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Hearing recovery after surgical resection of non-vestibular schwannoma cerebellopontine angle tumors

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1 Hearing recovery after surgical resection
2 of non-vestibular schwannoma
3 cerebellopontine angle tumors

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6
7

8 **Abstract**

9 **Purpose:** Post-operative outcomes for hearing after resection surgery to remove cerebellopontine angle (CPA) tumors other
10 than vestibular schwannomas (VS) are not well understood. This study presents a series of patients with significant post-
11 operative hearing recovery, trying to define the incidence among all patients operated on for removal of non-VS CPA tumors.

12 **Methods:** This is a retrospective observational case series of 8 patients among 69 operated on for removal of non-VS CPA
13 tumors between 2012 and 2020. All patients had pre- and post-operative hearing measurement with pure-tone average (PTA)
14 and speech discrimination score (SDS), according to the American Academy of Otolaryngology-Head and Neck Surgery
15 recommendations, auditory brainstem response (ABR) measurements and imaging.

16 **Results:** Six meningiomas and two lower cranial nerve schwannomas operated on with a retrosigmoid approach were
17 included for analysis. The mean pre-operative PTA and SDS were 58 ± 20.7 dB and $13\pm 17.5\%$, respectively. All patients had
18 pre-operative class D hearing and asynchronous ABRs. They all showed significant hearing recovery, with an improvement
19 of 36 ± 22.2 dB ($p=0.0025$) and $85\pm 16.9\%$ ($p=0.0001$) in PTA and SDS, respectively, with mean follow-up of 21 ± 23.5 months.
20 Seven patients recovered to a class A hearing level and one patient to class B. The ABRs became synchronous for three
21 patients. The incidence of auditory recovery was 13% for patients operated on with a conservative approach ($n=60$).

22 **Conclusion:** A significant post-operative improvement in hearing could be a reasonable expectation in non-VS tumors
23 extending into the CPA and a retrosigmoid approach should always be considered regardless of pre-operative hearing status.

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37 **Introduction**

38 The most common cerebellopontine angle (CPA) tumor is vestibular schwannoma (VS) which represents approximately 6%
39 of all intracranial [1] and 91% of CPA tumors [2]. Meningiomas are the second most common tumors of the CPA affecting
40 6% to 15% of patients [2]. Lower cranial nerve and trigeminal schwannomas are rare lesions and represent 0.7% and 1% of
41 CPA tumors, respectively [3].

42 Regardless of the tumor histology, hearing loss is one of the most common symptoms of CPA tumors [4–7]. To date, when
43 there is an indication for surgical treatment of these tumors, the choice of surgical approach is guided by the tumor size,
44 growth, location and hearing level [7, 8]. Although preservation of facial nerve function is still the main goal of surgery,
45 hearing preservation should be considered whenever possible [5, 6, 8, 9].

46 Apart from VS, where hearing preservation was obtained in 43% of patients in a large series [10] and significant hearing
47 recovery is not an expectable result, hearing recovery could be a reasonable expectation in non-VS CPA tumors since the
48 they arise outside the acoustic-facial bundle. Up to now, only a few case reports have been published on hearing recovery
49 after surgical resection of non-VS CPA tumors [4, 7, 11–15].

50 In this study, we evaluated the hearing results in non-VS CPA tumors with particular regard to those patients who had
51 significant hearing recovery, trying to analyze the incidence of such events and the possible surgical implications.

52
53 **Materials and methods**

54 This article follows the STROBE (STrengthening the Reporting of OBservational studies in Epidemiology) [16] guidelines
55 for the reporting of observational studies.

56
57 ***Study population***

58 This monocentric retrospective study, conducted in a tertiary referral center, included patients who experienced significant
59 hearing recovery after non-VS CPA tumor removal through a retrosigmoid approach between 2012 and 2020. All patients
60 gave their informed consent for the use of their clinical data. The study complied with Public Health code (CNIL #2211758).

61 The inclusion criterion was a post-operative hearing improvement of more than 30 dB in pure-tone audiometry (PTA) and/or
62 a 50% gain in the speech discrimination score (SDS).

63 Exclusion criteria were neurofibromatosis type II (NF2) related tumors, meningiomatosis, pseudotumors of the CPA
64 (arachnoid and epidermoid cysts), tumors of the central nervous system extending to the CPA (pilocytic astrocytoma, choroid
65 plexus papilloma, ependymoma, ganglioglioma) and revision surgical procedures.

