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Postoperative Cochlear Obliteration after Retrosigmoid Approaches in Patients with Vestibular Schwannoma

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Damit die Sichtbarkeit der Veränderungen in der Cochlea in den MRT-Untersuchungen verbessert wird, erfolgten die koronalen Rekonstruktionen der MRT-Untersuchungen, die der symmetrische Vergleich beider Cochleae erleichterte. Dabei handelt es sich um ein komplexes neuroradiologisches Verfahren. Die koronalen Rekonstruktionen der MRT-Untersuchungen wurden von Herrn Prof. E. Hofmann durchgeführt, welcher mir deren Ergebnisse zur Verfügung stellte.

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Widmung

Mardjan & Kiara

LIST OF ABBREVIATIONS

ABI..................... Auditory Brain stem Implantat

Ant .... Anterior

asc .... anterior semicircular canal

ASHA.....................American-Speech-Language-Hearing Association

CI .... Cochlear Implantat

CI .... Confidence Interval

CPA .... Cerebellopontine Angle

Coc .... Cochlea

CO .... Cochlear obliteration

dB .... Decibel

DRIVE .... Driven Equilibrium

ENT .... Ear, Nose and Throat

et al. .... et alii

EXT ....Extrameatal

F ....Female

Int ....Intrameatal

L .... Left

Lat ....Lateral

lsc .... lateral semicircular canal

m ....mild

mm.........................Millimeter

mo ....Month

mod ....moderate (hearing deterioration)

MRI .... Magnetic Resonance Imaging

NF II ....Neurofibromatosis Type II

nh .... normal hearing

p .... p-value

pr ....profound (hearing deterioration)

Preop .... Preoperative

Post .... Posterior

Postop .... Postoperative

psc .... posterior semicircular canal

qud .... quantitatively inexactly defined deaf

qunh .... quantitively inexactly defined normal hearing

qusl .... quantitatively inexactly defined, slight hearing deterioration

qust .... quantitatively inexactly defined, strong hearing deterioration

R ……………….... Right

Ref ……………… Reference

SD ………………. Standard deviation

se .... severe (hearing deterioration)

SSD ……………... single-sided deafness

Tu-d …………….. Tumor diameter

Vest ....Vestibule

VS ……………… Vestibular Schwannoma

Y.............................Year

1. SUMMARY

1.1. Summary in German (Zusammenfassung)

Vestibularschwannomen (VS) gehören zu den häufigsten Läsionen im Kleinhirnbrückenwinkel (CPA).[1] Obwohl große Läsionen selten die Funktion des Gesichtsnervs beeinträchtigen, wird der N. Cochlearis häufig durch den Tumor beeinträchtigt. Die Magnetresonanztomographie gehört zu dem Goldstandardbildverfahren zur Diagnose des Vestibularisschwannoms.[1] Zu den aktuellen Behandlungsoptionen gehören Beobachtung, chirurgische Resektion, fraktionierte Strahlentherapie und Radiochirurgie[1]. Die Ziele der VS-Operationen sind die Aufrechterhaltung der Funktion des N. Facialis, vorzugsweise die Erhaltung der Funktion des N. Cochlearis und eine möglichst radikale Tumorentfernung. Allerdings sind diese Ziele nicht immer realisierbar. Insbesondere der N. Cochlearis ist äußerst anfällig. Daher ist nach solchen Operationen häufig eine Verschlechterung des Hörvermögens unvermeidbar. Dank der Fortschritte in der Wiederherstellung des Gehörs bei den Patient:innen, die unter einem postoperativen Hörverlust leiden, können die Patient:innen mittlerweile mit Cochlea-Implantat (CI) bzw. mit auditorischem Hirnstammimplantat (ABI) versorgt werden. Trotz kontinuierlich verbesserter Ergebnisse bei ABI-Implantation ist CI noch immer eine bessere Technik zur Wiederherstellung des Hörvermögens vorausgesetzt, dass der Hörnerv erhalten geblieben und die Cochlea durchgängig ist.[3] Daher scheint eine obliterierte Cochlea im Falle einer CI-Implantation ein Hindernis oder zumindest eine große Herausforderung darzustellen.[7]

Während der retrosigmoidale Zugang bei Neurochirurgen sehr beliebt ist, findet der translabyrinthäre Zugang bei HNO-Ärzte großen Anklang. Könnte es nach einem Zugang häufiger zu einer Cochlea-Obliteration kommen, hätte dies zur Folge, dass die Wiederherstellung des Hörvermögens bei diesen Patienten weniger erfolgreich ist. Obwohl sich einige Studien mit der Wirkung der translabyrinthären Zugänge auf die Cochlea-Obliteration befasst haben, wurde bisher die Wirkung des retrosigmoidalen Zugangs auf Cochlea-Obliteration weniger untersucht. Daher besteht die Notwendigkeit die Wirkung des retrosigmoidalen Zugangs auf die Cochlea zu untersuchen. Sollte sich zeigen, dass die Cochlea-Obliteration nach den retrosigmoidalen Zugängen häufig auftreten, wäre es ratsam, eine frühe CI-Implantation nach VS-Operationen in Betracht zu ziehen, und zwar noch bevor die Obliteration erfolgt ist.

Darüber hinaus wurden die Häufigkeit der Obliteration in Bogengängen und ihre statistische Korrelation zur Cochlea-Obliteration untersucht. Außerdem wurden Patientenalter, Patientengeschlecht, die Lage des Tumors, Rezidiv-Operationen Tumordurchmesser, die Dauer der Operation, die Dauer der postoperativen MRT-Kontrollen und schließlich

postoperative Veränderung des Hörvermögens der Patienten untersucht. Die Studie wurde monozentrisch und retrospektiv durchgeführt. Es wurden nur Patienten eingeschlossen, bei denen postoperativ eine T2-gewichtete MRT(DRIVE-Sequenz) mit einem hochauflösenden Datensatz mit Submillimeterbereich durchgeführt wurde. Die letzte verfügbare MRT-Untersuchung wurde berücksichtigt. Die Bilder wurden interaktiv in der exakten Koronarebene neu formatiert. Die koronal umformatierten Bilder dienten dazu, die Sichtbarkeit der Obliteration in der MRT-Untersuchung zu verbessern und eine perfekte Rechts-Links-Vergleich der Innenohrdetails zu ermöglichen.[3]

Vestibularschwannome, die über subokzipitale retrosigmoidale Zugänge im Zeitraum von Januar 2008 bis Februar 2015 operiert wurden, wurden aus den Patientenakten ermittelt. Die Eingriffe erfolgten in Zusammenarbeit mit der HNO-Abteilung endoskopisch unterstützt in standardmäßiger mikrochirurgischer Technik und unter intraoperativem elektrophysiologischem Monitoring der Gesichts- und Hörnerven.

Kategoriale Daten wurden anhand absoluter und relativer Häufigkeiten zusammengefasst. Kontinuierliche Variablen wurden anhand von Mittelwert, Median und Standardabweichung charakterisiert. Der Zusammenhang zwischen zwei binären Variablen wurde mithilfe des Odds Ratio bewertet und mithilfe des Boschloo-Tests getestet. Um Unterschiede zwischen zwei Kategorien für eine kontinuierliche Variable zu testen, wurde ein Wilcoxon-Mann-Whitney-U-Test angewendet.

Insgesamt konnten 56 Patienten (33 weiblich, 23 männlich, Medianalter 23 Jahre) eingeschlossen werden. 32 % der Patienten zeigten Cochlea-Obliteration. Es konnte nicht nachgewiesen werden, dass Faktoren wie Alter, Tumordurchmesser sowie Tumor-Lokalisation und -Ausdehnung die Rate der Cochlea-Obliteration signifikant beeinflussen. Cochlea-Obliteration trat häufiger beim weiblichen Geschlecht auf (p-Wert von 0,09; Odds Ratio: 2,34 mit Konfidenzintervall 95% zwischen 0,969 und 7,864). Es stellte sich heraus, dass die Obliteration der Bogengänge und des Vestibulums der einzige Befund war, der bei Patient:innen mit Cochlea-Obliteration signifikant häufiger beobachtet wurde (p-Wert: 0,002; Odds Ratio: 12,36 und Konfidenzintervall 95 % zwischen 1,49 und 102,71). Da die Bogengänge häufiger betroffen sind, könnte die Nähe dieser Strukturen zur hinteren Gehörgangslippe eine wichtige Rolle bei der Anfälligkeit des Innenohrs für die Obliteration spielen. Die hintere Gehörgangslippe wurde intraoperativ ausnahmslos abgefräst, wodurch der intrameatale Teil des Tumors erreicht wurde. Die Beteiligung der hinteren Bogengänge ist aufgrund ihrer hohen Co-Obliterationsrate zusammen mit der Cochlea-Obliteration bemerkenswert. Vergleicht man die Rate der Cochlea-Obliteration nach retrosigmoidalen

Zugängen in der aktuellen Studie mit denen nach den translabyinthären Zugängen in der Literatur, sind retrosigmoidale Zugänge noch immer vorzuziehen. Eine differenzierte Untersuchung operativer Faktoren und ihr möglicher Beitrag zur Cochlea-Obliteration, eine prospektive Untersuchung der retrosigmoidalen und anderen Zugängen zu dem Kleinhirnbrückenwinkel und schließlich die Untersuchung des optimalen Zeitpunkts für die CI-Implantation nach der chirurgischen Entfernung von VS, wären künftig Gegenstand einer prospektiv randomisierten und kontrollierten Studie.

