Do cystic vestibular schwannomas have worse surgical outcomes? Systematic analysis of the literature

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Object. The goal of this study was to perform a systematic quantitative comparison of the surgical outcomes between cystic vestibular schwannomas (CVSs) and solid vestibular schwannomas (SVSs).

Methods. A review of English-language literature published between 1990 and 2011 was performed using various search engines including PubMed, Google Scholar, and the Cochrane database. Only studies that reported surgical results of CVSs in comparison with SVSs were included in the analysis. The primary end point of this study was surgical outcomes, defined by the following: 1) facial nerve outcomes at latest follow-up; 2) mortality rates; or 3) non–facial nerve complication index. Secondary end points included extent of resection and brainstem adherence.

Results. Nine studies comprising 428 CVSs and 1287 SVSs were included in the study. The mean age of patients undergoing surgery was 48.3 ± 6.75 and 47.1 ± 9 years for CVSs and SVSs, respectively (p = 0.8). The mean tumor diameter for CVSs was 3.9 ± 0.84 cm and that for SVSs was 3.7 ± 1.2 cm (p = 0.7). There was no significant difference in the extent of resection among CVSs and SVSs (81.2% vs 80.7%, p = 0.87) Facial nerve outcomes were significantly better in the cohort of patients with SVSs than in those with CVSs (52.1% vs 39%, p = 0.0001). The perioperative mortality rates for CVSs and SVSs were not significantly different (3% and 3.8%, respectively; p = 0.6). No significant difference was noted between the cumulative non–facial nerve complication rate (including mortality) among patients with CVSs and SVSs (24.5% and 25.6%, respectively; p = 0.75)

Conclusions. Facial nerve outcomes are worse in patients undergoing resection for CVSs than in patients undergoing resection for SVSs. There were no significant differences in the extent of resection or postoperative morbidity and mortality rates between the cohorts of patients with vestibular schwannomas.

Key Words • cystic vestibular schwannoma • acoustic neuroma • solid vestibular schwannoma

Vestibular schwannomas are the most common tumors occupying the cerebellopontine angle.7,19 Based on their consistency, they can be broadly categorized into SVSs (homogeneous or heterogeneous) and CVSs.13,25 It has been generally stated that CVSs are more aggressive, unpredictable variants of VSs, and patients present to their physicians after shorter symptomatic periods.4,9,13,25 Due to the improved understanding of CVSs, it was recommended in a 2003 consensus meeting that a VS with a cystic component (especially multicystic VSs and those with the cyst on the surface) should be categorized as a different group within VSs and should be appropriately analyzed and reported separately.13

It is widely believed that CVSs have less favorable surgical outcomes than SVSs with regard to facial nerve outcomes, surgery-related complications, and mortality.1,5,6,26,29,32 On the contrary, recently there have been reports that have shown no significant differences in the surgical outcomes among the 2 cohorts of VSs.9,10,25 To our knowledge, currently there is no systematic review in
the literature comparing the surgical outcomes between CVS and SVS. To address this question and summarize the evidence, we performed a quantitative analysis of the literature to elucidate if there was any difference in the surgical outcome among CVSs and SVSs. Additionally, this article will provide a brief synopsis of the literature to highlight the possible pathophysiology behind the development of the cystic component in a VS and operative considerations pertinent to CVS.

Methods

A review of the English-language literature published between 1990 and 2011 was done using various search engines including PubMed, Google Scholar, and the Cochrane database. Initially, the articles were identified using a combination of the following key words: “cystic vestibular schwannoma,” “solid vestibular schwannoma,” “vestibular schwannoma,” “acoustic neuroma,” “cyst,” “facial nerve,” and “surgical outcome.”

The abstracts of the various selected studies were screened, and only those studies that reported the surgical results of CVS in comparison with SVS were included in our analysis. The studies examining only 1 of the cohorts were excluded from the analysis. Furthermore, references from the selected studies were also screened to identify any missed studies.

The primary end point in our study was surgical outcomes defined by the following: 1) facial nerve outcomes at latest follow-up; 2) mortality rates; or 3) non–facial nerve complication index. Secondary end points included the extent of resection and brainstem adherence. As with most tumor studies, patient age and tumor size are important in determining surgical outcome. Thus, whenever possible, this pertinent information was noted, and a statistical comparison was performed to see if the difference in tumor size and age was significant between the cohorts.

