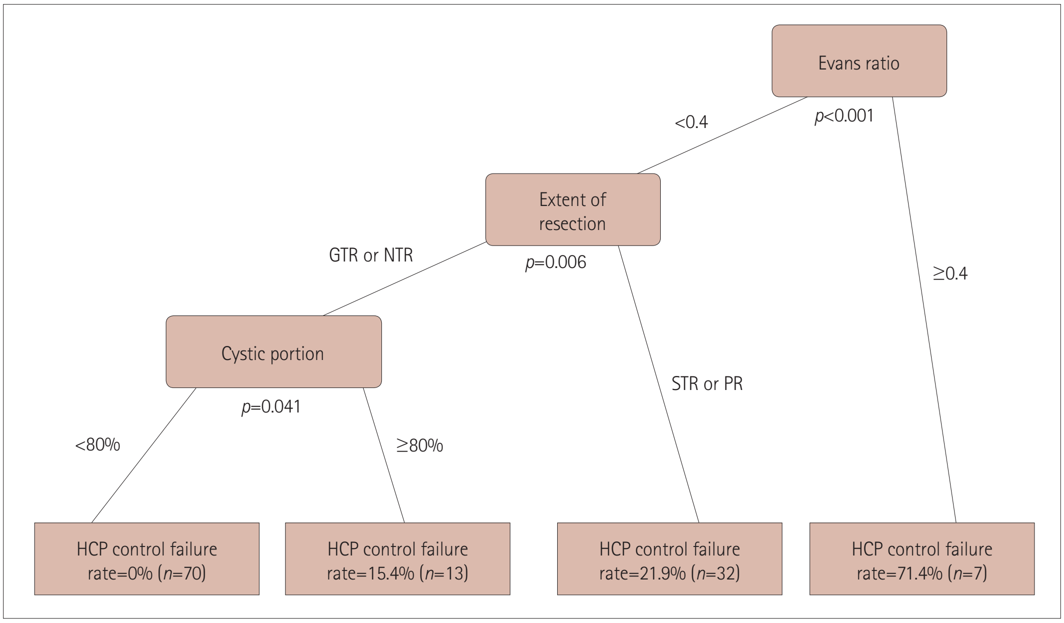

Fig. 2. Schematic flowchart of the rate of HCP control failure based on clinical factors. GTR: gross total resection, HCP: hydrocephalus, NTR: near-total resection.

tumor surface and severe hydrocephalus were significantly correlated with persistent hydrocephalus. Additionally, they found that tumor particles or bleeding during tumor resection can obstruct subarachnoid cisterns. These diverse features could account for the mixed characteristics of hydrocephalus. Obstructive hydrocephalus due to tumor compression of the fourth ventricle seems to resolve after total tumor removal, whereas communicating hydrocephalus often occurs after tumor resection due to obstruction of the arachnoid granules by CSF proteins, tumor debris, or hemorrhage.[1,2,4,15]

Lower age, larger tumor, tumor surface irregularity, severe hydrocephalus, and perilesional edema are well-known factors associated with poor hydrocephalus outcomes in patients with VS.[2,4,7,8,10,16-18] In our study, persistent hydrocephalus was associated with the severity of hydrocephalus (i.e., Evans ratio), the cystic portion, and extent of resection, but not with the tumor size or surface irregularity.

The effect of extent of the resection on hydrocephalus is controversial.[5,10,19,20] Won et al.[8] reported that STR may be sufficient for relieving obstruction. Morelli et al.[5] further found that the degree of tumor resection was not correlated with persistent hydrocephalus. However, some studies have found persistent hydrocephalus to be more common in STR groups.[19,21] Lee et al.[16] revealed that communicating hydrocephalus occurred in 4.1% of patients who underwent Gamma Knife radiosurgery. Some mechanisms have been proposed for understanding the pathophysiology of hydrocephalus after radiosurgery. Previous studies have described plugging of the arachnoid granulation by tumor cells.[4,16] Based on this theory, we hypothesized that the probability of releasing tumor cells is higher for STR or PR than for GTR or NTR. We found that the prognosis was better for GTR and NTR than for STR and PR, and therefore recommend that surgeons attempt at least NTR that leaves only the portion of the tumor that is inside the internal acoustic meatus.