1.2. Summary in English

Vestibular schwannomas (VSs) account for the most common lesions located in cerebellopontine angle (CPA)[1,3]. Although large lesions compromise seldom the facial nerve function, the cochlear nerve is not infrequently compromised by the tumor. Magnetic resonance imaging (MRI) belongs to the gold standard imaging method for the diagnosis of vestibular schwannoma[1]. “Current treatment options include observation, surgical resection, fractionated radiotherapy, and radiosurgery”.[1] (Goldbrunner, 2020) Goals of VS “surgery are maintenance of the facial nerve function, preferably preservation of the cochlear nerve function” (Hedjrat, 2017) and possibly a radical tumor removal.[1,3] However, these goals are not always necessarily feasible in reality. Specially, the cochlear nerve is extremely vulnerable. Therefore, a hearing deterioration and even hearing loss is often inevitable after such operations. Fortunately, there has been much advancement in reestablishing the hearing in patients suffering from the postoperative hearing loss. Cochlear Implant (CI) and Auditory Brain stem Implant (ABI) belong to two well-developed modalities addressing the postoperative hearing loss.[2,4] “In spite of continuously improving results in ABI implantations, CI is still a better technique for the restoration of hearing, if the auditory nerve is preserved and if the cochlea is patent”.[3] (Hedjrat, 2017) Hence an “obliterated cochlea seems to be an obstacle or at least a technical challenge in case of a CI”-implantation.[7] (Huibert Frans van Waegeningh, 2020) While standard retrosigmoid approaches are very popular among the neurosurgeons, the translabyrinthine ones find favor with the otolaryngologists. Could cochlear obliteration occur more frequently after one approach, the consequence would possibly be less success of hearing restoration among such patients. Although a few studies have addressed the effect of translabyrinthine approaches on cochlear obliteration so far, this issue has been even less frequently studied in patients after retrosigmoid approaches. Hence, “we decided to study the frequency of cochlear obliteration after retrosigmoid approaches” retrospectively.[3] (Hedjrat, 2017) Should cochlear obliteration frequently occur secondary to fibrosis or ossification of the cochlea after such an approach, it would be then advisable to consider an early CI implantation after VS operation before the cochlear obliteration has taken place. Additionally, we assessed the frequencies of obliteration in the semicircular canals and their possible statistical correlation to the cochlear obliteration. The study was conducted monocentric and retrospectively. Only patients were included, who underwent postoperatively T2-weighted MRI (DRIVE-sequence) with a submillimeter high-resolution dataset. The last available MRI exam was considered in our study. “The images were interactively reformatted in the exact coronal plane to enable us to make a perfect right–left match of the inner ear details. The coronal reformatted images served only to improve the conspicuity of obliteration”.[3] (Hedjrat, 2017)

Vestibular schwannomas, operated in our center through suboccipital retrosigmoid approaches, “were extracted for the period from January 2008 to February 2015. Standard microsurgical operations were performed endoscopically assisted” in cooperation with our ENT department.[3] (Hedjrat, 2017) Categorical data was summarized using absolute and relative frequencies. Continuous variables were characterized using mean, median, and standard deviation. The association between two binary variables was assessed using the Odds Ratio and tested using Boschloo’s test. Exact Wilcoxon-Mann-Whitney U-test was applied for testing differences between two categories for a continuous variable.

Thirty-two percent of suboccipital retrosigmoid approaches to VSs depicted cochlear obliteration to some extent in our center. Factors, such as age, reoperation, tumor diameter, Duration of the operations and reoperation were not associated with significantly higher rate of cochlear obliteration according to our study. Nevertheless, “cochlear obliteration was more common in females” in the studied population.[3] (Hedjrat,2017) (P-value: 0.09; odds ratio: 2.34 with 95% confidence interval (CI) between 0.696 and 7.864). The obliteration of semicircular canals and vestibule has turned out to be the only finding associated significantly with more frequent cochlear obliteration (p-value: 0.002; odds ratio: 12.36 and confidence interval 95 % between 1.49 and 102.71). Since semicircular canals are prone to be involved more frequently according to our data, the vicinity of these structures to the posterior lip of the meatus may play an important role in the susceptibility of the internal ear to the obliteration. The posterior lip of meatus was drilled unexceptionally in the patients’ cohort, through which the intrameatal part of the tumor was reached. Specially the involvement of posterior semicircular canals is noteworthy because of their high rates of co-obliteration with cochlea. Comparing the rate of cochlear obliteration after retrosigmoid approaches in the current study to those after translybyinthine ones in literature, retrosigmoid approaches seems still to be a better approach concerning the postoperative cochlear obliteration. The differentiated assessment of operative factors and their possible contribution to cochlear obliteration, multicentral assessment of both retrosigmoid and translabyrinthine approaches and finally the assessment of the optimal timing for CI implantation after the operative removal of VS would be subjects to future prospectively randomized and controlled studies.

2. INTRODUCTION

2.1. Study Overview

2.1.1. Vestibular Schwannoma (VS)

Schwannomas are benign tumors arising anywhere along the cranial or peripheral nerves. “Vestibular schwannomas, formerly termed acoustic neuromas, represent the third most common intracranial nonmalignant tumor entity after meningiomas and pituitary adenomas. They are the most common extra-axial posterior fossa tumors in adults, comprising over 80% of tumors in the cerebellopontine angle. In most cases the tumors present unilaterally; bilateral VS are a hallmark of neurofibromatosis type 2”.[1] (Goldbrunner, 2020) Although large lesions compromise seldom the facial nerve function, cochlear nerve is not infrequently compromised by the tumor. They can also compress brain stem resulting in functional disorders of long tracts.[1] “MRI is the method of choice for the identification of suspected VS, with contrast-enhanced T1-weighted scans considered to be the gold standard for the initial evaluation and postoperative assessment of recurrence or residual tumors”.[1] (Goldbrunner, 2020). “The choice of treatment depends on clinical presentations, tumor size, and expertise of the treating center”.[1] (Goldbrunner, 2020) Except for bevacizumab in treatment of VSs in patients with type II-neurofibromatosis, there is no pharmacotherapy in this field.[1] Observation belongs to the well-established work up in many patients with VS. In case of indicating therapy, stereotactic radiosurgery (SRS) is recommended for small- and medium-sized VS and in those without brain stem compression[1]. “The goals of VS surgery are the maintenance of the facial nerve function, preferably the preservation of the cochlear nerve function, and possibly a radical tumor remova”.[3] (Hedjrat, 2017) However, these goals are not always necessarily feasible in the reality. Despite constantly “electrophysiological monitoring of cochlear and facial nerves” “throughout the operation”, the cochlear nerve is still extremely vulnerable.[3] (Hedjrat, 2017) Therefore, hearing deterioration and frequently hearing loss are often inevitable after such operations.[1,2,3,4,5] Consequently, hearing restoration surgeries have gained increasingly in importance.[2,3,4] “The implantation of Cochlear Implant (CI) is a way to restore partly binaural hearing in single sided deafness”.[6] (West, 2019). Thinking of prerequisites for a promising CI-implantation a patent cochlea must logically be considered first. Some authors were thinking even of a simultaneous CI implantation because of ongoing cochlear ossification after the operation.[7]

The idea of cochlear patency as a requirement for later CI implantation persuaded us to assess the impact of retrosigmoid approaches on cochlea as a possible factor affecting the result of the hearing restoration after VS operations. This study was originally designed in 2015 and published in 2017. The entire study has been currently carefully revised and supplemented by further parameters and statistical work.

2.1.2. Surgical Approaches

There exist three surgical approaches to the VS: retrosigmoid, translabyrinthine, and middle fossa approaches. While the standard retrosigmoid approach is very popular among the neurosurgeons, the translabyrinthine one finds favor with the otolaryngologists. One major advantage of retrosigmoid approaches is the feasibility of a radical resection of large tumors with extrameatal extension. There is also an excellent view of cranial nerves. Furthermore, this approach facilitates the preservation of hearing during the resection of smaller tumors.[8]

2.1.3. Cochlear Nerve Vulnerability

Despite all advancements, the resection of VSs remains challenging because of the vulnerability of cochlear and facial nerves. Therefore, hearing deterioration and commonly hearing loss are often inevitable.[9] “Warren III et al. described the T2-weighted magnetic resonance findings after hearing preservation surgery for acoustic tumor removal”.[3] (Hedjrat,2017) “Loss of inner ear signals on T2-weighted images correlates with the loss of hearing postoperatively, whereas preserved inner ear signal correlates with hearing preservation after the middle fossa surgery for VS removal”.[3,10] (Hedjrat, 2017) (Warren, 2006) Belal et al. concluded that both retrosigmoid and middle fossa approaches belong to hearing preserving approaches.[22] Nevertheless, the risk of postoperatively profound hearing loss exists.[11]

2.1.4. Hearing Restoration after Vestibular Schwannoma (VS) Operation

Fortunately, there has been much advancement in reestablishing the hearing in patients suffering from the postoperative hearing loss. Cochlear Implant (CI) and Auditory Brain stem Implant (ABI) belong to two well-developed modalities addressing the postoperative hearing loss2,9. “In spite of continuously improving results in ABI implantations, CI is still a better technique for the restoration of hearing, if the auditory nerve is preserved and if the cochlea is patent”.3 (Hedjrat,2017) Hence, “the success rate of a CI-implantation in the presence of severe cochlear ossification or obliteration is strongly restricted due to the technical challenges and due to the histological factors”.[3,12] (Hedjrat, 2017) (Trinh, 2000) “Ossification can compromise the implantation of cochlear electrodes; therefore, cochlear implantation is ideally considered before any ossification is initiated. It can be argued" that patients who are at the risk of postoperative deafness, should be considered as potential candidates for simultaneous CI or placeholder implantation.[7] (Huibert Frans van Waegeningh, 2020)

2.1.5. Objective of The Study

Concerning the chance of aural rehabilitation, we do assume that retrosigmoid approaches to VSs should be safer than translabyrinthine ones. Should cochlear obliteration occur more frequently after one approach, the likelihood of hearing rehabilitation could be diminished as well. There are few publications in PubMed discussing this subject. According to these studies, MRI exams have turned out to be the most sensitive imaging method to demonstrate cochlear obliteration postoperatively.[10] According to another study, in which the sensitivity of MRI concerning the identification of cochlear obstruction was assessed, "preoperative high-resolution T2 MRI may be useful in predicting cochlear obstruction in patients with a prior history of bacterial meningitis".[13] (Isaacson B, 2009) While a few studies have been addressing the effect of translabyrinthine approaches on cochlear obliteration, this issue has been less frequently studied in patients after retrosigmoid approaches. Hence, we decided to study the frequency of cochlear obliteration after retrosigmoid approaches retrospectively. Should cochlear obliteration occur secondary to the fibrosis or the ossification of cochlea after this approach, it would be advisable to consider the CI-implantation after VS operation before the cochlear obliteration has occurred. Additionally, we assessed the frequencies of the obliteration in semicircular canals and their possible correlation to the cochlear obliteration.

Besides comparing our results to those after translabyrinthine approaches in literature, we also assessed the frequency of other variables like age, gender, tumor diameter, duration of the operation, reoperation, main tumor location and their statistical significance between those with and without cochlear obliteration. Thinking of a possible correlation between surgical traumas and cochlear obliteration, the duration of the whole operation has also been assessed and considered as an indirect indicator for the operative traumas. Finally, patients´ perioperative hearing capabilities were figured out according to the patients´ files.

