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# Dispersed Bone Spicules as a Cause of Postoperative Headache after Retrosigmoid Vestibular Schwannoma Surgery: A Myth?

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Abstract Keywords - bone spicule - retrosigmoid - suboccipital - acoustic neuroma - vestibular schwannoma - headache	<b>Objectives</b> Dispersion of bone dust in the posterior fossa during retrosigmoid craniectomy for vestibular schwannoma (VS) resection could be a source of meningeal irritation and lead to development of persistent postoperative headaches (POH). We aim to determine risk factors, including whether the presence of bone spicules that influence POH after retrosigmoid VS resection. <b>Design</b> Present study is a retrospective case series. <b>Setting</b> The study was conducted at a tertiary skull-base referral center. <b>Participants</b> Adult patients undergoing VS resection via a retrosigmoid approach between November 2017 and February 2020 were included for this study. <b>Main Outcome Measures</b> Development of POH lasting ≥ 3 months is the primary outcome of this study. <b>Results</b> Of 64 patients undergoing surgery, 49 had complete data (mean age, 49 years; 53% female). Mean follow-up time was 2.4 years. At latest follow up, 16 (33%) had no headaches, 14 (29%) experienced headaches lasting <3 months, 19 (39%) reported POH lasting ≥3 months. Twenty-seven (55%) patients had posterior fossa bone spicules detectable on postoperative computed tomography (CT). Age, gender, body mass index, length of stay, tumor diameter, size of craniectomy, the presence of bone spicules, or the amount of posterior petrous temporal bone removed from drilling did not differ significantly between patients with POH and those without. On multivariate logistic regression, patients with POH were less likely to have preoperative brainstem compression by the tumor (odds ratio [OR] = 0.21, <i>p</i> = 0.028) and more likely to have higher opioid requirements during hospitalization (OR = 1.023, <i>p</i> = 0.045).

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**Conclusion** The presence of bone spicules in the posterior fossa on postoperative CT did not contribute to headaches following retrosigmoid craniectomy approach for VS resection.

# Introduction

Management strategies for vestibular schwannoma (VS) have undergone tremendous evolution over the past few decades. Although historically craniotomy and complete tumor removal was the ultimate goal, many current treatment paradigms have shifted toward more conservative strategies such as observation. When surgery is undertaken, greater emphasis is placed on the preservation of neurologic function and maximization of the patient's quality of life (QOL).<sup>1</sup> While significant technical advances in microsurgical resection have been made, surgery can still be debilitating largely owing to the unique anatomical location where the tumor resides. Morbidities associated with surgery include facial weakness or paralysis, facial numbness, hearing loss, and postoperative headaches (POH). While the immediate onset of headaches after craniotomy is not uncommon and can often be attributed to incisional pain, transient alterations in cerebrospinal fluid (CSF) flow and meningeal irritation may also contribute.<sup>2</sup> However, POH that persists for weeks to months after surgery can be profoundly debilitating, potentially resulting in the use of excess opioid medications, and ultimately significantly impacting the patient's QOL.

While there is no current standardized method to assess POH after craniotomy for VS resection, Harner et al have developed quantitative methods to characterize POH in general.<sup>3,4</sup> In 2004, the diagnostic criteria for postcraniotomy headache was defined by the International Headache Society, where chronic postcraniotomy headache was defined as headache occurred within 7 days after craniotomy, located directly within the surgical area, and persists beyond 3 months postoperatively.<sup>5</sup> Nonetheless, most previously published literature suffer from limitations including small patient population, study accrued over a long period of time, a lack of detailed characteristics, and inconsistent definitions on POH, and multiple surgeons with heterogeneity in surgical techniques.