We presumed that the CSF diversion procedure without tumor resection could be an alternative treatment option for symptomatic communicating hydrocephalus with small to medium-sized VS in the elderly. Morelli et al.[5] reported that 11 of 14 patients who had hydrocephalus with a posterior fossa tumor showed improvement through biopsy and ETV, without tumor resection. Preoperative management before tumor resection should be considered if a patient has an initial Evans ratio of >0.4. A preresectional VP shunt was an effective option for the patients in the present study who had an Evans ratio of >0.4.

Endoscopic third ventriculostomy

Previous studies have found that the success rate of ETV is high (50–80%) in hydrocephalus secondary to posterior fossa tumors.[5,22,23] The reported complication rate of preresectional ETV has varied between 5.9% and 8.1%.[10] ETV has a low morbidity (<0.1%) and provides permanent shunting in obstructive hydrocephalus.[24] Hayhurst et al.[25] reported on the efficacy of ETV in cerebellopontine-angle tumors, with seven (63.6%) of 11 patients (8 with VS, 1 with meningioma, 1 with melanocytoma, and 1 with jugular foramen schwannoma) remaining shunt free without surgery-related complications. That is the only previous report discussing cerebellopontine-angle tumors and hydrocephalus. Our study included 57 patients who underwent preresectional ETV. Appropriate patient selection may result in ETV being a useful procedure for decreasing the intracranial pressure or minimizing cerebellar retraction during tumor resection. Furthermore, since lowering the intracranial pressure improves symptoms, tumor resection can be delayed long enough to permit evaluation of the patient prior to performing surgery for resection on an elective basis. In addition, glucocorticoids can be administered as an adjunctive therapy during the delay period. In our study, the opening-pressure data showed that the intracranial pressure was moderate to high in 21 (75%) of 28 patients. This indicates that ETV is a useful method for decreasing intracranial pressure and relieving acute symptoms before performing resection.

However, the present study did not obtain better outcomes in the ETV group, which might have been due to the type of hydrocephalus not being clear in these patients. Patients exhibited characteristics of either obstructive or communicating hydrocephalus, and so ETV alone was not an ideal procedure. Moreover, patients who underwent ETV had larger ventricles than did patients in the primary resection group (Evans ratio: 0.33 vs. 0.31), which was associated with worse outcomes in the multivariate analysis. Further studies should therefore investigate whether large ventricles are an indication for preresectional ETV.

In conclusion, severe hydrocephalus, the cystic portion, and incomplete resection (STR or PR) are associated with persistent hydrocephalus after tumor resection. An individual treatment strategy should be established for each patient to avoid an unnecessary CSF diversion procedure before performing tumor resection. Future randomized prospective studies should further evaluate the clinical outcomes for hydrocephalus in patients with VS. Finally, we recommend removing as much of the tumor as possible in order to avoid an adjuvant CSF diversion procedure.

Author Contributions

Conceptualization: Sang Woo Song. Data curation: Dong-Won Shin. Formal analysis: Dong-Won Shin, Sang Woo Song. Funding acquisition: SangJoon Chong. Investigation: Young-Hoon Kim. Methodology: Young Hyun Cho. Project administration: Seok Ho Hong. Resources: Dong-Won Shin, Sang Woo Song. Supervision: Jeong Hoon Kim. Validation: Sang Woo Song. Visualization: Dong-Won Shin. Writing—original draft: Dong-Won Shin. Writing—review & editing: Sang Woo Song.

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Conflicts of Interest

The authors have no potential conflicts of interest to disclose.

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