2.2. Relating Subjects

For the sake of completeness, historical aspects and anatomical considerations relating to such approaches are reviewed briefly here. Subsequently, the material and methods are introduced and finally, the results will be presented and discussed in detail.

2.2.1. History of Diagnosis and Treatments of Vestibular Schwannoma (VS)

The application of the microscope in operation rooms has revolutionized the neurosurgical practices since 1921. The skull base surgeries have turned out to be more accessible after this invention. The removal of VSs was carried out for the first time in the 18th century. Sir Charles Bell (1774-1842) was pioneer in the operation of a cerebellopontine angle (CPA) tumor in 1833.[14] Nevertheless, the diagnosis could be made after the autopsy.[14] Charles Balance succeeded for the first time to remove a vestibular schwannoma in 1894.[14] R. Panse suggested the translabyrinthine approach in 1904, which was primarily unsuccessful.[14] Even attempts to remove the tumor through combined suboccipital and petrosal approaches failed.[14] "Cushing realized that none of approaches attempted by his predecessors, had provided sufficient working place. He decided to do a "bilateral craniotomy and drainage of CSF via tapping of the lateral ventricle".[14] (Baird, 2012) "His attempts to lower the mortality rate led him to forgo a complete resection, instead debulking the tumor through a capsular incision and leaving the capsule behind".[14] (Baird, 2012) Dandy could improve the Cushing`s technique. He was in favor of a "smaller unilateral flap and craniectomy in the lateral position".[14] (Baird, 2012) "In general, facial paralysis was felt to be preferable than the tumor recurrence".[14] (Baird, 2012) Hugh Cairns was the first one who recognized the importance of sparing the facial nerve during the resection of a VS and reported his success in this issue in 1931. Both microsurgical techniques and application of facial nerve monitoring have extremely improved the safety of removal of VSs nowadays.[14]

2.2.2. Anatomical Aspects[8,15,16,17]

Internal ear "consists of the osseous labyrinth and the contained membranous labyrinth".[17] (Gray´s Anatomy, 1989) The osseous labyrinth lies in petrous temporal bone and consists of a complex series of cavities in petrous temporal bone. The membranous labyrinth corresponds a complex set of interconnected membranous sacs and ducts and vestibulocochlear nerve.[17]

2.2.3. Osseous Labyrinth

"The osseous labyrinth consists of three parts: vestibule, semicircular canals, and cochlea".[17] (Gray´s Anatomy, 1989) "Vestibule is the central part of the osseous labyrinth and lies medial to the tympanic cavity, posterior to the cochlea and anterior to the semicircular canals". (Gray´s Anatomy, 1989) Three semicircular canals are connected to each other. Based on their relations to each other they are called anterior (superior), posterior and lateral (horizontal). "They lie posterior and superior to the vestibule and open into it by five openings".[17](Gray`s Anatomy, 1989) "The cochlea shaped like a conical snail-shell, is the most anterior part of the labyrinth, lying anterior to the vestibule".[17] (Gray`s Anatomy, 1989)

2.2.4. Vestibulocochlear Nerve

"The vestibulocochlear nerve divides deep in the internal acoustic meatus into anterior cochlear and posterior vestibular components.[17] (Gray`s Anatomy, 1989) "The internal acoustic meatus is separated at its lateral fundus from the ear by a vertical plate divided unequally by a transverse crest, above which anteriorly is a facial canal conducting its nerve through the petrous bone to the stylomastoid foramen. Posterior to this a small, depressed superior vestibular area present openings for nerves to the utricle, the larger of the vestibular sac and for anterior und lateral semicircular ducts".[17](Gray`s Anatomy, 1989) "Below the crest is an anterior cochlear area in which a spiral of small holes, the tractus spiralis foraminosus, encircles the central cochlear canal".[15] (Gray`s Anatomy, 1989)

"The nerves in the lateral part of the internal acoustic meatus are facial, cochlear, inferior and superior vestibular nerves. The position of the nerves is the most constant in the lateral portion of the meatus".[16] (Rhoton, 2003) "The facial and superior vestibular nerves are superior to the crest. The facial nerve is anterior to the superior vestibular nerve and is separated from it at the lateral end of the meatus by a vertical ridge of bone, called the vertical crest (a.k.a. "Bill`s bar" after William House). The cochlear and inferior vestibular nerves run below the transverse crest with the cochlear nerve located anteriorly".[16] (Rhoton, 2003) "The labyrinthine artery which supplies the labyrinthine structures, is arising from the anterior inferior cerebellar artery or the basilar artery. It divides at the internal meatus into cochlear and vestibular rami".[17] (Gray`s Anatomy, 1989)

2.3. Surgical Approaches to The Cerebellopontine Angle (CPA)

Retrosigmoid, translabyrinthine and middle fossa approaches belong to standard approaches to the CPA. Retrosigmoid and translabyrinthine approaches are introduced in detail below.

2.3.1. Retrosigmoid Approach

The retrosigmoid approach is directed through a lazy S-shaped scalp incision across the asterion. The trepanation is directed to the intradural exposure of the plane between the posterior face of the temporal bone and the petrosal cerebellar surface. “When removing the posterior meatal wall, it is often necessary to sacrifice the subarcuate artery”.[16] (Rhoton, 2003) “The posterior semicircular canal and its common crus with the superior semicircular canal, both of which are situated just lateral to the posterior meatal lip and should be preserved when removing the posterior meatal wall if there is the possibility of preserving hearing. Hearing may be lost if these structures are damaged.”[16] (Rhoton, 2003)

2.3.2. Translabyrinthine Approach

The translabyrinthine approach is still a favorite among otolaryngologists. “A complete mastoidectomy is performed with skeletonization of the tegmen and the bone overlying the sigmoid sinus. The compact of bone of the labyrinth is identified and the lateral semicircular canal used as a landmark for anatomic positioning of the facial nerve. Labyrinthectomies are completed by drilling down the superior petrosal sinus. The lateral semicircular canal is opened until the ampula reached anteriorly. The facial nerve is completely skeletonized from the mastoid segment around the genu to the tympanic segment. The vestibule is opened widely. It is important to extend far enough laterally to allow identification of Bill`s bar and therefore the anterior superior facial nerve. Once the bone between the middle fossa dura mater and superior internal acoustic canal is removed the facial nerve identified, the posterior fossa dura mater is incised.”[17] (Gray`s Anatomy, 1989)

3. MATERIAL & METHODS

3.1. Material

3.1.1. Inclusion Criteria

We retrospectively reviewed data from patients´ records. Vestibular schwannomas operated from January 2008 to February 2015 in our center were extracted. Standard microsurgical operations were performed in cooperation with our ENT department. The operations have been carried out by experienced surgeons. “After the extirpation of the extrameatal part of the tumor, the intrameatal part” was resected by an experienced otologist via “unroofing the internal acoustic canal”.[3] (Hedjrat, 2017) All removed tumors were histologically examined. Only cases with schwannoma of vestibulocochlear nerve were included. “Only patients were included who underwent a postoperative T2-weighted MRI (DRIVE-sequence) with a submillimeter high-resolution dataset to evaluate cochlea on both sides”.[3] (Hedjrat, 2017)

3.1.2. Exclusion Criteria

- Lack of at least one pre- and postoperative MRI exam
- -All space occupying lesions in CPA with histological diagnosis other than vestibular schwannoma
- Preoperative cochlear obliteration
- -Simultaneous ABI-implantation

3.1.3. MRI Scan

The study was conducted retrospectively. The MRI scans were performed by scanners (Ingenia^{TM}; Philips Healthcare, Best, Netherland). The last available MRI study was considered in this study. “The images were interactively reformatted in the exact coronal plane to enable us to make a perfect right–left match of the inner ear details. The thickness of the reformatted slice was 0.3 mm. To search for any obliteration, these reformations were manually scrolled symmetrically from the cochlear apex anteriorly to the most posterior extension of the posterior semicircular canal posteriorly”.[3] (Hedjrat, 2017). **(►Figurs.1-3)**

Figure 1: Intra- extrameatal vestibular Schwannoma in T2- and T1- weighted MRIs with gadolinium, patent cochleas and VS on the right are visible

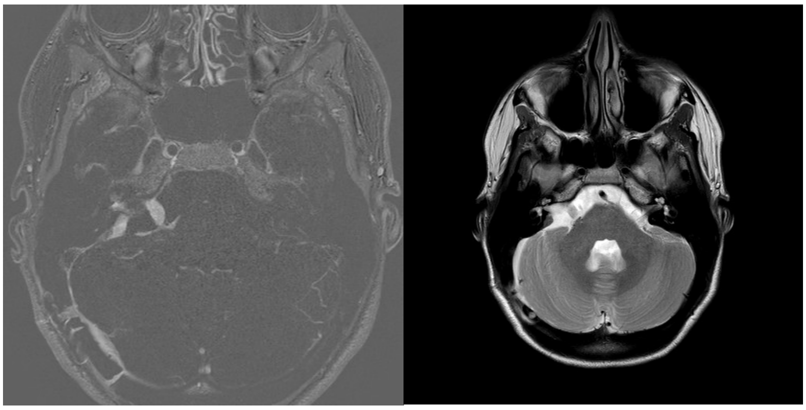


Figure 2: Last postoperative MRI with cochlear obliteration on the right side

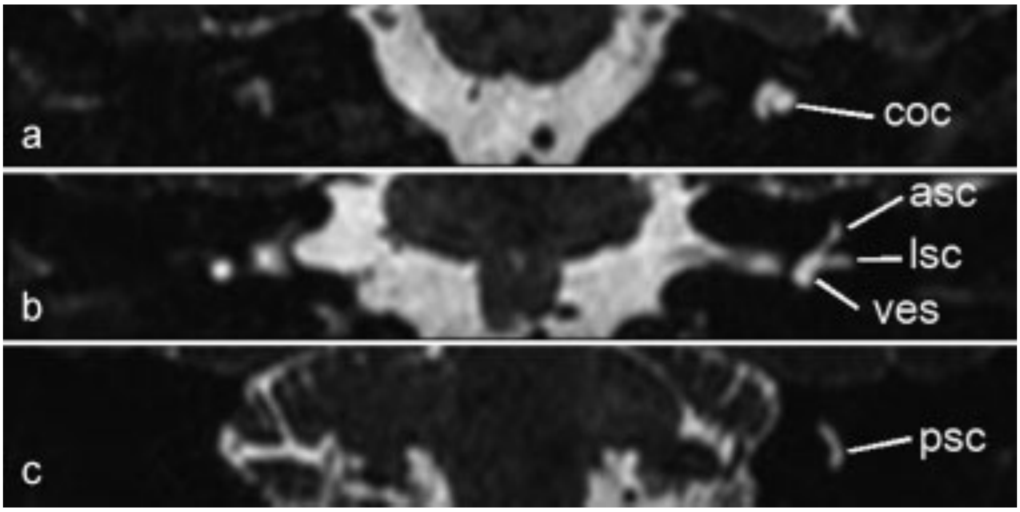


Figure 3: "Reformatted coronal examination with detailed exposure of cochlea (coc), anterior semicircular canal (asc), lateral semicircular canal (lsc), posterior semicircular canal (psc), and vestibule (ves), obliteration of inner ear on the right side".[3]

3.1.4. Definition of Intra- /Extrameatal Tumor Location

Samii defined the intrameatal origin of schwannomas in his popular classification (Hannover tumor extension classification system).[8] According to his classification, tumors originate from the intra meatal part of the nerve even in the lowest class. In other words, exclusively extrameatal tumor does not exist in his classification. Hence, the unroofing of the internal acoustic canal seems to be inevitable in many cases. Nevertheless, we decided for the sake of simplicity to divide the vestibular schwannomas in our studied cohort into two categories exclusively intrameatal and combined.