Several previous studies have attempted to characterize the incidence and risk factors for the development of POH after VS resection. In general, POH is thought to be more common and more severe after suboccipital or retrosigmoid approaches when compared with the middle cranial fossa or translabyrinthine craniotomy approach.<sup>2,6,7</sup> While the exact mechanism by which POH persists is still incompletely understood, it has been hypothesized that POH could result due to the development of scarring adhesions between the dura and the neck musculature, dural tension resulted from direct dural closure, entrapment of occipital nerve fibers, and aseptic meningitis from the use of fibrin glue intraoperatively.<sup>8–10</sup> As such, techniques for improving wound closure to prevent dural adhesions have been described and are commonly employed today.<sup>10</sup> Still, one of the current leading hypotheses of POH is the development of meningeal irritation due to the spillage of bone spicules in the posterior fossa after drilling of the internal auditory canal (IAC), while the subarachnoid space is exposed.<sup>8,11–13</sup> Nevertheless, direct radiographic evidence that supports this hypothesis is scant.

Accordingly, we aimed to evaluate the risk factors, including the presence of bone spicules detectable on postoperative computed tomography (CT) that influence the degree and severity of POH after retrosigmoid craniectomy for resection of VS. Furthermore, we provided an in-depth and comprehensive analysis of radiographic characteristics associated with the development of POH.

# **Materials and Methods**

# **Patient Selection**

Approval was obtained from the Institutional Review Board at University of California San Diego Health. Retrospective chart review was performed on consecutive cases of retrosigmoid craniectomy with attempted hearing preservation between November 2017 and February 2020. Inclusion criteria were age greater than or equal to 18 years, confirmed diagnosis of vestibular schwannoma, and duration of postoperative follow-up  $\geq$  6 months.

## **Surgical Approach**

All patients received a lumbar drain prior to surgical incision. The drain was clamped initially. The patient was placed supine in the Mayfield 3-point fixation device. The retrosigmoid craniectomy approach began with a postauricular lazy S-shaped incision. The deep fascia was incised in an L-shaped incision. The suboccipital muscles were retracted and an approximate  $3 \text{ cm} \times 3 \text{ cm}$  retrosigmoid craniectomy was performed. CSF was drained via the lumbar drain as needed throughout the procedure. Copious irrigation was performed to remove all visible bone spicules prior to opening of the dura. The dura was then opened in a cruciate fashion, the trigeminal nerve rootlet and the lower cranial nerves were systematically identified. Once the cerebellopontine angle (CPA) portion of the tumor was carefully debulked centrally until the tumor remaining was located in the IAC and attached laterally, the wound was copiously irrigated again and large pieces of gelatin sponges (Gelfoam) were placed in the cisternal spaces to prevent accumulation of blood products and bone spicules. The dura over the posterior petrous ridge and posterior lip of the IAC was opened. Intradural drilling of the IAC was accomplished using sequentially smaller diamond burrs. The bone overlying the IAC, superior and inferior bony troughs were drilled from the porous laterally toward the fundus. Once the drilling was complete, further tumor debulking was performed for the intracanalicular portion of the tumor.

For closure of the bony defect over the IAC, a small piece of abdominal fat graft obtained via a lower abdominal quadrant incision was placed in the posterior lip of the porus. The fat was held in place using a piece of surgicel packing. The Gelfoam pieces were removed after confirmation of hemostasis. The dura was tacked together using Nurolon sutures. Dural closure was augmented with a piece of onlay dural graft. An additional piece of abdominal fat graft was used to fill the craniectomy defect. Next, a mesh cranioplasty was fashioned out of titanium mesh and secured using micro screws circumferentially. The bone flap was not replaced. The deep fascia and the scalp was then closed in layers in a standard fashion. No drain was used. A compressive mastoid dressing was placed for 1 to 2 days postoperatively. Patients are routinely discharged after an average of 3 days.

#### Assessment of Postoperative Headache

A questionnaire consisted of nine multiple choice questions was designed to delineate the following characteristics: the presence of preoperative headaches, the onset and duration of POH, the frequency and intensity of POH, whether overthe-counter or narcotic medications were needed for analgesia, and the impact of POH on quality of life (> Supplementary Table S1 [available in the online version). The intensity of headaches was quantified using the visual analogue scale from 1 to 10; with 10 being the most severe headaches, the patient has ever experienced. Additional information collected included demographics, tumor size, length of stay, and the amount of analgesic medications patients received during the hospitalization. A letter explaining the study and the questionnaire were sent to the study cohort electronically. A second letter and questionnaire were sent to nonrespondents. The answers to the questionnaires were reviewed independently by two investigators.

