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Reliability of clinical diagnosis of masses of the cerebellopontine angle: A retrospective multi-institutional study

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A B S T R A C T

Objectives: To assess the accuracy of pre-operative diagnosis of masses of the cerebellopontine angle (CPA) when compared to surgical pathology.
Design: Retrospective chart review.
Participants: Patients who underwent surgery for CPA masses at two tertiary care institutions from 2007 to 2017.
Main outcome measures: Percent concordance between pre-operative and surgical pathologic diagnosis; sensitivity, specificity, positive predictive value, and negative predictive value for predicted diagnoses.
Results: Concordance between pre-operative diagnosis and surgical pathology was 93.2% in 411 sampled patients. Concordance was 57.9% for masses other than vestibular schwannoma. Prediction of vestibular schwannoma and meningioma had high positive (0.95 and 0.97, respectively) and negative (0.76 and 0.99, respectively) predictive values. Prediction of facial neuroma had sensitivity of 0.13 and positive predictive value of 0.25. Headache ($p = 0.001$) and facial weakness ($p = 0.003$) were significantly associated with different pathologic profiles. Hearing loss was associated with differences in diagnostic prediction ($p = 0.02$) but not with differences in surgical pathology ($p > 0.05$).
Conclusions: Comparison between pre-operative predicted diagnosis and surgical pathology for cerebellopontine angle masses is presented. Vestibular schwannoma and meningioma were effectively identified while rarer CPA masses including facial neuroma were rarely identified correctly. Clinicians caring for patients with CPA masses should be mindful of diagnostic uncertainty which may lead to changes in treatment plan or prognosis.

1. Introduction

Approximately 10% of intracranial tumors arise in the cerebellopontine angle (CPA) and 80% of these are vestibular schwannomas [1,2]. The majority of the remaining 20% are meningiomas, with rare incidence of facial or trigeminal schwannomas, epidermoid cysts (primary cholesteatomas), glomus jugulare tumors, arachnoid cysts, giant cell tumors, metastatic deposits, and other masses [3]. Each of these masses requires specialized treatment and carries a unique prognostic profile. Therefore, clinical differentiation between masses of the CPA is critical for optimal treatment planning [4].

While surgical pathology is the diagnostic gold standard, clinical and radiologic features help differentiate between CPA masses. Magnetic resonance imaging (MRI) is the most powerful noninvasive diagnostic tool for this purpose, and many CPA masses have distinct classic MRI features which may help with identification [5–8]. Patient demographics, medical history, and presenting symptoms can also be helpful in predicting tumor pathology. However, no imaging modality or array of clinical features correlates perfectly with any diagnosis.

The purpose of this study was to evaluate the accuracy of pre-operative diagnostic predictions of CPA mass pathology compared with surgical pathology. As the majority of CPA masses are vestibular schwannomas, focus was directed toward prediction of other diagnoses. This work informs treatment planning and helps establish realistic expectations for physicians and patients.

2. Methods

2.1. Ethical considerations

All data in this study were anonymized in compliance with the Health Insurance Portability and Accountability Act of 1996. This work was approved by the Yale University School of Medicine and Providence-Providence Park Hospital Internal Review Boards.

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2.2. Patient selection

Patients were identified by searching records of the Yale-New Haven Health System (New Haven, CT, USA) and the Michigan Ear Institute (Farmington Hills, MI, USA) for patients seen in otology clinics with ICD-10 code D33.3 or ICD-9 code 225.1 ("benign neoplasm of cranial nerves") between 2010 and 2017. Records were individually examined and excluded if masses were not located in the CPA or if surgical pathology was not available. Patients who already had a known diagnosis or had previously undergone treatment for a CPA mass were also excluded.

2.3. Pathologic prediction and surgical pathology

Records were examined for predicted tumor pathology. An unambiguous or probable diagnosis documented at any pre-operative visit (for example, "vestibular schwannoma" or "CPA mass, likely vestibular schwannoma") was evaluated as a prediction of that diagnosis. Cases without any prediction, uncertain predictions, or predictions of multiple diagnoses (for example, "vestibular schwannoma vs. meningioma") were evaluated as an unknown preoperative diagnosis. Surgical pathology was determined based on review by a board-certified pathologist. Discrimination between schwannomas by neural origin (vestibular, facial, trigeminal, etc.) was based on intraoperative findings.