Relative rates of facial nerve outcomes at the last follow-up were compared. Good facial nerve outcome was defined as House-Brackmann Grade I or II. The studies that reported good facial nerve outcomes as Grades I–III were excluded from the main analysis; their results were analyzed and reported separately.1,29 Since there was a possibility that a patient could have more than 1 type of non-auditory facial complication, we analyze the non-auditory facial complications, such as CSF leak, lower cranial nerve deficits, and stroke, as the total cumulative complication percentage per cohort (non-auditory facial complication index).

Statistical Analysis

The Fisher exact test was used to analyze the binary variables, while an independent sample t-test was used to determine the statistical difference among the continuous variables. The result was considered statistically significant at p < 0.05.

Results

After the initial screening, 35 unduplicated studies were reviewed, from which 10 studies comparing the results of CVS versus SVS were extracted. Two studies comparing the results of fractionated stereotactic radiotherapy between the groups were excluded from the analysis of the surgical outcomes.24,28 Overall, 9 studies including 428 CVSs and 1287 SVSs were included in our review (Table 1). The mean age of patients undergoing surgery for CVSs and SVSs was 48.3 ± 6.75 and 47.1 ± 9 years, respectively; this difference was not significant (p = 0.8). The mean tumor diameter of the CVSs was 3.9 ± 0.84 cm and that of the SVSs was 3.7 ± 1.2 cm; this difference was also not significant (p = 0.7). The 2 studies that did not report their mean tumor sizes did mention in their methods section that the patients were recruited only after matching the tumor sizes.6,10

Extent of Resection

To analyze the extent of resection, data were available for 341 patients with CVSs and 1210 with SVSs (Table 2). The extent of resection was classified into GTR and STR. Authors of 1 study divided their results into 3 categories that included GTR, near-total resection, and STR.9 For this paper, we included the patients undergoing near-total resection in the STR group. There was no significant difference with regard to the extent of resection among surgery for CVSs and SVSs (81.2% and 80.7%, respectively; p = 0.87) (Fig. 1).

Facial Nerve Preservation Rate

For analysis of the facial nerve function, good outcome was defined as House-Brackmann Grade I or II at the latest follow-up (Table 3). A total of 302 patients with CVSs and 959 patients with SVSs were analyzed. Patients from 2 studies were excluded from this analysis (analyzed separately) since they reported good outcome as House-Brackmann Grades I–III, and no detailed table was available from which information pertaining to House-Brackmann Grade I or II could be extracted. Facial nerve outcomes at the last follow-up were significantly better in the cohort of patients with SVSs than for those with CVSs (52.1% and 39%, respectively; p = 0.0001) (Fig. 2). Facial nerve preservation rates in the studies that reported good outcomes as House-Brackmann Grades I–III were also significantly better for patients with SVSs than for those with CVSs (78.3% and 65.2%, respectively; p = 0.03).1,29

![Fig. 1. Bar graph showing a comparison of the extent of resection between CVSs and SVSs.](image-url)
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Mortality and Non–Facial Nerve Morbidity

To analyze the perioperative mortality and morbidity rates, data were available for 293 patients with CVSs and 800 patients with SVSs (Table 4). The mortality rate was not significantly different between the groups (3% and 3.8%, respectively; p = 0.6). Furthermore, no significant difference was noted between the cumulative non-audiofacial complication rate (including mortality) among the CVS and SVS cohorts (24.5% and 25.6%, respectively; p = 0.75) (Fig. 3).

Brainstem Adherence

Only 3 studies had tabulated the comparative frequencies of tumor-brainstem adherence. To analyze the same, data were available for 94 patients with CVSs and 356 patients with SVSs. Patients with SVSs had a significantly higher rate of brainstem adherence than those with CVSs (86.8% and 77.6%, p = 0.03 [Table 5]).

Discussion

The incidence of CVSs based on the current review of comparative studies range from 4% to 23% (mean 13.5% [Table 1]). Previous contemporary studies noted the incidence of CVSs as ranging from 5.7% to 48%. Generally, CVS is considered to be a more aggressive and less predictable tumor than SVS. Patients with CVSs also tend to have shorter symptomatic periods. In our review of the literature, the mean duration of symptoms was noted in 3 studies (Table 1), and a trend of a shorter duration of symptoms was noted in patients with CVSs, although the difference was not significant (18.7 vs 23.3 months, p = 0.3).

Fundová et al. pointed out that the heterogeneity in the incidence of CVS will likely remain until an effective...