#### **Analysis of Radiographic Data**

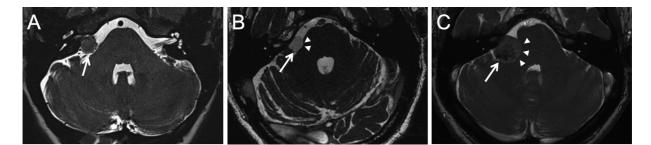
Preoperative magnetic resonance images (MRIs) were performed within 3 months prior to surgery and analyzed by two independent board-certified radiologists blinded to outcome. Image analysis was performed using our institutional PACS database (Agfa, United States). Absolute tumor measurements were made using a combination of axial volumetric steady-state free precession (SSFP) sequences, as well as axial and coronal T1-weighted postgadolinium MRI contrast imaging. Parameters queried included the transverse tumor size, location relative to the CPA cistern and IAC. Additional metrics included the presence of contact or compression of the adjacent middle cerebellar peduncle and potential extension to the root entry zone of the ipsilateral trigeminal nerve (**-Fig. 1**). Postoperative CTs were obtained immediately after surgery per protocol utilizing 0.625-mm axial acquisition with 2.5-mm axial, coronal, and sagittal reformats. Measurements include the presence and amount of bone spicules in the posterior fossa (**-Fig. 2**), the presence of pneumocephalus or evidence of blood products distal to the craniectomy (**-Fig. 3**), the size of the craniectomy defect and petrous bone defect after drilling of IAC, and the presence of distant hemorrhage within the infratentorial and supratentorial compartments (**-Fig. 3**).

#### **Statistical Analysis**

Statistical analysis was done using SPSS v.21.0 (IBM Inc., Armonk, New York, United States). Categorical variables were analyzed using the Pearson's Chi-square statistic. Radiographic measurements between patients with persistent POH versus those without were compared using univariate analysis. Association with persistent POH was evaluated using logistic regression where development of POH was the dependent dichotomous variable, and independent variables were age, gender, laterality, body mass index (BMI), presence of preoperative headache (dichotomous), preoperative tumor characteristics on MRI, medication usage postoperatively (continuous), and postoperative CT findings including the presence of bone spicules (dichotomous). Results were summarized using odds ratios (OR) and 95% confidence intervals (CI). Multivariable models were developed using stepwise selection, with the p-value cut-off of 0.05 for a variable to enter or leave the model. All tests were two-sided and p < 0.05was considered statistically significant.

#### Results

A total of 49 patients met criteria and were included in the analysis. Demographic statistics are outlined in **-Table 1**. There were 26 women (53.1%) and 23 men (46.9%). The median age was  $49 \pm 9$  years (range: 31–69 years) and the mean BMI was  $26.6 \pm 6.3$  kg/m<sup>2</sup> (range: 16.5–46.4 kg/m<sup>2</sup>). The mean tumor size, measured as the maximum transverse tumor diameter, was 16.9 mm (range: 12–28 mm). Over half of the tumors (n = 28 of 49, 57.1%) were under 15 mm in size.



**Fig. 1** Axial heavily T2-weighted sequences demonstrating the spectrum of findings associated with the cisternal components of VS (A–C, arrow), including absence of contact with the ipsilateral middle cerebellar peduncle (arrow, A), contact and mild compression of the ipsilateral middle cerebellar peduncle (B, arrowheads) and moderate compression of the ipsilateral middle cerebellar peduncle (C, arrowheads).



**Fig. 2** Bone spicules on post-operative head CT examinations after retrosigmoid craniectomy for VS resection. A single bone spicule is noted in (A) (arrow) along the posterior margin of the resection cavity, abutting the right flocculus. CT examination of a separate patient (B and C) demonstrated multiple bone spicules along the posterior resection cavity (B, arrow) and contouring the craniectomy site (C, arrow). CT, computed tomography; VS, vestibular schwannoma.



**Fig. 3** Spectrum of imaging findings on post-operative head CT after retrosigmoid craniectomy. Noncontrast CT examinations performed after retrosigmoid craniectomy demonstrating focal subarachnoid hemorrhage in the cerebellopontine angle cistern (A, arrow), distal hemorrhage along the left tentorial leaflet (B, arrow) as well as various degrees of pneumocephalus (moderate in C, arrowheads). CT, computed tomography.