2.4. Other collected variables

Cases were examined for demographic, clinical, and surgical characteristics. Demographics included age at presentation and gender. Clinical characteristics included tumor laterality, tumor volume in cubic centimeters, and presenting symptoms, including facial weakness, facial numbness or trigeminal neuralgia, vertigo, headache, and hearing loss and/or tinnitus. Tumor volume was based on pre-operative imaging, when available, and was estimated by using the formula $0.5 \times L \times W \times H$, where L, W, and H are the greatest length, width, and height of the tumor, respectively [9]. Facial weakness was evaluated using the House-Brackmann scale [10] and was considered present for any scale value > 1. Hearing loss and/or tinnitus were evaluated as "present" or "absent."

2.5. Data analysis

All analysis was performed using SPSS Statistical Software for Windows (IBM, Armonk, NY, USA). Concordance between pre-operative diagnosis and surgical pathology was measured as a percentage. For each pre-operatively predicted diagnosis present in the sample, sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were calculated for matching surgical pathology. Statistical significance between categorical variables was determined using the chi-squared test. Significance was set at $p < 0.05$.

3. Results

A total of 411 patients met inclusion criteria with diagnoses by one of eleven board-certified neurotologic surgeons. Characteristics of the patient sample are shown in Table 1. Average age was 53.1 years and 55.7% of patients were female. Vestibular schwannoma was the most common predicted and actual diagnosis, accounting for over 90% of each group. Other diagnoses included meningioma, facial neuroma, epidermoid cyst, trigeminal neuroma, and endolymphatic sac tumor. No preoperative diagnosis was documented in 11 cases (2.7%).

Comparison of predicted and surgical pathology is shown in Table 2. Overall concordance was 93.2%, and 96.5% of predicted diagnoses of vestibular schwannoma were confirmed on surgical pathology. Concordance between predicted and actual diagnosis for non-vestibular schwannoma masses was 57.9%. Measures of prediction accuracy are shown in Table 3. Prediction of vestibular schwannoma and meningioma had high positive (0.95 and 0.97, respectively) and negative (0.76 and 0.99, respectively) predictive values, while prediction of facial neuroma had a sensitivity of 0.13 and a positive predictive value of 0.25. While the majority of vestibular schwannomas and meningiomas were correctly identified, identification of facial neuromas was unreliable with 1 correct identification, 3 false positives and 7 false negatives.

Associations between presenting symptoms and expected and final surgical pathology are shown in Table 4 and Table 5. Hearing loss, vertigo, facial numbness, and facial weakness were all significantly associated with differences in predicted pathology ($p < 0.05$). However, only headache ($p = 0.001$) and facial weakness ($p = 0.003$) were associated with differences in actual surgical pathology. No patients with facial neuroma presented with facial weakness. Headache was present in each of the single patients with trigeminal neuroma and endolymphatic sac tumor.

Table 1
Demographic, disease, and surgical characteristics of patient sample.

Characteristic	% (n = 411)
Age	
< 40	16.8
40–59	50.9
60–79	31.6
≥80	0.7
Gender	
Male	44.3
Female	55.7
Side	
Right	52.6
Left	47.4
Presenting symptoms	
Hearing loss/tinnitus	70.1
Facial weakness	5.6
Headache	12.4
Vertigo	55.5
Facial numbness/neuralgia	13.6
Tumor volume (cm^3)	
< 0.5	21.7
0.5–1.9	17.5
2.0–4.9	15.8
> 5.0	24.3
Unknown	20.7
Predicted pathology	
Vestibular schwannoma	91.0
Meningioma	4.9
Facial neuroma	1.0
Epidermoid	0.5
Unknown	2.7
Surgical pathology	
Vestibular schwannoma	90.8
Meningioma	5.8
Facial neuroma	1.9
Epidermoid	1.0
Trigeminal neuroma	0.2
Endolymphatic sac tumor	0.2

4. Discussion

4.1. Novel findings and clinical applicability

Surgery of the cerebellopontine angle carries significant morbidity, with risk of cerebrospinal fluid leak, meningitis, facial paralysis, possible or implicit hearing and vestibular loss, and death [11,12]. In addition, the vast majority of CPA masses are benign and slow-growing. As a result, many physicians and patients opt for nonsurgical

Table 2
Predicted pathology vs. final surgical pathology. Data given as number of patients (percent). Percentages are of patients with a predicted tumor pathology, by row. Shaded cells represent correct predictions. VS, vestibular schwannoma; ELS, endolymphatic sac.