66

67 *Pre-operative assessment*

68 Before surgery, all patients underwent a clinical examination (facial nerve function was evaluated according to the House-
69 Brackmann (HB) grading system [17]), hearing assessment and neuroradiological examinations (high-resolution computed
70 tomography and magnetic resonance imaging [MRI]).

71

72 *Audiometric tests*

73 All patients were evaluated before surgery and post-operatively (at 1 month and at the last visit) by the same audiologist
74 using similar testing equipment and procedures (pure-tone and monosyllabic speech audiometry). Audiometric data included
75 PTA, calculated as the mean of the thresholds at frequencies of 0.5, 1, 2 and 3 kHz and SDS, calculated using a standardized
76 presentation up to 40 dB sensation level or maximum comfortable loudness (whichever was lower). The differences between
77 pre- and post-operative PTA and SDS were calculated (respectively Δ PTA and Δ SDS). Hearing function was graded
78 according to the American Academy of Otolaryngology – Head and Neck Surgery (AAO-HNS) guidelines: **Class A:** PTA \leq 30
79 dB and SDS \geq 70%; **Class B:** PTA $>$ 30 dB and \leq 50 dB and SDS \geq 50%; **Class C:** PTA $>$ 50 dB and SDS \geq 50%; **Class D:** PTA
80 any level and SDS $<$ 50%) [18]. Hearing recovery was defined as described above corresponding to a change in the AAO-
81 HNS hearing class from non-useful (Class D) to useful or normal hearing (Class A and B).

82 Pre-operative and post-operative auditory brainstem responses (ABR) using click were collected. Five waves (I-V) were
83 recorded in the first 10 ms after broad-band and high-intensity stimuli. Three 90 dB acquisitions were made, followed by a
84 decrease by 10 dB ranging up to the hearing threshold. **ABR were classified as: Synchronous: reproducible ABR waves in
85 three 90 dB stimulations and good visualization of wave V which decreased in intensity and increased in latency with
86 decreasing stimulus intensity; Augmented inter-peak latency: good visualization of the ABR waves, but with a I-V inter-peak
87 interval in the homolateral ear increasing by more than 0.5 ms compared to the contralateral ear; or Asynchronous: no
88 visualization of a reproducible wave V, even at high-intensity stimulation. A detailed analysis of ABR curves has been carried
89 out.**

90

91 *Tumor imaging*

92 Pre-operative MRI allowed morphological characterization of the tumors for diagnostic orientation, measurement of their
93 sizes and analysis of the acoustic-facial bundle position. The MRI protocol included at least a high-resolution 3D T2-weighted
94 image (wi) to analyze the position of the acoustic-facial bundle and a 3D T1-wi after gadolinium chelate injection, allowing
95 tumor characterization and measurements of tumor size in three axial directions (anterior-posterior, medio-lateral and
96 superior-inferior). Brainstem displacement with or without mass effect in the fourth ventricle was collected. Meningiomas

97 were classified according to the modified Desgeorges and Sterkers classification: Posterior petrous (P); Meatus and auditory
98 canal invasion (M); Anterior petrous (A); Anterior petrous and meatus (AM); Posterior petrous and meatus (MP), and anterior
99 and posterior petrous but also meatus (AMP) [19].

100

101 *Surgery*

102 We used two classifications usually used for VS. The quality of resection was classified following the Monfared classification
103 as gross-total resection (no tumor remnant was visible at the end of surgery), near-total resection (the tumor remnant measured
104 less than 5x5x2 mm over the brainstem and the facial nerve) or sub-total resection (the tumor was resected 80% to 90% by
105 volume and 60% to 70% by surface area) [20]. The Jackler classification was used to describe the acoustic-facial bundle
106 position with regard to the tumor: **Facial nerve course pattern I:** anterior-inferior shift of the VII-VIII bundle; **Facial nerve**
107 **course pattern II:** anterior shift of the VII-VIII bundle; **Facial nerve course pattern III:** superior shift of the VII-VIII
108 bundle; **Facial nerve course pattern IV:** posterior shift of the VII-VIII bundle [21, 22].

109 The anatomopathological results were listed, and the meningiomas were graded from I to III according to the World Health
110 Organization (WHO) classification (2007 or 2016).

111

112

113 *Post-operative assessment*

114 Complications of surgery were assessed. Post-operative facial (HB) and lower cranial nerve functions were evaluated at the
115 last follow-up. Audiometric tests and ABRs were performed at the last visit.