Characteristics	Results (% or range)
Number of patients	49
Age (yrs)	49.1 ± 9.1 (31–69)
Follow-up (yrs)	2.4±0.6 (1.5-3.5)
Gender	
Male	23 (46.9)
Female	26 (53.1)
BMI (kg/m <sup>2</sup> )	26.6±6.3 (16.5-46.4)
Tumor size	
Maximum transverse diameter (mm)	16.9±3.5 (12–28)
0–15 (mm)	28 (57.1)
15.1–25 (mm)	20 (40.9)
Laterality	
Right	22 (44.9)
Tumor location	
IAC dominant	10 (20.4)
CPA dominant	29 (59.2)
IAC = CPA	8 (16.3)
Length of stay (d)	3.0±0.8 (2-5)

**Table 1** Demographics of the study population

Abbreviations: BMI, body mass index; CPA, cerebellopontine angle; IAC, internal auditory canal.

In terms of location, 10 patients (20.4%) had tumors located within the IAC (dominant), 29 had tumors located mostly within the CPA (dominant), and 8 (16.3%) tumors were located in both the IAC and CPA.

Details on the characteristics of headaches are shown in **- Table 2**. Among all patients who completed the survey, 12 (24.5%) patients reported having preoperative headaches. POH developed in 33 patients (67.3%). Among them, nearly half of which resolving within 3 months after surgery (n = 14of 33, 42.4%) and 19 patients had chronic POH that persisted beyond 3 months. Fourteen (28.6%) patients developed POH that lasted more than 12 months. Thirteen patients (42.4%) who experienced POH reported headaches occurring at least daily. The majority of POH lasted less than 4 hours in duration (n = 29 of 33, 87.9%) and most POH required either no treatment (n = 6, 18.2%) or over-the-counter analgesia such as acetaminophen or nonsteroidal anti-inflammatory drugs (NSAIDs) (n = 21, 63.6%). Nearly 80% of all patients (n = 39) reported being able to work despite the presence of headaches.

Compared with patients without persistent POH, those with persistent POH that lasted 3 months or greater were less likely to have brainstem compression by the tumor preoperatively (16.7 vs. 63.3%, p = 0.025), more likely to have areas of hemorrhage distal to the tumor site (36.8 vs. 20.0%, p = 0.04), and consumed higher amount of opioid medications during their hospitalization (53.6 vs. 23.6 mg, p = 0.005; **- Table 3**). Interestingly, the proportion of patients with bone spicules

Characteristics	Results (% or range)
Number of surveys completed	49
Preoperative headache	12 (24.5)
Postoperative headache	33 (67.3)
Duration of headache (mo)	
<1	11 (33.3)
1–3	3 (9.1)
3–6	1 (3.0)
6–12	4 (12.1)
>12	14 (42.4)
Frequency of headache	
Less than once weekly	12 (36.4)
Multiple times per week	7 (21.2)
Daily	10 (30.3)
Multiple times per day	4 (12.1)
Length of headache episode (h)	
<1	10 (30.3)
1-4	19 (57.6)
>4	4 (12.1)
Treatment	
None	6 (18.2)
Over-the-counter medication	21 (63.6)
Narcotic medication	3 (9.1)
Other	3 (9.1)
Able to work	
Yes	39 (79.6)
No	10 (20.4)

**Table 2** Survey results on the characteristics of pre- and postoperative headaches

present within the posterior fossa on the CT scan did not differ significantly between the two groups (42.1 vs. 63.3%, p = 0.167). Furthermore, the amount of bone spicules in the posterior fossa, categorized as either absent (n = 22), minimal (n = 20, defined as having only one visible spicule on CT shown in **~ Fig. 2A**), or moderate (n = 7, defined as having more than one spicule shown in **~ Fig. 2B**, and **C**) also did not correlate with the development of headaches (p = 0.24). Clinical factors including age, gender, BMI, tumor size, and the presence of a history of headaches preoperatively did not differ significantly between the two cohorts. Postoperative CT imaging characteristics, such as the presence of pneumocephalus, craniectomy diameter, and the size of the IAC/petrous bone defect were not significantly different.