3.1.5. Definitions of Cochlear Obliteration

“Obliteration was assumed if there existed a reduction of signal or even a complete signal dropout in the corresponding structures (cochlea, vestibulum, and lateral, posterior, or anterior semicircular canals)”.[3] (Hedjrat,2017) Furthermore, “the size and the location of tumors, their” relationship “to the internal acoustic” meatus were figured out.[3] (Hedjrat, 2017) We decided to improve the exposure of inner ear structures through the “reconstruction of thin-slice coronal” exams.[3] (Hedjrat, 2017) “The coronal reformatted images in absolutely symmetrical way enabled us to compare the left and right sides” more precisely.[3] (Hedjrat, 2017) “Cochlear obliteration was also visible in source images but the peri- and endolymphatic fluid were more conspicuous in the symmetrical images. There was no banding artifact in the DRIVE-sequence”.[3] (Hedjrat, 2017) Patients with the evidence of preoperatively cochlear obliteration were excluded.

We could not evaluate the whole available MRI studies for each patient with such demanding reconstructing procedures; therefore, we decided to reconstruct the last available MRI study to prevent to miss cases with possibly later cochlear obliteration. Nevertheless, we were aware of the potential of a selection bias. Since our case study was planned retrospectively, a selection bias could sometimes be inevitable. However, our intention was to figure out the potential statistical relationship between retrosigmoid approaches and cochlear obliteration.

3.1.6. Data Collection

“Histological diagnosis, gender, age of patients, and side of operation” were assessed according to medical records.[3](Hedjrat, 2017) The main location of the tumors was defined according to their relationship to the internal acoustic canal. Those tumors located exclusively inside the acoustic canal were classified as intrameatal. Tumors located in both intra- and extrameatal compartments were classified as Intra/ Extra. The length of the follow-up was determined based on last available MRI examinations. The greatest measurable tumor dimension on axial images were also determined. “An exact volumetric examination of the tumors was technically not possible”.[3] (Hedjrat, 2017) Thinking of a possible correlation between the surgical traumas and cochlear obliteration, the duration of the whole operation was also assessed and considered as an indirect indicator for the operative challenges.

3.1.7. Revision of Criteria

The Data of this study has been already published in the Journal of Neurosurgery B in September 2017. As a matter of homogeneity, we decided to exclude all cases, in whom an additional surgical trauma could have occurred. These supplementary procedures had surely prolonged the duration of the operations and might have additionally caused some local traumas to the inner ear. Therefore, patients, on whom a brain stem implant (ABI) was implanted subsequently, must be excluded in the current assessment.

There are also differences concerning the definition of the tumor location between the published article and the current study. After careful review of tumor locations in preoperative MRI, no exclusively extrameatally locating tumor existed in our series.

3.2. Methods

Categorical data in this monocentric retrospective study was summarized using absolute and relative frequencies. Continuous variables using mean, median, and standard deviation. The association between two binary variables was assessed using the Odds Ratio and tested using Boschloo’s test. Exact Wilcoxon-Mann-Whitney U-test was applied for testing differences between two categories for a continuous variable.

4. RESULTS

“84 patients with space-occupying lesions in CPA were operated from January 2008 to February 2015 in the neurosurgical Ward, Klinikum Fulda, Germany”.[3] (Hedjrat, 2017) 65 patients had primarily met the inclusion criteria in the original study. “In one patient, cochlear obliteration had already been identified in the preoperative MRI” exams, who was excluded as well[3]. (Hedjrat, 2017) Compared with our previously published data in 2017, 9 additional patients must be excluded in the current study. In 6 patients, an ABI was implanted subsequently during the same operation and in three patients, there exist histological or topographical discrepancies to the inclusion criteria, which were overlooked in the former study and could be detected in our current review. Therefore, finally 56 patients (33 females, 23 males, median age: 53 years) met the criteria and were included in the current study. The patients´ data are listed in the ►**Table 1 & 2**. In two patients, vestibular schwannoma was accompanied with type II neurofibromatosis (NF II).

4.1. Patients´ Characteristics

Table 1: Patients´characteristics

Pat.-No	Ref.-No	Age	Gender	Follow-up (mo)	Diagnose	Post-operative Cochlear Obliteration	Side	Tu-d	Re-OP
1	1	65	F	65	VS	No	L	29	Yes
2	4	49	M	78	VS	No	R	7	Yes
3	5	74	M	61	VS	No	L	39	Yes
4	6	46	M	28	VS	No	R	8	No
5	11	58	F	19	VS	Yes	R	14	No
6	12	75	M	44	VS	No	L	7	No
7	13	72	M	5	VS	Yes	L	18	No
8	15	53	M	14	VS	No	R	15	No
9	16	42	F	60	VS	No	R	15	No
10	17	64	F	29	VS	No	L	16	Yes
11	18	21	M	6	NFII/VS	No	L	13,5	Yes
12	19	39	F	45	VS	No	R	15,6	No
13	20	69	F	78	VS	No	R	8	Yes

Pat .- No	Ref .- No	Age	Gender	Follow -up (mo)	Diagnose	Post-operative Cochlear Obliteration	Side	Tu-d	Re-OP
14	23	64	F	2	VS	No	R	17	No
15	24	34	F	59	VS	Yes	R	30	No
16	25	37	F	47	VS	No	R	30	No
17	26	53	F	37	VS	Yes	L	18	No
18	27	44	F	48	VS	No	L	15	Yes
19	28	56	M	60	VS	No	L	24	Yes
20	29	53	M	60	VS	No	L	12	No
21	30	61	F	33	VS	Yes	L	16	Yes
22	31	78	F	56	VS	No	L	10	Yes
23	32	85	F	48	VS	No	R	23	Yes
24	33	62	M	30	VS	No	L	8	No
25	34	70	F	47	VS	Yes	L	23	No
26	35	50	M	53	VS	No	R	16	No
27	40	51	F	5	VS	No	R	25	No
28	41	60	F	36	VS	No	L	19	No
29	42	72	F	44	VS	No	L	22	No
30	44	69	F	37	VS	Yes	L	17	No
31	45	32	M	40	VS	No	R	12	No
32	46	61	M	3	VS	No	L	13	Yes
33	49	35	F	4	VS	Yes	L	32	Yes
34	50	42	M	11	VS	No	L	28	No
35	51	80	M	1	VS	Yes	R	32	Yes
36	52	43	F	9	NFII/VS	No	R	28	Yes
37	53	71	F	21	VS	Yes	L	15	No
38	56	53	F	26	VS	Yes	L	14	No
39	58	47	M	33	VS	No	L	9	Yes
40	61	49	M	27	VS	No	L	33	No
41	62	46	F	15	VS	Yes	R	16	No
42	63	26	M	7	VS	No	R	26	Yes
43	64	43	M	6	VS	No	L	14	No
44	65	78	F	2	VS	No	L	12	No
45	66	49	F	16	VS	No	R	16	Yes
46	67	63	F	18	VS	Yes	L	14	No

Pat.-No	Ref.-No	Age	Gender	Follow-up (mo)	Diagnose	Post-operative Cochlear Obliteration	Side	Tu-d	Re-OP
47	70	50	M	9	VS	Yes	R	18	No
48	71	72	M	13	VS	Yes	R	32	No
49	72	70	F	16	VS	Yes	R	8	No
50	73	52	M	12	VS	Yes	L	19	Yes
51	78	58	F	4	VS	No	R	16	No
52	80	64	F	3	VS	Yes	L	16	Yes
53	81	35	F	4	VS	No	R	34	Yes
54	82	71	F	3	VS	No	R	14	Yes
55	83	35	M	2	VS	No	L	39	Yes
56	84	23	F	2	VS	Yes	R	28	Yes

►**Table 1:** Patients´ characteristics: Ref.: Reference; M: male; F: female; VS: vestibular schwannoma; NFII: neurofibromatosis type II; L: left; R: right; Tu-d: Tumor diameter; Re-OP: Re- or recurrent operation

Further patients' characteristics are depicted in ►**Table 2.** Since the usual audiometric exams were not available for many patients, we decided to modify ASHA-hearing classification to include even those without audiometric exams into the study.