Predicted pathology	Surgical pathology					
	VS	Meningioma	Facial neuroma	Epidermoid	Trigeminal neuroma	ELS tumor
VS	361 (96.5)	4 (1.1)	7 (1.9)	1 (0.3)	1 (0.3)	0 (0.0)
Meningioma	1 (5.0)	19 (95.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Facial neuroma	2 (50.0)	0 (0.0)	1 (25.0)	1 (25.0)	0 (0.0)	0 (0.0)
Epidermoid	0 (0.0)	0 (0.0)	0 (0.0)	2 (100.0)	0 (0.0)	0 (0.0)
Unknown	9 (81.8)	1 (9.1)	0 (0.0)	0 (0.0)	0 (0.0)	1 (9.1)

Table 3
Measures of test accuracy for pre-operative diagnoses. PPV, positive predictive value; NPV, negative predictive value. VS, vestibular schwannoma. Trigeminal neuroma and endolymphatic sac tumor were not predicted and are excluded.

Predicted pathology	Sensitivity	Specificity	PPV	NPV
VS	0.97	0.65	0.97	0.76
Meningioma	0.79	1.00	0.95	0.99
Facial neuroma	0.13	0.99	0.25	0.98
Epidermoid	0.50	1.00	1.00	1.00

Table 4
Symptoms at presentation by expected pathology. Data given as number of patients (percent of patients with expected diagnosis), by row. Bold numbers indicate statistical significance. VS, vestibular schwannoma.

Expected pathology	Symptoms				
	Hearing loss/ tinnitus	Vertigo	Headache	Facial numbness/ neuralgia	Facial weakness
VS	272 (72.7)	211 (56.4)	44 (11.8)	50 (13.4)	14 (3.7)
Meningioma	11 (55.0)	13 (65.0)	3 (15.0)	1 (5.0)	0 (0.0)
Facial neuroma	1 (25.0)	0 (0.0)	1 (25.0)	1 (25.0)	1 (25.0)
Epidermoid	0 (0.0)	0 (0.0)	0 (0.0)	2 (100.0)	0 (0.0)
Unknown	7 (63.9)	4 (36.4)	3 (27.3)	2 (18.2)	2 (18.2)
p value	**0.02**	**0.04**	> 0.05	**0.006**	**0.03**

Table 5
Symptoms at presentation by final surgical pathology. Data given as number of patients (percent of patients with pathologic diagnosis), by row. Bold numbers indicate statistical significance. VS, vestibular schwannoma; ELS, endolymphatic sac.

Surgical pathology	Symptoms				
	Hearing loss/ tinnitus	Vertigo	Headache	Facial numbness/ neuralgia	Facial weakness
VS	270 (72.4)	207 (55.5)	43 (11.5)	53 (14.3)	12 (3.2)
Meningioma	14 (58.3)	15 (62.5)	3 (12.5)	1 (4.2)	0 (0.0)
Facial neuroma	5 (62.5)	5 (62.5)	3 (37.5)	0 (0.0)	0 (0.0)
Epidermoid	1 (25.0)	0 (0.0)	0 (0.0)	2 (50.0)	1 (25.0)
Trigeminal neuroma	0 (0.0)	1 (100.0)	1 (100.0)	0 (0.0)	0 (0.0)
ELS tumor	1 (100.0)	0 (0.0)	1 (100.0)	0 (0.0)	1 (100.0)
p value	> 0.05	> 0.05	**0.001**	> 0.05	**0.003**

management, including observation or stereotactic radiosurgery [13]. While these options are successful in appropriate patient populations, they require a high degree of diagnostic certainty based on available clinical data. Vestibular schwannoma, meningioma, and facial neuroma can all be treated with surgical resection, stereotactic radiosurgery or observation in appropriate clinical settings, however the expected responses and progression of symptoms vary [14,15]. A suspected diagnosis of meningioma affects surgical planning [16], and surgical excision or stereotactic radiosurgery for facial neuromas often results in facial palsy [17] which is not expected with these treatment modalities for vestibular schwannomas [18]. Epidermoid cysts do not respond to stereotactic radiosurgery and resection is frequently complicated by cranial neuropathy [19]. Therefore, accurate prediction of CPA tumor pathology has significance for treatment planning and prognostication.