Univariate logistic regression analysis was performed to identify clinical and radiographic factors associated with the development of chronic persistent POH (**-Table 4**). Among the variables examined, only the presence of tumor brainstem compression on preoperative MRI was negatively associated

with persistent POH (OR = 0.24, p = 0.03). Increased postoperative use of oxycodone was associated with a higher likelihood of developing chronic POH (OR = 1.03, p = 0.011). Notably, demographic variables (age, gender, and BMI), having a history of headaches, and tumor size were not associated with chronic POH. None of the radiographic findings delineated on postoperative CT, including the presence of bony spicules, pneumocephalus or hemorrhage were associated with an increased likelihood of POH.

A multivariate regression model was developed to adjust for potential confounders (**-Table 5**). The presence of brainstem compression on preoperative MRI was again associated with a lower likelihood of developing chronic POH (OR = 0.21, p = 0.028), whereas postoperative oxycodone use during hospitalization was associated with an increased likelihood of POH (OR=1.023, p=0.045). Notably, the presence of bony spicules within the posterior fossa postoperatively was not associated with POH despite adjusting for other covariates.

# Discussion

In this series, we demonstrated that postcraniotomy headaches occurred in approximately two-thirds of patients undergoing retrosigmoid craniectomy for resection of VS, and less than 40% of patients had persistent headaches lasting for more than 3 months after surgery. The majority of patients with POH required only over-the-counter analgesia medications and were able to work despite their headaches. While bony spicules in the posterior fossa that were large enough to be detected on CT scan were present in over half of the patients (Fig. 2), this was not associated with an increased likelihood of developing POH. Of all the clinical and radiographic factors examined, preoperative brainstem compression by the tumor was found to be protective of POH (Fig. 1), while the amount of opioid medications required during the hospital stay was associated with increased likelihood of POH.

In the literature, the reported prevalence of POH after VS surgery is highly variable. In one study, up to one-third of VS patients reported headaches at 3 months postoperatively; and 16 to 64% reported chronic POH lasting greater than 3 months.<sup>14</sup> Earlier studies published in the 1990s found that after suboccipital craniotomy, 17 to 70% of patients reported POH.<sup>6,8,15,16</sup> Although the incidence of POH typically declines over time, it can persist for years and significantly impact the patient's QOL postoperatively; in a large series of 251 patients followed for an average of 8.9 years, 93 patients (37.1%) still reported headaches. Furthermore, 27 patients (10.7%) reported considerable difficulties with daily living due to POH.<sup>12</sup> Today, the goal of VS management continues to shift from complete tumor excision to preservation of neurologic function. As such, there is an ever-increasing emphasis on identifying the etiology and risk factors for the development of POH, and ultimately reducing its incidence and impact on the QOL.

The suboccipital (retrosigmoid) craniotomy approach is one of the most commonly utilized approaches for resection

Variable	Persistent headache (n = 19)	No persistent headache ( $n = 30$ )	p-Value
Age (y)	$47.0\pm8.5$	$50.5\pm9.3$	0.192
Female n (%)	13 (68.4)	13 (43.3)	0.086
Laterality (right) n (%)	8 (42.1)	14 (46.7)	0.754
BMI (kg/m <sup>2</sup> )	25.9±5.4	27.1±6.8	0.501
Preoperative headache n (%)	4 (21.1)	8 (26.7)	0.656
Preoperative radiographic features			
Transverse tumor size (mm)	$15.8\pm2.6$	17.4±3.8	0.126
Brainstem compression n (%)	5 (16.7)	19 (63.3)	0.025
Trigeminal compression n (%)	6 (31.6)	17 (56.7)	0.159
Dominant JV/TS n (%)	4 (21.1)	12 (40.0)	0.451
Mass effect on TS n (%)	4 (21.1)	8 (26.7)	0.711
Postoperative CT n (%)			
Bone spicules	8 (42.1)	19 (63.3)	0.167
Pneumocephalus	1 (5.3)	5 (16.7)	0.252
Distal hemorrhage	7 (36.8)	6 (20.0)	0.04
Size of craniectomy (cm)	$3.0\pm0.4$	$3.0 \pm 0.4$	0.634
IAC/Petrous bone defect (mm)	$4.4 \pm 1.1$	$4.5 \pm 1.6$	0.841
Cerebellar SDH thickness (mm)	7.0±1.5	6.2±2.4	0.208
In-hospital medication			
Dexamethasone (mg)	2.7±8.2	4.0±9.9	0.646
Fentanyl (µg)	$420.9\pm296.2$	395.5±306.6	0.777
Ondansetron (mg)	37.1±19.5	26.8±18.1	0.068
Oxycodone (mg)	53.6±43.8	23.6±26.4	0.005