116

117 *Statistical analysis*

118 Results are presented as mean \pm SD for continuous variables and as numbers and percentages for categorical variables.
119 Statistical analysis was performed using Prism (GraphPad Software, San Diego, CA, USA). The pre-operative and post-
120 operative audiological results were compared using two-way ANOVA and Mann–Whitney tests. Differences between groups
121 were considered to be significant for $p \leq 0.05$.

122

123 Results

124 *Patients*

125 Among 99 patients operated on between December 2012 and January 2020 for non-VS CPA tumors, 69 were eligible for this
126 study, from whom 60 were operated on with a retrosigmoid approach (**Fig. 1**). A significant post-operative hearing recovery

127 was found in eight patients who were included in this study, representing 13.3% (8/60) of all non-VS CPA tumors operated
128 on with a conservative approach. Patient characteristics for inclusion are detailed in the flow chart (**Fig. 1**).
129

130 *Baseline characteristics*

131 Baseline characteristics of the 8 patients with hearing recovery are described in Table 1. Their mean age was 58 ± 9.9 years
132 [40–72 years]. The right side was involved in half of the cases. One patient had pre-operative grade II HB facial nerve
133 function. All patients had a significant degree of pre-operative hearing loss. For all patients but one, who had a sudden hearing
134 loss which was unresolved after 5 days of corticosteroid therapy, the hearing loss was progressive, with an average evolution
135 of 1 year. Patients were not premedicated with steroids or other drugs in the pre-operative period.

136 Tinnitus and balance disorder were present in one and four cases, respectively. Two patients were experiencing hemifacial
137 hypoesthesia. Regarding lower cranial nerve function, one patient, affected by a lower cranial nerve schwannoma, had a X
138 and XI palsy. One of the patients had morning headaches suggesting early intracranial hypertension.

139

140 *Pre-operative assessment*

141 *Hearing*

142 Complete audiological data were available for all eight patients (Table 1). The mean pre-operative PTA was 58 ± 20.7 dB and
143 SDS was $13\pm 17.5\%$. All patients presented with class D hearing. ABR were asynchronous for all patients, **but in 3 patients,**
144 **we identified the isolated presence of wave I at 90 dB stimulation.**

145

146 *Imaging*

147 In all cases, the pre-operative MRI allowed a correct diagnosis of tumor histology. The mean tumoral measurements in the
148 three axial directions were 32 ± 5.8 mm, 28 ± 6.9 mm, and 31 ± 5.0 mm for anterior-posterior, medio-lateral and superior-inferior
149 diameters, respectively.

150 Six patients had a significant brainstem compression (**Fig. 2**), four with and two without fourth ventricle
151 displacement/compression. No hydrocephalus was observed pre-operatively. Four patients showed internal auditory canal
152 invasion.

153 Regarding the displacement of the acoustic-facial bundle, in two cases, an anterior course was observed, while it was anterior-
154 superior in two cases, superior in two others and no nerve deviation and posterior-inferior switch in the two remaining
155 patients.

156

157 **Surgery**

158 All patients were operated on with a retrosigmoid approach using a continuous facial nerve monitoring system (NIM3®,
159 Medtronic, Minneapolis, MN, USA).

160 Intraoperative displacement of the acoustic-facial bundle by the tumor was as follows: two patients had facial nerve course
161 pattern I, one had pattern II, and five had pattern III. Gross total resection was achieved in four cases, and sub-total resection
162 in four (Table 1). MRI analysis of the VII-VIII bundle displacement matched the intraoperative observed displacement in
163 five cases.

164 Regarding the histological analysis, the most common lesion was CPA meningioma (n=6), followed by lower cranial nerve
165 schwannoma (n=2) (Table 1). Four of the six meningiomas were classified as grade I in the WHO classification, and the other
166 two as grade II. The proportion of grade I and grade II in our series was comparable to the proportion in the entire cohort (52
167 grade I WHO and 8 grade II WHO).

168

169

170 *Post-operative assessment*

171 **Hearing**

172 The mean follow-up was 21±23.5 months [1–54 months]. At the last visit, ΔPTA was 36±22.2 dB, with a significant
173 improvement at all frequencies ($p<0.0001$, two-way ANOVA, n=8, **Fig. 3A**), and ΔSDS was 85±16.9% ($p=0.0002$, Mann–
174 Whitney test, n=8, **Fig. 3B**). There was no significant difference between the hearing results at 1 month and at the last visit,
175 or the mean PTA (20±9.7 dB vs 18±10.6 dB, $p=0.25$, Mann–Whitney test), or the mean SDS (95±8.8% vs 92±18.9%,
176 $p>0.999$, Mann–Whitney test). Table 1 shows the results for all patients at the last visit.