In this study, overall concordance between predicted and actual diagnosis was high at 93.2%, while concordance for non-vestibular schwannoma diagnoses was lower at 57.9%. Therefore, 42% of patients with meningioma or other, rarer tumors of the CPA were initially either not diagnosed or misdiagnosed. Predicted diagnoses were based on a combination of radiologic and clinical features. Radiologic findings are the most powerful data used to distinguish masses of the CPA. On MRI imaging, vestibular schwannomas are typically T1 isointense and T2 hyperintense with intense enhancement on post-contrast images. They may be homogenous, heterogeneous, or cystic in appearance [20] and can exhibit a layer of fluid between the lateral tumor aspect and the fundus of the internal auditory canal [21]. Facial neuroma can be seen as an enlargement of the facial nerve but is highly variable in appearance [22]. They are similar in composition to vestibular schwannomas and therefore may be difficult to distinguish radiologically. In comparison, meningiomas are typically T1 and T2 isointense with gadolinium contrast enhancement, along with enhancement of the surrounding dura and typically without IAC widening [5,7]. Epidermoid cysts and arachnoid cysts are irregular, typically T1 hypointense and T2 hyperintense lesions which mimic fluid-filled cysts, and tend to encase cisternal nerves and vessels rather than displacing them. While epidermoid cysts are hyperintense on FLAIR and diffusion-weighted imaging (DWI), arachnoid cysts are FLAIR and DWI suppressed. Solitary metastatic deposits to the CPA have been reported many years after diagnosis and treatment of primary malignancy [23]. These masses are highly variable in appearance and prognostic consequences of misdiagnosis are severe [6]. Computed tomography (CT) imaging is also occasionally employed in the evaluation of CPA tumors. Although less discriminatory for soft tissue, CT imaging is very sensitive for bony changes which may be seen in certain pathologies, including endolymphatic sac tumors or metastatic deposits [24]. Importantly, none of these findings is perfectly sensitive and specific, leading to diagnostic uncertainty [6,8].

While clinical features may give additional diagnostic clues, CPA masses are very difficult to distinguish based on clinical presentation [25]. Some authors report a lower incidence of hearing and balance dysfunction among tumors other than vestibular schwannoma, although these symptoms remain common [3,16]. This belief may affect diagnostic prediction: while the presence of hearing loss or tinnitus was statistically significantly associated with predicted diagnosis in the present work (favoring vestibular schwannoma), it was not statistically significantly associated with actual surgical pathology, suggesting that clinicians may be overestimating its diagnostic importance. Four of 5 (80%) patients with facial neuromas and 3 of 14 (21%) patients with meningiomas who presented with hearing loss or tinnitus were initially misdiagnosed with vestibular schwannomas. Facial weakness was associated with certain non-schwannoma diagnoses, and interestingly,

facial neuromas were not associated with facial weakness in this sample. Likewise, headache was associated with unusual masses including facial and trigeminal neuroma and endolymphatic sac tumor. While sample sizes for these uncommon masses were very small in this study, headache or facial weakness to an unusual degree may warrant concern for these diagnoses.

4.2. Strengths and limitations

To our knowledge, this work represents the only evaluation of the accuracy of clinical diagnosis of CPA tumors to date. This work establishes the confidence with which providers caring for these patients can proceed with treatment planning and prognostication based on imaging and clinical findings. This was executed with a large sample size consistent in demographic, clinical and tumor characteristics with previous large series, suggesting generalizability [26]. However, several limitations of this study should be addressed. Masses of the CPA other than vestibular schwannomas are rare, and evaluation of rarer CPA masses requires larger multi-institutional review. While this study included eleven neurotologic surgeons at two institutions, it may not perfectly represent the neurotologic community as a whole. This sample only included patients who underwent surgery to ensure availability of surgical pathology, so it likely sampled patients of younger age and with larger tumors than the overall population of patients with CPA masses. Finally, information about the specific decision-making leading to predicted diagnosis was not available, so the independent contributions of imaging and clinical data are unknown.

5. Conclusions

A comparison of pre-operative predicted diagnosis and surgical pathology for cerebellopontine angle tumors is presented. Overall concordance between pre-operative and actual diagnoses was 93.2%. Concordance fell to 57.9% when examining tumors other than vestibular schwannoma. While vestibular schwannoma and meningioma were usually correctly identified, predictive ability was poor for rarer CPA masses including facial neuroma. Clinicians caring for these patients should be mindful of diagnostic uncertainty which may lead to changes in treatment plan or prognosis.

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Disclosures/conflicts of interest

None.