Pat.-No	Ref.-No	Tumor location	Postop. obliteration of semicircular canals & vest.	Operation duration (hours)	Preop. Hearing	Postop. Hearing
1	1	Ext/Int	post.	5.8	7	10
2	4	Int	lat./post. /ant. / vest.	4.3	10	10
3	5	Ext/Int	post.	4.3	10	10
4	6	Int	ant.	2.7	4	7
5	11	Ext/Int	lat./post. /ant. /vest.	5.5	9	0
6	12	Ext/Int	lat./ant.	3.4	7	7
7	13	Ext/Int	lat./hint. /ant./vest.	7	9	9
8	15	Ext/Int	-	4.7	5	7
9	16	Int	lat./post.	5	7	10
10	17	Ex/Int	-	2.5	2	2
11	18	Ext/Int	lat.	6	7	0
12	19	Ext/Int	-	4.3	5	7
13	20	Int	lat./post.	4	5	0
14	23	Int/Ext	-	5.3	9	9
15	24	Ext/Int	lat./post. /ant.	9.5	8	9
16	25	Ext/Int	post.	6	1	9
17	26	Ext/Int	lat./post./ant./vest.	8.8	2	7
18	27	Ext/Int	-	6	5	7
19	28	Ext/Int	lat./post.	7	10	10
20	29	Ext/Int	post. /ant.	4.5	2	10
21	30	Ext/Int	lat./post./ant./vest.	5.2	10	10
22	31	Ext/Int	post. /ant.	3.1	10	10
23	32	Ext/Int	lat./ant.	6.5	5	10
24	33	Int	-	3.8	7	0
25	34	Ext/Int	lat./post. /ant./vest.	6.2	7	10
26	35	Ext/Int	post. /ant.	6.5	10	10
27	40	Ext/Int	post.	7.5	7	0

Pat.-No	Ref.-No	Tumor location	Postop. obliteration of semicircular canals & vest.	Operation duration (hours)	Preop. Hearing	Postop. Hearing
28	41	Ext/Int	-	9.7	8	10
29	42	Ext/Int	lat./post. /ant.	4.5	8	0
30	44	Ext/Int	lat./post. /ant.	3.5	5	10
31	45	Ext/Int	lat./post. /ant.	4.1	7	10
32	46	Int/Ext	-	6.2	6	6
33	49	Ext/Int	lat./post. /ant./vest.	8.1	7	7
34	50	Ext/Int	-	6.5	7	0
35	51	Ext/Int	-	5	10	0
36	52	Ext/Int	post.	3.8	10	10
37	53	Ext/Int	lat./post./ant./vest.	3	6	0
38	56	Ext/Int	lat./post. /ant.	8.3	8	7
39	58	Int/Ext	-	4.7	8	9
40	61	Ext/Int	-	6.9	6	10
41	62	Int	lat./post. /ant./vest.	4.7	9	10
42	63	Ext/Int	-	6.9	5	0
43	64	Ext/Int	-	4.3	8	0
44	65	Ext/Int	-	4.3	9	9
45	66	Ext/Int	-	5.3	6	8
46	67	Int	lat./post. /ant./vest.	6	9	9
47	70	Ext/Int	lat./post. /ant. /vest.	6.3	10	10
48	71	Ext/Int	lat./post. /ant. /vest.	6	10	10
49	72	Ext/Int	lat./post. /ant. /vest.	4.4	6	10
50	73	Ext/Int	lat./post. /ant.	4.9	6	10

Table 2: Patients´characteristics (contd.)

Pat.-No	Ref.-No	Tumor location	Postop. obliteration of semicircular canals & vest.	Operation duration (hours)	Preop. Hearing	Postop. Hearing
51	78	Ext/Int	lat./post. /ant. /vest.	5.7	10	10
52	80	Ext/Int	lat./post. /ant. /vest.	5.3	8	10
53	81	Ext/Int	lat./post. /ant. /vest.	9.7	6	10
54	82	Int	-	3.2	7	0
55	83	Ext/Int	lat./post. /ant. /vest.	10.9	7	10
56	84	Ext/Int	lat./post. /ant. /vest.	6.1	2	10

►**Tables 2:** Patients´characteristics (contd.) Ref.: Reference; Preop.: preoperative; Postop: postoperative. Int: intra meatal; Ext: extrameatal; lat: lateral; post: posterior; ant: anterior; vest: vestibule. Pre- and postoperative hearing using a modified ASHA-Hearing-Classification 10: deaf (quantitatively inexactly defined); 9: profound, >90 dB; 8: severe, 56-90 dB; 7: strong (quantitatively inexactly defined); 6: moderate, 41-55 dB; 5: slight (quantitatively inexactly defined); 4: mild, 26-40 dB; 3: slight, 16-25 dB; 2: normal (quantitively inexactly defined); 1: normal: 10 to 15 dB; 0: missing information

4.2. Cochlear Obliteration

Two patients´ groups, those with and without cochlear obliteration are listed separately in ►**Tables 3 & 4**. The statistical comparison of these groups is summarized in ►**Table 5**. Finally, statistical results concerning their different characteristics are summarized in ►Table 6. Many of these data are also depicted in the following graphics. (►**Graphic 1 – 17**)

4.2.1. Patients' Characteristics in Cases with Cochlear Obliteration

In a total of "18 patients (32%), "the cochlea" cannot "be identified in the last follow-up control".[3] (Hedjrat, 2017)

►**Table 3**: Patients` characteristics in cases with cochlear obliteration

Pat-No	Reference-No.	Age (y)	Gender	Follow-up (mo)	Tumor Diagnosis
1	11	58	F	19	VS
2	13	72	M	5	VS
3	24	34	F	59	VS
4	26	43	F	37	VS
5	30	61	F	33	VS
6	34	70	F	47	VS
7	44	69	F	37	VS
8	49	35	F	4	VS
9	51	80	M	1	VS
10	53	71	F	21	VS
11	56	53	F	26	VS
12	62	46	F	15	VS
13	70	50	M	9	VS
14	71	72	M	13	VS
15	72	70	F	16	VS
16	73	52	M	12	VS
17	80	64	F	3	VS
18	84	23	F	2	VS

Table 3: Patients` characteristics in cases with cochlear obliteration

4.2.2. Patients' Characteristics in Cases without Cochlear Obliteration

No cochlear obliteration was detected in 38 Patients. Their characteristics are listed in the ►**Table 4.**

Table 4: Patients' characteristics in cases without cochlear obliteration

Pat-No	Reference-No.	Age (y)	Gender	Follow-up (mo)	Tumor Diagnose
1	1	65	F	65	VS
2	4	49	M	78	VS
3	5	74	M	61	VS
4	6	46	M	28	VS
5	12	75	M	44	VS

Pat-No	Reference-No.	Age (y)	Gender	Follow-up (mo)	Tumor Diagnose
6	15	53	M	14	VS
7	16	42	F	60	VS
8	17	64	F	29	VS
9	18	21	M	6	NFII/VS
10	19	39	F	45	VS
11	20	69	F	78	VS
12	23	64	F	2	VS
13	25	37	F	47	VS
14	27	44	F	48	VS
15	28	56	M	60	VS
16	29	53	M	60	VS
17	31	78	F	56	VS
18	32	85	F	48	VS
19	33	62	M	30	VS
20	35	50	M	53	VS
21	40	51	F	5	VS
22	41	60	F	36	VS
23	42	72	F	44	VS
24	45	32	M	40	VS
25	46	61	M	3	VS
26	50	42	M	11	VS
27	52	43	F	9	NFII/VS
28	58	47	M	33	VS
29	61	49	M	27	VS
30	63	26	M	7	VS
31	64	43	M	6	VS
32	65	78	F	2	VS
33	66	49	F	16	VS
34	67	63	F	18	VS
35	78	58	F	4	VS
36	81	35	F	4	VS
37	82	71	F	3	VS
38	83	35	M	2	VS

►**Table 4** Patients' characteristics in cases without cochlear obliteration

4.2.3. Statistical Comparisons

Thirty-eight patients (68%) showed no cochlear obliteration after the retrosigmoid approaches. Cochlear obliteration was observed in 18 patients (32%). It was more common in females. Using Boschloo's test, the odds Ratio is 2.34 with 95% Confidence Interval 0.70-7.86 and p-value 0.09. "The median age of patients with cochlear obliteration was "59.5 years, "which was not significantly different from" those without cochlear obliteration (52.5 years).[3] (Hedjrat, 2017) (► **Table 5**).

Table 5: Comparisons of statistical characteristics in cases with and without cochlear obliteration

Characteristics	Without cochlear obliteration	With cochlear obliteration
Number of patients	38	18
Age (years)		
Range	21 – 85	23 – 80
Average	53.7	56.8
Median	52.5	59.5
Gender		
F/M	1.1	2.6
Follow up (months)		
Range	2 – 78	1 – 59
Average	31.1	19.9
Median	29.5	26
Operation duration (hours)		
Range	2.5 - 10.9	3 - 9.5
Average	5.4	6
Median	5.1	5.8
Tumor Localization		
Intrameatal	7	1
Combined	31	17

►**Table 5:** Comparisons of statistical characteristics in cases with and without cochlear obliteration

4.3. Data Summary

Table 6: Data Summary

Characteristics	Patients N (%)
Age (years)	
Median	53
Average	54.7
Range	21 – 85
Standard deviation	15.5
Gender	
Male	23 (41)
Female	33 (59)
Female/Male ratio	1.4
Operation duration (hours)	
Median	5.3
Average	5.60
Range	2.5 – 10.9
Standard deviation	1.86
Follow-up interval (months)	
Median	23.5
Average	27,5
Range	1 – 86
Standard deviation	22.4
Obliteration	
Cochlea	18 (32)
Lateral semicircular canal	30 (54)
Posterior semicircular canal	34 (60)
Anterior semicircular canal	30 (54)
Vestibule	18 (32)
Combined obliteration (cochlea & semicircular canals)	17 (30)
No obliteration	15(26)
Median age (years)	50.5
Female/Male ratio	1.1

Characteristics	Patients N (%)
Cochlear obliteration	
Median age (years)	59.5
Female	13
Male	5
Female/male ratio	2.6
Tumor location	
Exclusively intrameatal	8 (14)
Combined	46(82)
Tumor diameter (mm)	
Median	16
Average	19.1
Range	7 – 39
Standard deviation	8.43
Postoperative hearing	
Deterioration	25 (44)
Recurrent/Re-Operation	24 (43)
With cochlear obliteration	6 (11)
Without cochlear obliteration	18 (32)
Primary Operation	32 (57)
With cochlear obliteration	12 (21)
Without cochlear obliteration	20 (36)