177 After surgery, all patients but one recovered from a pre-operative hearing class D to a post-operative class A; the last patient
178 recovered to class B.

179 Concerning ABRs, three of the five available post-operative ABRs became synchronous, one became synchronous with
180 increased interpeak interval I-V, and only one remained asynchronous.

181

182 **Complications**

183 Regarding early post-operative complications, one patient experienced a post-operative cerebrospinal fluid leak (7 days after
184 surgery) which required revision surgery.

185 One patient had a well-tolerated post-operative paralysis of the X and XI nerves (Patient 5) and another had reversible grade
186 II facial paralysis that required no further treatment (Patient 1). The patient presenting pre-operative grade II HB facial nerve

187 function recovered to grade I (Patient 8). Lower cranial nerve functions were improved in Patient 7, with disappearance of
188 the XIth nerve paralysis, improved laryngeal sensitivity, but persistence of ipsilateral vocal cord palsy.

189

190 Imaging

191 Post-operative imaging was available for seven patients. Three had a residual tumor, located in the jugular foramen in two
192 and in the cavernous sinus in one patient (Table 1). All but one residual tumor were stable; the last one showed growth that
193 was treated with Gamma-knife stereotactic radiosurgery.

194

195 Discussion

196 Analyzing our results, among the 69 patients operated on for a non-VS CPA tumor at our institute, we were surprised to note
197 that the incidence of significant hearing recovery was 13.3% after tumor removal with a retrosigmoid approach. These
198 patients experienced a recovery from non-useful hearing (class D) to useful hearing with intelligibility (class A or B), that
199 probably represents a substantial improvement in their everyday quality of life. During the same period, in nine cases, we
200 used a translabyrinthine approach for non-VS CPA tumor removal (**Fig. 1**), because of significant pre-operative hearing loss.
201 It is likely that some of them would have experienced hearing recovery if we had used a retrosigmoid approach in those cases.
202 Therefore, at present, **the retrosigmoid approach is the preferred option when dealing with non-VS CPA tumors despite the**
203 **hearing level and/or the tumor volume, and this has represented an important change in our daily practice.**

204 In the literature, there are a few reports [4, 7, 11–15] on hearing recovery after CPA tumor removal (Table 3), most being
205 case reports generally concerning meningiomas, arachnoid and epidermoid cysts. We decided not to include the cysts in our
206 series because they were not “true” tumors with different biological and histopathological behaviors. Only one study reported
207 a large series of CPA meningiomas [4] and found some degree of hearing improvement in 40 of 421 cases. Unfortunately,
208 they used the Hannover Audiological Classification making comparison with the present study difficult.

209 Although preservation of hearing in surgical treatment of VS has been emphasized and discussed in the literature [10], little
210 is known about auditory function in non-VS tumors of the CPA. However, extrapolating data on hearing preservation in VS
211 surgery to the post-operative evolution of hearing for non-VS CPA tumors is probably a mistake. First, in VS,
212 pathophysiological evidence indicates that hearing loss is explained by compression of either the cochlear nerve and/or the
213 labyrinthine artery in the internal auditory canal (IAC) with a direct association between VS tumor size and hearing loss [23].
214 In the case of labyrinthine artery compression, vascular damage to the cochlea with no conceivable recovery could explain
215 the hearing loss. The significant recovery of hearing obtained in this series suggests that the vascular etiology was not
216 involved, similar to a report by Lanzino et al. [7] who described hearing recovery after marsupialization of a CPA arachnoid

217 cyst in a patient who had recordable pre-operative otoacoustic emissions (OAEs) with an asynchronous ABR. The presence
218 of OAEs pre-operatively may predict the integrity of vascular supply to the cochlea and correlation studies would be
219 necessary to define their function in pre-operative care [24]. Similarly, the presence of wave I in the pre-operative ABR,
220 which indicates the cochlear synapse function, could have the same significance and be a good prognostic factor for hearing
221 recovery [25]. Indeed, we found the presence of wave I pre-operatively even in the case of asynchronous ABR, and it could
222 be helpful to use OAEs as an additional tool to select cases with a greater chance of hearing recovery.