<table>
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<th>TABLE 1: Study type and basic demographic details of the available comparative studies in the literature*</th>
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| Authors & Year | Level of Evidence | Study Setting | No. of Patients | Mean Age (yrs) | Tumor Size (cm) | Incidence of CVS (%) | CVS | SVS | CVS | SVS | CVS | SVS | CVS | SVS | CVS | SVS | CVS | SVS | CVS | SVS | CVS | SVS | CVS | SVS | CVS | SVS | CVS | SVS | CVS | SVS | CVS | SVS | CVS | SVS | CVS | SVS | CVS | SVS | CVS | SVS | CVS | SVS | CVS | SVS | CVS | SVS | CVS | SVS | CVS | SVS | CVS | SVS | CVS | SVS | CVS | SVS | CVS | SVS | CVS | SVS | CVS | SVS | CVS | SVS | CVS | SVS | CVS | SVS | CVS | SVS | CVS | SVS | CVS | SVS | CVS | SVS | CVS | SVS | CVS | SVS | CVS | SVS | CVS | SVS | CVS | SVS | CVS | SVS | CVS | SVS | CVS | SVS | CVS | SVS | CVS | SVS | CVS | SVS | CVS | SVS | CVS | SVS | CVS | SVS | CVS | SVS | CVS | SVS | CVS | SVS | CVS | SVS | CVS | SVS | CVS | SVS | CVS | SVS | CVS | SVS | CVS | SVS | CVS | SVS | CVS | SVS | CVS | SVS | CVS | SVS | CVS | SVS | CVS | SVS | CVS | SVS | CVS | SVS | CVS | SVS | CVS | SVS | CVS | SVS | CVS | SVS | CVS | SVS | CVS | SVS | CVS | 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standard classification system is universally used. There have been numerous attempts in the literature to propose a standard classification (Fig. 4). Most of the studies considered VSs to be cystic if the mean diameter of the cyst was more than two-thirds the diameter of the tumor on MRI imaging. Among the available studies, the most extensive classification system has been proposed by Piccirillo et al. (Table 6 and Figs. 5 and 6); nevertheless, the need to standardize a criterion for CVS remains.

Pathophysiology of Cyst Formation

Vestibular schwannomas are composed of 2 types of tissue that were originally described by Antoni in 1920. Type A tissue is formed by a compact interwoven bundle of long bipolar spindle cells that have a tendency to palisade. Type B tissue is characterized by the presence of loosely organized tissue with small round satellite cells and tumor cell polymorphism.

While the exact pathogenesis of CVS remains unclear, various observations and hypotheses have been put forth. Originally, it was thought that the cyst formation was due to the increased cell growth rate. However, later studies did not find any difference in the proliferative index of CVSs compared with SVSs. Now it is believed that the unpredictable and rapid growth in CVSs is due to the expansion of the cyst itself.

Charabi et al. concluded that the formation of cysts was due to the degeneration of tumor tissue. The authors observed the production of a myxomatous material in small cystic areas by Antoni Type B tissue and hypothesized that the former may eventually coalesce into larger cysts and compress the surrounding Antoni Type A cells. Their finding that the cyst walls consisted of Type A tissue and that the inner tissue was made up of Antoni Type B tissue has drawn general agreement. Some investigators have explained the presence of cysts by the difference in the distribution of Antoni cells and the degeneration of tumor tissues. However, recent studies have not found any relationship between the distribution of cysts and the 2 types of tissues.

An impairment of the blood-tumor barrier leading to an extravasation of serum proteins has also been proposed as a reason for the increase in cyst size. Protein secretion by the tumor cells, due to an osmotic effect, augmenting the accumulation of fluid within the cyst is also thought to contribute to an increase in size. While these mechanisms may explain the expansion of already present cysts, they do not explain their genesis.

While massive intratumoral hemorrhage has been classically attributed to an increase in the size of the tumor, the role of microhemorrhages has also come to light as a possible reason for the presence of cysts. Park et al. documented the presence of significantly increased histological evidence of microhemorrhage, such as hemosiderin-laden macrophages, hemosiderin deposits, thrombotic vessels, and abnormal vessel proliferation, in CVSs compared with their solid counterparts (Fig. 7).

Another interesting observation is the increased expression of MMP-2 in the cyst fluid and cyst-lining wall of the tumor. The proteolytic enzyme MMP-2 has been shown to be present in renal cystic lesions and ovarian cystic neoplasms and is thought to significantly contribute to the genesis of the cyst as well as to its biological invasiveness. Although it was thought that the presence of MMP-2 may explain the increased adhesion of the tumor to the neighboring neurovascular structures, our review of the literature showed that SVSs had a significantly higher probability of adherence to the brainstem.