►**Table 6:** Data summary

4.4. Graphics

4.4.1. Age

Figure 4 / ►***Graphic 1:*** Age Distribution

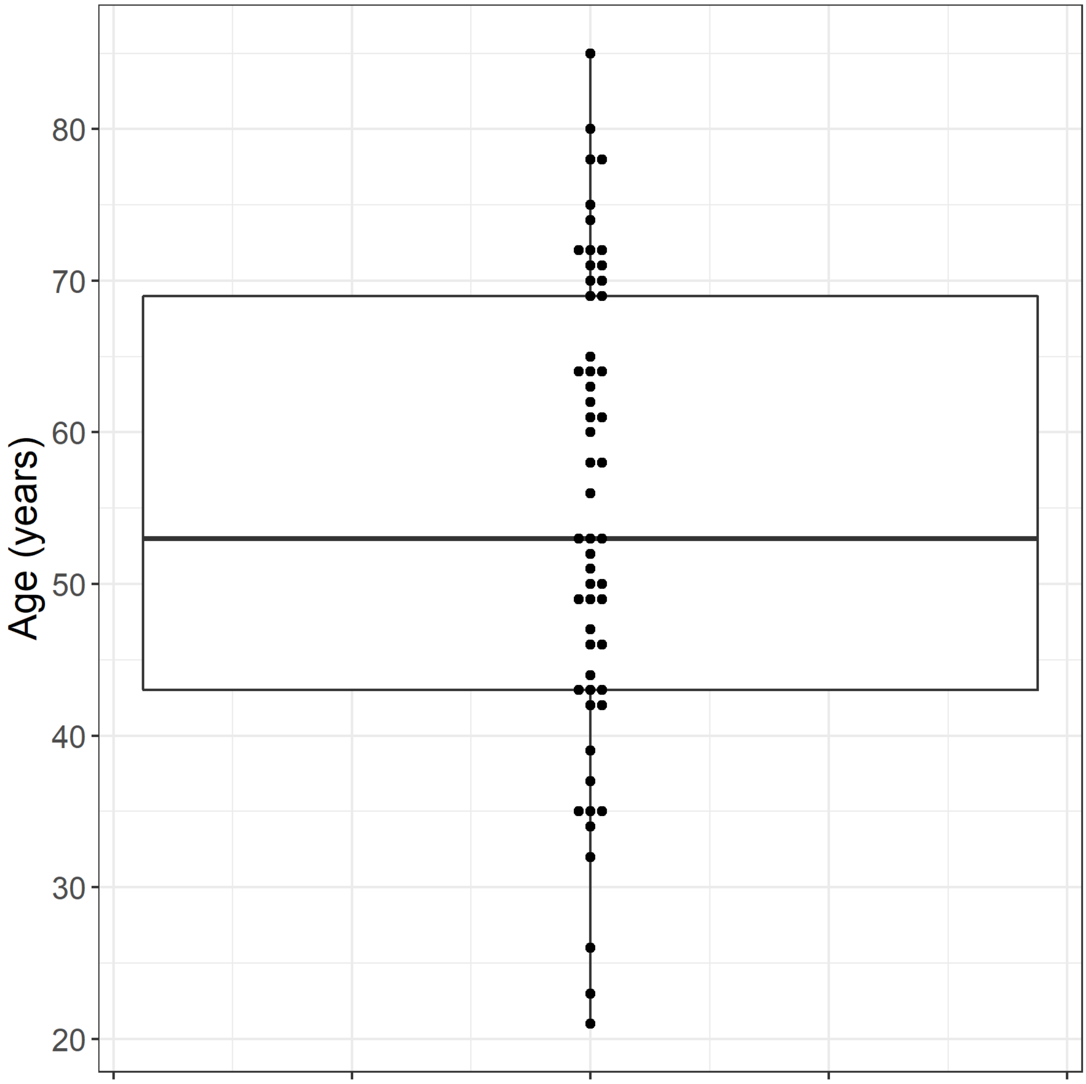
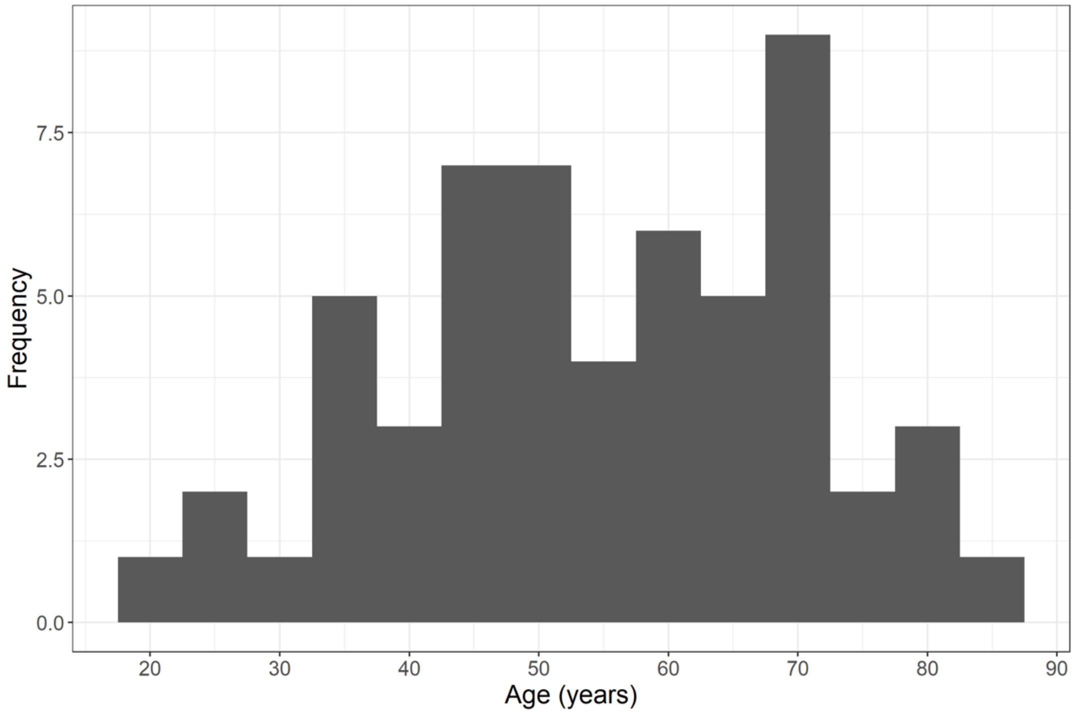
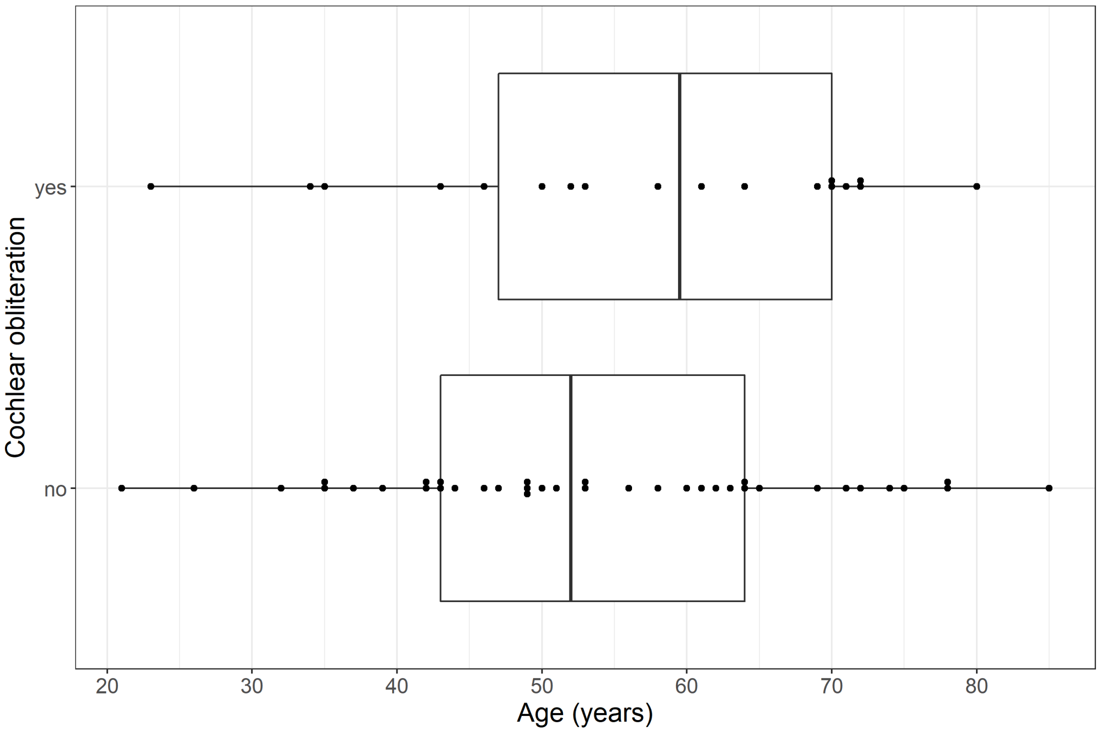


Figure 5 / ►***Graphic 2:*** Age Distribution



No statistically significant differences exist between the patients with and without cochlear obliteration according to Exact Wilcoxon-Mann-Whitney test (p-value: 0.4). (►**Graphic 3**)

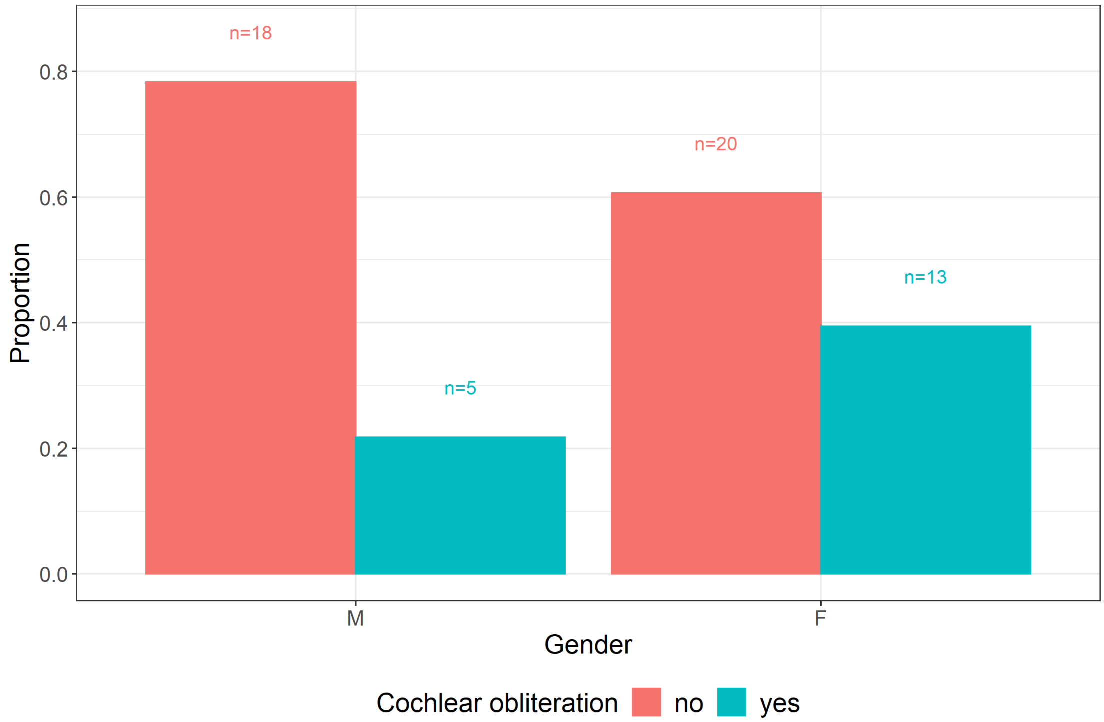
Figure 6 /►***Graphic 3:*** Cochlear Obliteration and Age