223 In addition, histological evidence of invasion of the cochlear nerve by VS was reported by Neely et al. [26]. In contrast, in
224 non-VS CPA tumors, although the pathophysiology evidence is poor, hearing loss is probably due to cochlear nerve
225 compression without invasion [14], which would not cause irreversible damage to the nerve and the cochlea, making hearing
226 improvement possible. Indeed, we know that damage to the cochlear nerve cannot be repaired, but compression by a tumor
227 may cause neurapraxia that, once the pressure is alleviated, allows return of axonal transmission and hearing recovery. Thus,
228 the decompression of the cochlear nerve by the tumor removal could allow spectacular recovery of the SDS, as illustrated in
229 our series.

230 Regarding other post-operative functional outcomes, a good post-operative facial nerve function was obtained in all patients,
231 despite the presence of relatively large lesions, underlining the fact that, when dealing with large CPA lesions, the facial
232 nerve is not at increased risk during a retrosigmoid approach compared to a translabyrinthine approach. Finally, the choice
233 of the extent of resection in our series was mainly decided after considering lower cranial nerve function. In two cases, the
234 lesion arose from these nerves and a gross-total resection might have led to lower cranial nerve injury.

235 Surgery is not the sole option for treating these lesions. Gamma-knife stereotactic radiosurgery has been employed in the
236 treatment of meningiomas [27] and lower cranial nerve tumors [28]. Results on hearing preservation have been published
237 [27] and a mention of hearing improvement has been reported in that series without any audiological data. Because of the
238 volume of tumors in our cases, radiosurgery was not indicated as first-line treatment. In addition, chemotherapy with
239 bevacizumab could be associated with an improvement in hearing in NF2-related VS, but this treatment is reserved for
240 patients with NF2 and no indications are accepted for other kinds of CPA tumor. The mechanism of hearing recovery is
241 thought to be a decrease in intraneural edema and vascular shrinkage of the tumor which would decrease the compression on
242 the nerve and blood vessels [29].

243 There are some important limitations that could affect the generalizability of our findings. First, the retrospective nature of
244 this study encompasses biases that are difficult to overcome. Also, we did not use intraoperative auditory monitoring in this
245 study. Looking at our cases, pre-operative ABR were asynchronous in almost all patients making this kind of monitoring
246 impossible. Monitoring with cochlear nerve action potentials (CNAP) would have provided interesting information about the

247 variation of this potential during manipulation of the tumors with the possibility of individualizing some surgical
248 steps/maneuvers important for hearing recovery [30]. Finally, we tried to highlight anatomic, audiological or radiological
249 factors to compare the different groups presented in the flow chart (**Fig. 1**), but the heterogeneity of their presentation and
250 the relatively small number of patients did not allow us to constitute a statistically significant control group.

251

252 **Conclusion**

253 **We would like to alert readers to the potential for significant post-operative hearing recovery in non-VS CPA tumors and**
254 **stress the importance of considering a conservative surgical approach, even in cases of severely impaired hearing and large**
255 **tumors. Relying on tumor size and hearing status for choosing the translabyrinthine approach (as classically performed for**
256 **VS) should not be adopted in non-VS CPA tumors. Larger multi-center studies examining this topic would help corroborate**
257 **our results.**

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336 **Figure legends**

337 **Fig. 1** Flow chart of the study population

338 Δ PTA: difference between pre- and post-operative pure tone average; Δ SDS: difference between pre- and post-operative
339 speech discrimination score.

340

341 **Fig. 2** Axial and coronal views of MRI scans (cerebellopontine angle meningioma) from Patient 1

342 Pre-operative Fast imaging employing steady-state acquisition in axial (**A, upper left**) and coronal (**B, lower left**) images
343 showing a stage IV tumor with brainstem compression; and post-operative axial (**C, upper right**) and coronal (**D, lower**
344 **right**) images showing a total tumor resection with acoustic-facial bundle visualization.

345

346 **Fig. 3** Evolution of hearing between the pre-operative period and the final post-operative visit

347 **A:** Pre- and post-operative mean of thresholds of the tonal audiogram at 500, 1000, 2000, and 3000 Hz, showing a significant
348 improvement of thresholds ($p=0.0152$, $p=0.0054$, $p=0.0002$ and $p=0.0017$, respectively; two-way ANOVA with SIDAK's
349 multiple comparison test).

350 **B:** Significant improvement of the pre- and post-operative speech discrimination score ($p=0.0002$, Mann–Whitney test).

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