**Table 3** Clinical and radiographic factors associated with postoperative persistent headache, defined as patient reportedheadaches lasting 3 months or greater after craniotomy

Abbreviations: BMI, body mass index; CT, computed tomography; IAC, internal auditory canal; JV, internal jugular vein; TS, transverse sinus; SDH, subdural hematoma.

of VS owing to its wide exposure to the posterior fossa and access to tumors in the CPA. Furthermore, it is a hearingpreserving approach useful in patients with VS and serviceable hearing. However, retrosigmoid approaches have been historically associated with a higher incidence of POH when compared with the translabyrinthine or middle cranial fossa approaches. Specifically, the incidence of POH in patients undergoing retrosigmoid craniotomy ranged from 34 to 73%.<sup>6,9,14,15</sup> In contrast, the frequency of POH after translabyrinthine approach is significantly less. In a series of 251 patients undergoing either retrosigmoid or translabyrinthine VS resection, Levo et al found the rate of POH was 42.5% in the retrosigmoid group compared with only 17.3% in the translabyrinthine group. In multivariate analysis, the retrosigmoid surgical approach the most important risk factor linked to severe POH (OR = 3.9, p = 0.026).<sup>12</sup>

To date, numerous studies have been performed to investigate the etiology of POH after retrosigmoid craniotomy. One proposed mechanism of headaches includes adherence of cervical or nuchal musculature to the posterior fossa which has been supported by histologic studies demonstrating the fusion of musculature with dura.<sup>6</sup> Activation of neck muscles could lead to stimulation of dural nociceptive fibers and result in pain in the vertex, frontal, and occipital regions. This is in accordance with anecdotal observations that posttussive headaches are common after retrosigmoid craniotomies. To prevent dural adhesions, technical modifications in wound closure such as using extradural adipose tissue graft have been employed to reduce the incidence of chronic POH.<sup>10</sup> Other techniques included the use of mesh cranioplasty or reintroduction of autologous bone or bone substitutes. However, results from these studies are mixed.<sup>6,8,9,17</sup>