4.4.2. Gender

Considering a possible effect of gender on cochlear obliteration, statistically significant differences was not recognized according to these data. These binary variables are compared according to Boschloo`s test. P-value is 0.09. The odds ratio is 2.34 with 95% confidence interval (CI) between 0.696 and 7.864. Nevertheless, a tendency of the higher chance of cochlear obliteration can be demonstrated in females according to these data. (►**Graphic 4**)

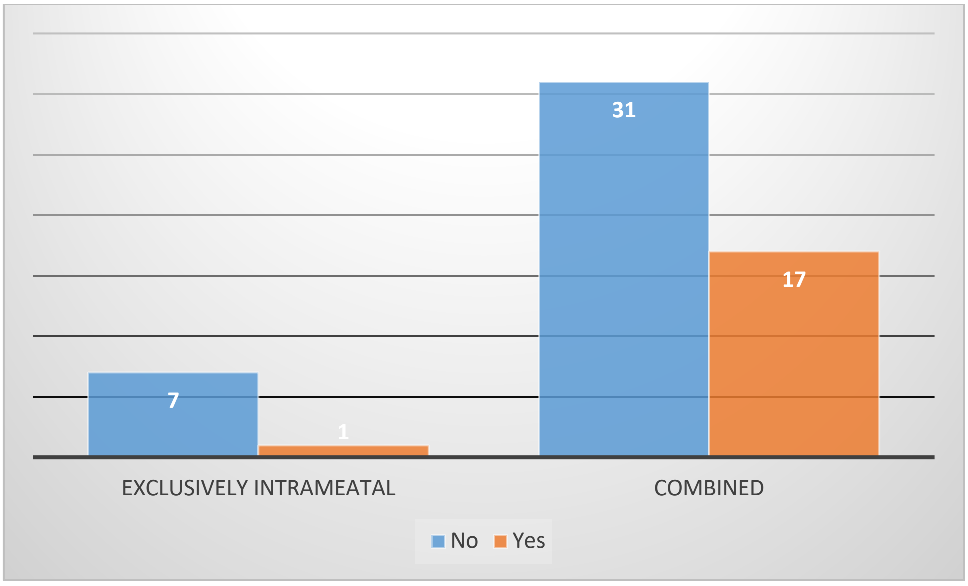
Figure 7 / ►***Graphic 4:*** Cochlear Obliteration and Gender



4.4.3. Tumor Location

Vestibular schwannomas were located mainly combined intra- and extrameatally (82.1%). We could find exclusively intrameatal vestibular schwannomas in 14.3% of patients` cohort. (►**Graphic 5**). Due to low number of intrameatally locating tumors, no statistically significant conclusion can be drawn.

Figure 8 / ►***Graphic 5***: Cochlear Obliteration and Tumor Location



4.4.4. Tumor Size

4.4.5. Tumor Diameter

The greatest measurable diameter on axial images was considered. An exact volumetric analysis of the tumors was technically not possible. Nevertheless, we decided to study a possible relationship between the tumor diameter and cochlear obliteration (►**Graphic 6**). A range of 8 - 32 mm (median 18 mm and the average of 20.3 mm) was detected in the cohort with cochlear obliteration. These two categories with continuous variables were assessed with exact Wilcoxon-Mann-Whitney test, P-value is 0.2. A statistically significant correlation between tumor diameter and cochlear obliteration does not exist (►**Graphic 7**).

Figure 9 / ►**Graphic 6**: Distribution of Tumor Diameter

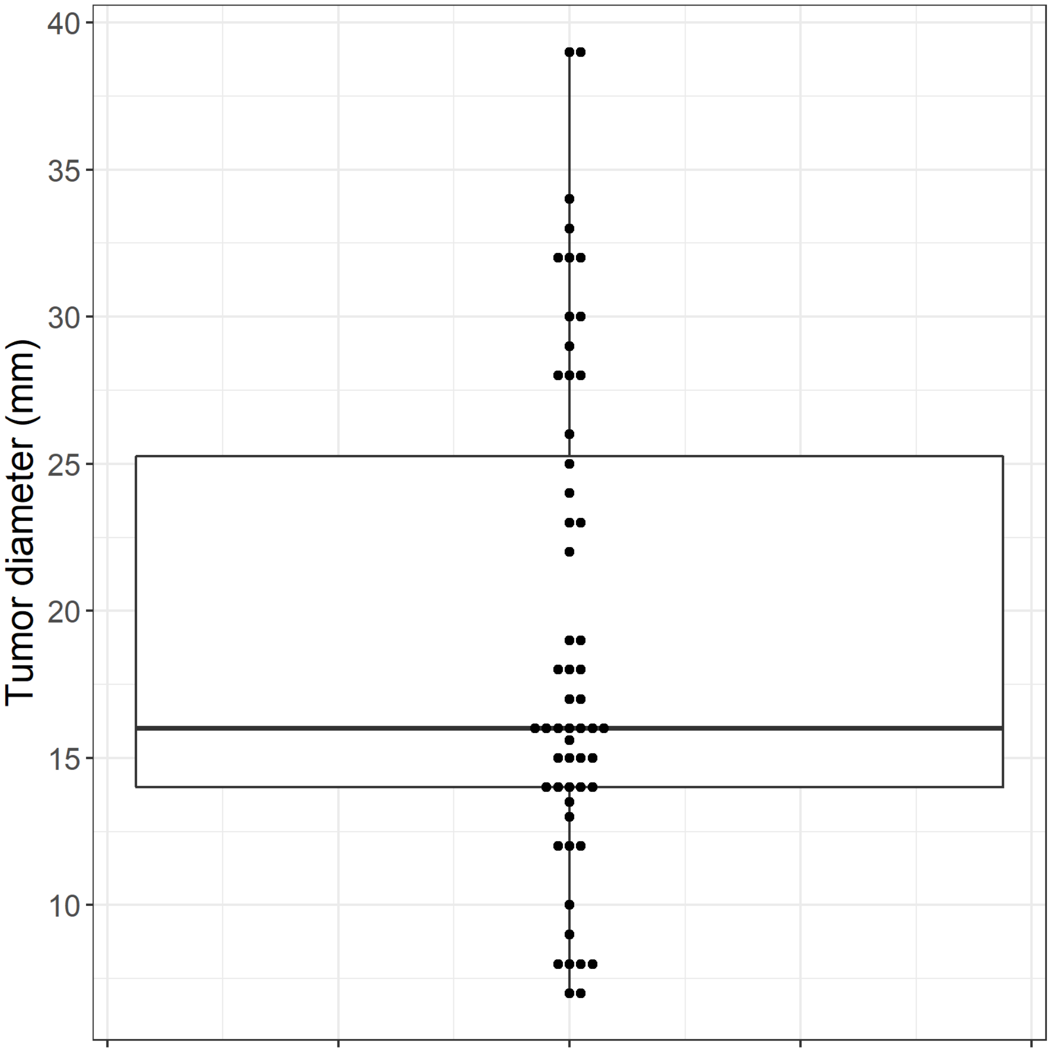
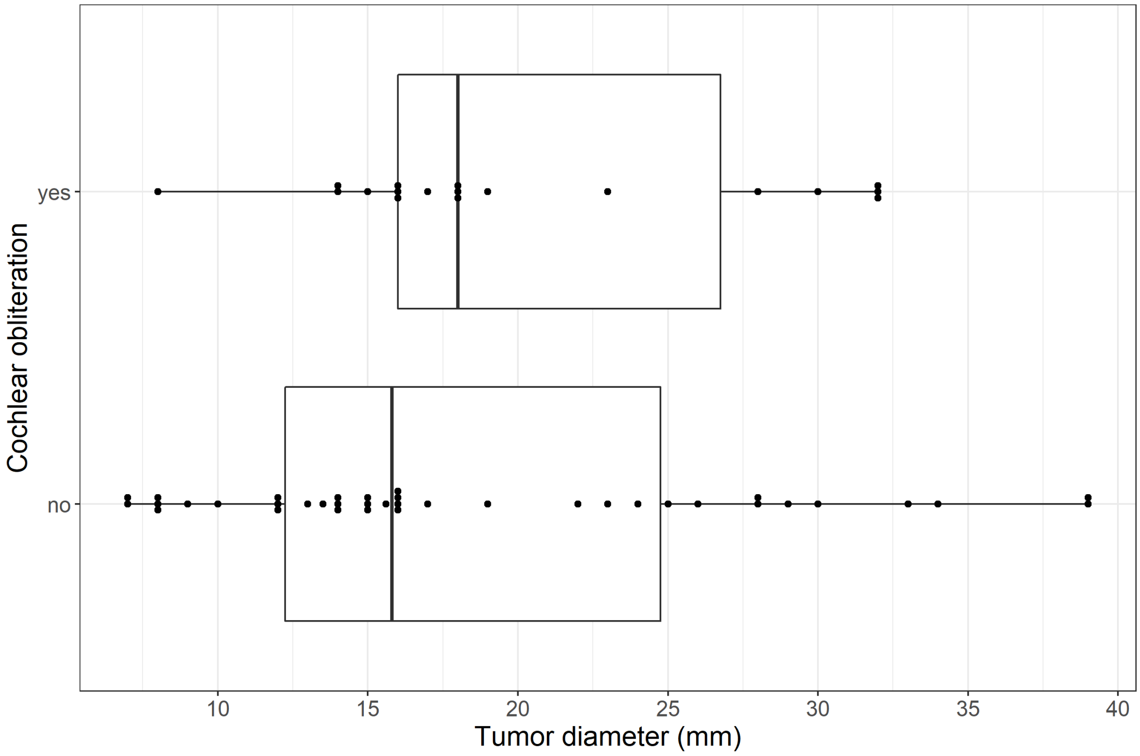


Figure 10 / ►**Graphic 7**: Cochlear Obliteration in Relation to Tumor Diameter



4.4.6. Duration of Operation

As an additional indirect parameter for the tumor-size, we studied the duration of operations (►**Graphics 8 & 9**). Theses continuous variables were analyzed according to exact Wilcoxon-Mann-Whitney test.