References

[1] Nikolopoulos TP, Fortnum H, O'Donoghue G, et al. Acoustic neuroma growth: a systematic review of the evidence. Otol Neurotol 2010;31:478–85.
[2] Springborg JB, Poulsgaard L, Thomsen J. Nonvestibular schwannoma tumors in the cerebellopontine angle: a structured approach and management guidelines. Skull Base 2008;18:217–27.
[3] Moffat DA, Ballagh RH. Rare tumours of the cerebellopontine angle. Clin Oncol (R Coll Radiol) 1995;7:28–41.
[4] Friedmann DR, Grobelny B, Golfinos JG, et al. Nonschwannoma tumors of the cerebellopontine angle. Otolaryngol Clin North Am 2015;48:461–75.
[5] Carlson ML, Van Abel KM, Driscoll CL, et al. Magnetic resonance imaging surveillance following vestibular schwannoma resection. Laryngoscope 2012;122:378–88.
[6] Farid N. Imaging of vestibular schwannoma and other cerebellopontine angle tumors. Oper Tech Otolaryngol Head Neck Surg 2014;25:87–95.
[7] Saloner D, Uzelac A, Hetts S, et al. Modern meningioma imaging techniques. J Neurooncol 2010;99:333–40.
[8] Guermazi A, Lafitte F, Miaux Y, et al. The dural tail sign–beyond meningioma. Clin Radiol 2005;60:171–88.
[9] Monga SP, Wadleigh R, Sharma A, et al. Intratumoral therapy of cisplatin/epinephrine injectable gel for palliation in patients with obstructive esophageal cancer. Am J Clin Oncol 2000;23:386–92.
[10] Yen TL, Driscoll CL, Lalwani AK. Significance of House-Brackmann facial nerve grading global score in the setting of differential facial nerve function. Otol Neurotol 2003;24:118–22.
[11] Becker SS, Jackler RK, Pitts LH. Cerebrospinal fluid leak after acoustic neuroma surgery: a comparison of the translabyrinthine, middle fossa, and retrosigmoid approaches. Otol Neurotol 2003;24:107–12.
[12] Sanna M, Taibah A, Russo A, et al. Perioperative complications in acoustic neuroma (vestibular schwannoma) surgery. Otol Neurotol 2004;25:379–86.
[13] Smouha EE, Yoo M, Mohr K, et al. Conservative management of acoustic neuroma: a meta-analysis and proposed treatment algorithm. Laryngoscope 2005;115:450–4.
[14] DiBiase SJ, Kwok Y, Yovino S, et al. Factors predicting local tumor control after gamma knife stereotactic radiosurgery for benign intracranial meningiomas. Int J Radiat Oncol Biol Phys 2004;60:1515–9.
[15] McRackan TR, Wilkinson EP, Brackmann DE, et al. Stereotactic radiosurgery for facial nerve schwannomas: meta-analysis and clinical review. Otol Neurotol 2015;36:393–8.
[16] Voss NF, Vrionis FD, Heilman CB, et al. Meningiomas of the cerebellopontine angle. Surg Neurol 2000;53:439–46. [discussion 46–7].
[17] Angeli SI, Brackmann DE. Is surgical excision of facial nerve schwannomas always indicated? Otolaryngol Head Neck Surg 1997;117:S144–7.
[18] Brackmann DE, Cullen RD, Fisher LM. Facial nerve function after translabyrinthine vestibular schwannoma surgery. Otolaryngol Head Neck Surg 2007;136:773–7.
[19] Safavi-Abbasi S, Di Rocco F, Bambakidis N, et al. Has management of epidermoid tumors of the cerebellopontine angle improved? A surgical synopsis of the past and present. Skull Base 2008;18:85–98.
[20] Charabi S, Tos M, Thomsen J, et al. Cystic vestibular schwannoma–clinical and experimental studies. Acta Otolaryngol Suppl 2000;543:11–3.
[21] Goddard JC, Schwartz MS, Friedman RA. Fundal fluid as a predictor of hearing preservation in the middle cranial fossa approach for vestibular schwannoma. Otol Neurotol 2010;31:1128–34.
[22] Wiggins 3rd RH, Harnsberger HR, Salzman KL, et al. The many faces of facial nerve schwannoma. AJNR Am J Neuroradiol 2006;27:694–9.
[23] Yuh WT, Mayr-Yuh NA, Koci TM, et al. Metastatic lesions involving the cerebellopontine angle. AJNR Am J Neuroradiol 1993;14:99–106.
[24] Luff DA, Simmons M, Malik T, et al. Endolymphatic sac tumours. J Laryngol Otol 2002;116:398–401.
[25] Lalwani AK. Meningiomas, epidermoids, and other nonacoustic tumors of the cerebellopontine angle. Otolaryngol Clin North Am 1992;25:707–28.
[26] Brackmann DE, Bartels LJ. Rare tumors of the cerebellopontine angle. Otolaryngol Head Neck Surg 1979;1980(88):555–9.