Table 4         Results of univariate analysis of clinical and radiographic factors associated with	h persistent postoperative headaches
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Variable	No persistent headache (n=30)	Persistent headache (n = 19)	OR	95% CI	p-Value
Age (y)	$50.5\pm9.3$	$47.0\pm8.5$	0.96	0.90-1.02	0.191
Female n (%)	13 (43.3)	13 (68.4)	2.83	0.85–9.47	0.091
Laterality right n (%)	14 (46.7)	8 (42.1)	1.20	0.38-3.84	0.755
BMI (kg/m <sup>2</sup> )	27.1±6.8	$25.9\pm5.4$	0.97	0.88-1.07	0.494
Preoperative headache n (%)	8 (26.7)	4 (21.1)	0.73	0.19–2.88	0.657
Preoperative MRI					
Transverse tumor size (mm)	17.4±3.8	$15.8\pm2.6$	0.86	0.70-1.05	0.131
Brainstem compression n (%)	19 (63.3)	5 (26.3)	0.24	0.07-0.87	0.030
Trigeminal compression n (%)	17 (56.7)	6 (31.6)	0.42	0.12-1.43	0.163
Mass effect on TS n (%)	8 (27.5)	4 (21.1)	0.77	0.19-3.08	0.711
Postoperative CT					
Bone spicules n (%)	19 (63.3)	8 (42.1)	0.42	0.12-1.45	0.171
Pneumocephalus n (%)	5 (16.7)	1 (5.3)	0.29	0.03-2.70	0.275
Distal hemorrhage n (%)	6 (20.0)	7 (36.8)	3.47	0.71-17.0	0.125
Size of craniectomy (cm)	$3.0\pm0.4$	$3.0\pm0.4$	0.66	0.13-3.45	0.626
Petrous bone defect (mm)	4.5±1.6	4.4±1.1	0.96	0.62-1.48	0.837
Cerebellar SDH thickness (mm)	$6.2\pm2.4$	$7.0\pm1.5$	1.22	0.90-1.65	0.208
Headache intensity at discharge	2.8 ± 1.7	3.0±2.4	1.09	0.81-1.46	0.557
In-hospital morphine milligram equivalent	$114.5\pm68.3$	$164.6\pm99.0$	1.01	1.00-1.02	0.054
Dexamethasone (mg)	$4.0\pm9.9$	2.7 ± 8.2	1.03	0.99–1.07	0.121
Fentanyl (µg)	$395.5\pm306.6$	$420.9\pm296.2$	1.00	0.99–1.00	0.772
Ondansetron (mg)	$26.8 \pm 18.1$	37.1 ± 19.5	1.03	0.99–1.06	0.076
Oxycodone (mg)	$23.6\pm26.4$	$53.6\pm43.8$	1.03	1.01-1.04	0.011

Abbreviations: BMI, body mass index; CI, confidence interval; CT, computed tomography; MRI, magnetic resonance imaging; OR, odds ratio; TS, transverse sinus; SDH, subdural hematoma.

**Table 5** Results of multivariate regression analysis of prognosticfactors for persistent postcraniotomy headache after retrosigmoidVS resection

Variables	OR	95% CI	p-Value
Brainstem compression	0.206	0.05-0.84	0.028
In-hospital opioid use, MME	1.023	1.00-1.05	0.045

Abbreviations: CI, confidence interval; MME, morphine milligram equivalent; OR, odds ratio.

One of the main technical differences between retrosigmoid and translabyrinthine approaches that may contribute to the propensity of POH development is the presence of bone dust in the posterior fossa (**-Fig. 2**). In the suboccipital approach, drilling of the petrous face of IAC takes place intradurally after the posterior fossa dura is opened. By contrast, drilling during the translabyrinthine and middle fossa approaches is performed prior to opening of the dura. Therefore, any bone dust or spicules generated from drilling could then be dispersed in the subarachnoid space within the posterior fossa and cause meningeal irritation or aseptic meningitis.<sup>6,12,18,19</sup> This theory has been partly supported by several retrospective studies. In one the earliest studies by Catalano et al, 84 patients undergoing retrosigmoid craniotomy were divided into the following three groups: (1) those who underwent standard craniectomy, (2) those who underwent primary cranioplasty after tumor resection, and (3) those who underwent "residue trapping" where Gelfoam pieces were placed intraoperatively to prevent bone dust entry into the CSF cisterns. Patients who had Gelfoam pieces placed to collect bone dust had the lowest incidence of POH (10%) compared with the other groups (64–81%).<sup>8</sup> Jackson et al evaluated whether intradural drilling could lead to POH by comparing patients who underwent VS resection versus patients who underwent retrosigmoid vestibular nerve section where no IAC drilling was required. In this series of over 500 patients, a significantly higher proportion of VS patients experienced POH compared with vestibular nerve section patients (54 vs. 5%, p < 0.01).<sup>11</sup> Nonetheless, the authors did not demonstrate any radiographic evidence of bone dust in the posterior fossa. Schaller and Baumann compared procedural characteristics, laboratory findings of aseptic meningitis, and radiographic findings between patients with and without POH. In the headache group, there was a higher incidence of drilling of the posterior aspect of IAC and the presence of speckled calcification along the brain stem suggestive of bone spicules. However, no statistical significance was provided.<sup>9</sup>