TABLE 5: Analysis of studies reporting the comparative frequencies of tumor-brainstem adherence

<table>
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<tr>
<th>Cohort</th>
<th>Yes (%)</th>
<th>No</th>
<th>Total</th>
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<tbody>
<tr>
<td>CVS</td>
<td>73 (77.6)</td>
<td>21</td>
<td>94</td>
</tr>
<tr>
<td>SVS</td>
<td>309 (86.8)</td>
<td>47</td>
<td>356</td>
</tr>
<tr>
<td>total</td>
<td>382</td>
<td>68</td>
<td>450</td>
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* Data available from the 3 studies that reported brainstem adherence show that SVSs have a significantly higher rate of adherence than CVSs (p = 0.03).
Operative Considerations

Surgery for CVSs can be technically challenging. Standard surgical approaches (translabyrinthine, middle fossa, and retrosigmoid) have been used to resect CVSs. The patient’s hearing status, size of the tumor with respect to cisternal and metal segments, brainstem compression, and surgeon’s preference all play an integral role in determining which surgical approach is used. However, irrespective of which approach is used, there are fundamental differences and pertinent considerations while resecting CVSs versus SVSs.

Generally, the following are important factors that govern the surgical strategy among CVS treatment.

**Number and Size of the Cysts.** Multiple cysts in a tu-
mor can be challenging because of the heterogeneity in the consistency of the tumor. Resection usually proceeds more rapidly through cystic areas. Nevertheless, tumors with large cystic components can be difficult to resect. Removal of large cyst contents can cause deformation of the tumor structure and subsequently may change the structural integrity by lowering the internal resistance. Cyst decompression is also likely to alter the existing relationship to adjacent structures, especially the facial nerve.

**Thickness of the Cyst Wall.** The thickness of the cyst wall is an important feature on preoperative imaging. Thinner cyst walls provide less of a barrier and can be easily breached during dissection. This can be especially problematic if the cystic component is anterior or adherent to the facial nerve. One can imagine traversing a cyst with a thin wall and injuring the facial nerve due to the minimal barrier afforded by the wall. A thin cyst wall also provides a minimal subarachnoid plane for dissection. Therefore, it is suggested that the tumor should always be sharply dissected from the facial nerve, thus eliminating the traction forces associated with blunt dissection. Also, using higher-voltage stimulation for facial nerve monitoring has been advocated in some studies. This can potentially allow for earlier identification and preservation of the facial nerve while working in the cystic component.

**Location of the Cyst Wall.** Cystic areas along the tumor periphery can cause loss of the dissection plane, especially when the cyst is in the anterior portion of the tumor in contact with the facial nerve. Similar issues may arise when the cystic component is located more...
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medially against the brainstem. On the other hand, these technical challenges may not be as evident in the centrally located cysts.

Adherence to Neighboring Neurovascular Structures. Individual cystic tumors may be notoriously adherent to neurovascular structures and may make the resection difficult. Historically, it was thought that the presence of a cyst increased the risk of adherence to these neurovascular structures; however, our systematic review found that SVSs were more likely to be adherent to the brainstem than CVSs (Table 5). Hence, even though adherence of CVSs may be a factor in making the resection difficult, this is likely also the case with SVSs.

Study Limitations

Our current quantitative study is based on the results of 2 studies with Level II evidence and 7 studies with Level III evidence; therefore, the results should be interpreted with caution. Having said that, performing a prospective controlled study and comparing the surgical outcomes between SVSs and CVSs may be difficult in terms of accruing enough patients to achieve desirable statistical power. Thus, a systematic review such as ours does evaluate a relatively large patient population and provides some trends for interpretation. A comparison of hearing outcomes was reported by only 2 studies and thus could not be considered as a potential primary end point. Lastly, stereotactic radiosurgery is an important component of the treatment paradigm for all types of VSs. Our study does not incorporate results of this treatment modality since there were only limited comparative series.

Conclusions

Facial nerve outcomes are worse in patients undergoing resection for CVSs than in those undergoing resection for SVSs. There were no significant differences in the extent of resection or postoperative morbidity and mortality rates between CVS and SVS treatment. Further prospective comparison studies are required to validate the results of the current study.

Disclosure

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author contributions to the study and manuscript preparation include the following: Conception and design: Thakur, Guthikonda. Acquisition of data: Thakur, Khan. Analysis and interpretation of data: Thakur, Shorter, Sonig. Drafting the article: Thakur, Khan, Shorter. Critically revising the article: Nanda, Sonig, Gardner, Guthikonda. Approved the final version of the manuscript on behalf of all authors: Nanda. Statistical analysis: Thakur, Khan. Administrative/technical/material support: Nanda. Study supervision: Gardner, Guthikonda.

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