Over the years, microsurgical techniques for retrosigmoid craniotomy have evolved and several measures have been taken to mitigate the risk of bone dust dispersion. These include the use of Gelfoam packings over the CSF cisterns located both superior and inferior to the IAC to prevent bone dust dispersion,<sup>8</sup> the use of fine diamond burrs and copious suction irrigation during drilling to minimize bone spicules and remove bone dust efficiently. In our study, surgical techniques were consistent throughout by the same neurotologist/neurosurgeon team, and no clinical spillage of bone spicules into the posterior fossa was observed intraoperatively. Despite all of these maneuvers, the presence of bony spicules was still identified in 55% of postoperative CT scans as seen from calcifications along the brain stem (Fig. 2). This suggests that microscopic dispersion of bone dust still occurs during IAC drilling. Nonetheless, the presence of bony spicules was not associated with a higher incidence of POH even when confounding covariates are taken into account. In the future, the development and refinement of novel technologies, such as ultrasonic bone aspirators, may become a useful tool in further facilitating the removal of bone granules during intradural drilling compared with a standard otologic drill.<sup>19</sup>

In the literature, other demographic and clinical factors implicated in the development of POH included patient age and tumor size. Specifically, some studies have shown that younger patients under 65 years of age were far more likely to develop POH compared with those older than 65 years.<sup>20</sup> In an Acoustic Neuroma Association survey of over 1,600 VS patients, those who younger than 55 were three times more likely to report a more severe POH than those greater than 75 years of age and consider POH as a significant morbidity.<sup>2</sup> Several studies have also found an inverse relationship between tumor size and the development of POH. Schaller and Baumann examined 155 patients who underwent retrosigmoid resection of VS and had headaches at 3 months after surgery.<sup>9</sup> When patients with headaches were compared with those without, those with chronic POH tended to

have smaller diameter tumors. In a retrospective survey study of 192 patients, 64% of patients developed POH and over half of whom had persistent POH at a mean follow-up of 5 years. Tumor size was found to be significantly smaller in the group without POH in multivariate analysis after accounting for age, gender, and existence of preoperative headaches.<sup>14</sup>

We identified, for the first time, preoperative brainstem compression by the tumor may be a protective factor for the development of POH ( $\succ$  Fig. 1). The precise mechanism by which this occurs is not clear and further investigations are certainly needed. It is possible that preoperative brainstem compression may have provided "conditioning" for the brain to tolerate tumor-related mass effects and resulted in a reduced likelihood of postoperative obstruction of CSF outflow. Given the small sample size in the series, validation of this finding in larger cohorts is warranted. Future work is needed to quantify the degree of brainstem compression and correlate with the development and severity of POH. Furthermore, we found that the amount of opioid medications required during a patient's hospitalization was associated with the development of POH. This information may be useful in counseling patients regarding their recovery and likelihood of developing POH over time.

## Limitations

This study has several limitations. Due to its retrospective nature, there is limited ability to adjust for unknown confounders. Follow-up time is relatively short; longer duration of observation and follow-up may provide additional data on the chronicity and progression of POH. Only one CT scan obtained on postoperative day 1 was available which limits the evaluation of the ultimate fate of these bone spicules, especially in the subset of patients whose POH persist. Subsequent CT scans may be useful in the future to serially assess the location of bony spicules in these patients. Although other survey-based studies have identified similar trends in POH and large-scale surveys have been conducted by the Acoustic Neuroma Association, the use of a survey instrument may suffer from recall bias.<sup>2</sup> Objective data, such as the incidence of narcotic use over time and QOL questionnaires, may help validate our findings. Future investigations could utilize a multi-institutional cohort in a prospective study design where preoperative and POH and other morbidities could be completed in a systematic manner.

## Conclusion

In summary, we demonstrated that although POH occur frequently after retrosigmoid craniotomy, few patients are debilitated by it and most POH are well controlled with overthe-counter medications. Posterior fossa bone spicule is a common radiographic finding observed in over half of the patients. However, the presence of posterior fossa bone spicules detectable on CT is not associated with the development of chronic POH after VS resection via the retrosigmoid approach.

#### **Previous Presentations**

This study was presented as a poster at the 154th American Otological Society Annual Virtual Spring Meeting on April 2021.

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Conflict of Interest

None declared.

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