Figure 11 / ►***Graphic 8***: Operation Duration

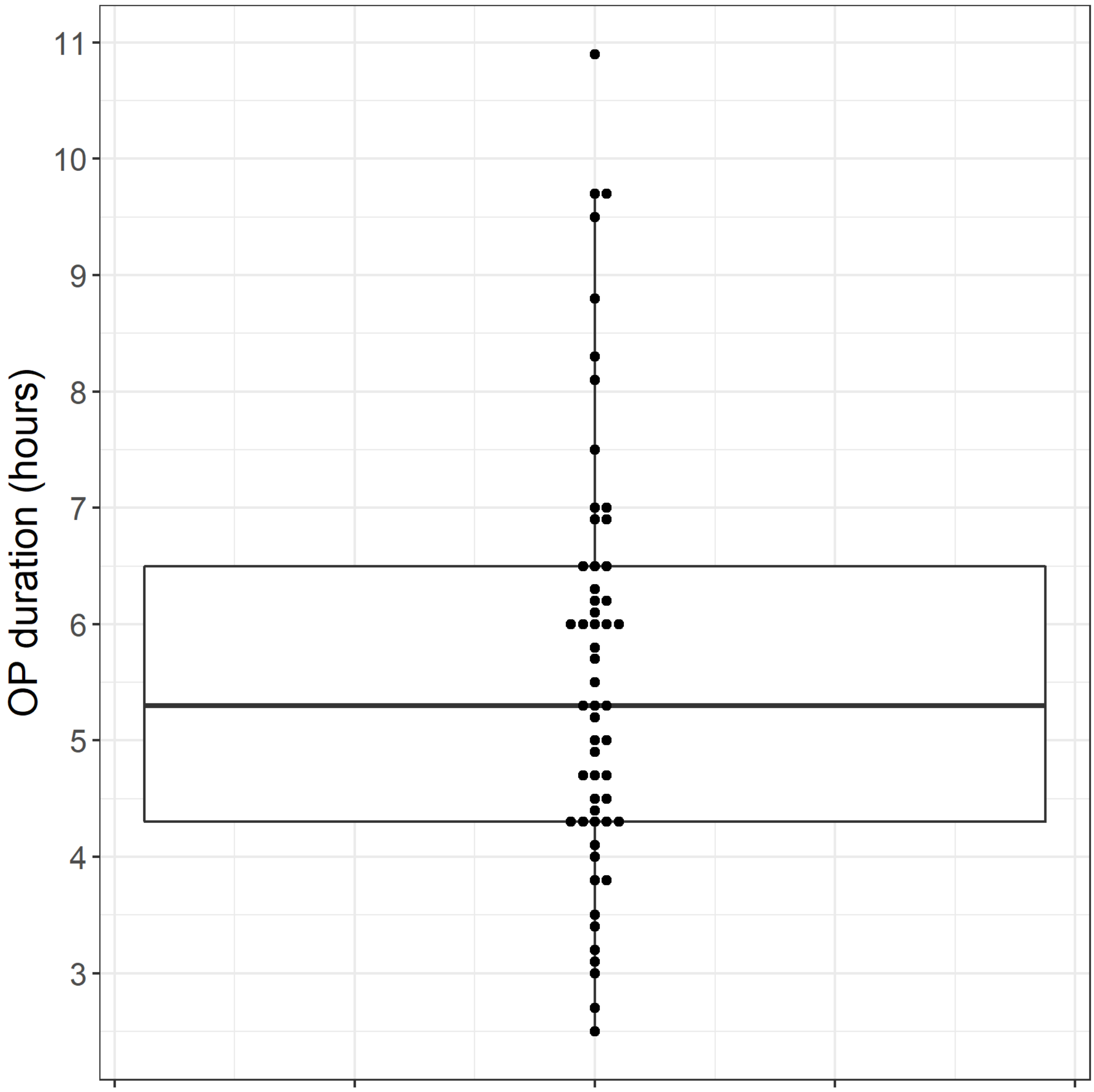
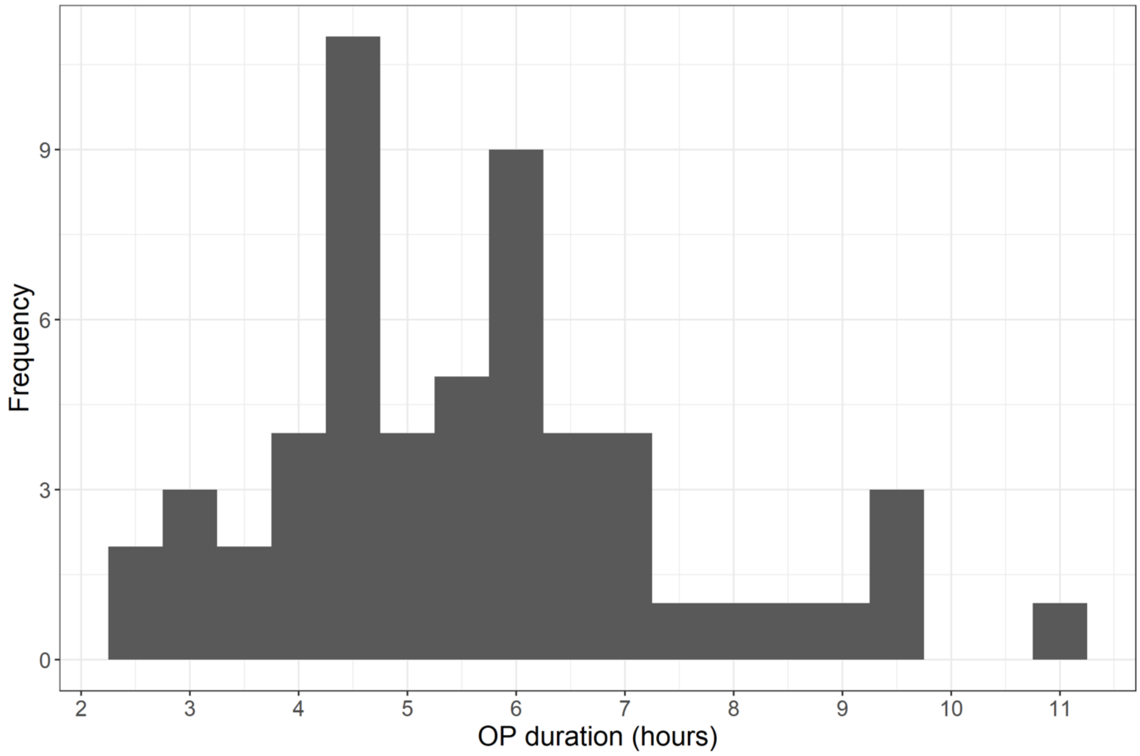


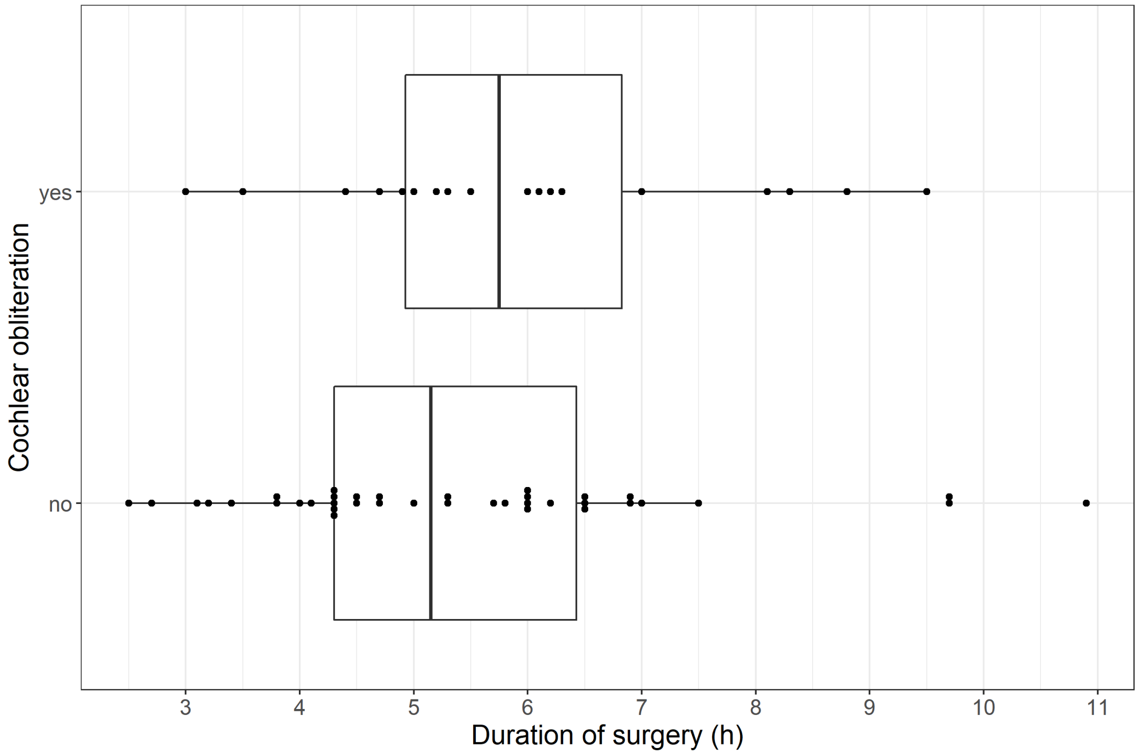
Figure 12/ ►***Graphic 9***: OP Duration



4.4.7. Significance

Neither the tumor diameter, nor the operation duration can statistically be considered as significant factors for precipitating cochlear obliteration according to these data (p-value: 0.2). The alternative hypothesis is not equal 0. Nevertheless, a trend seems to exist towards more frequently cochlear obliteration with increasing both the tumor diameter and the duration of the operation. (►**Graphic 7 &10**)

Figure 13 /► ***Graphic 10*** Cochlear Obliteration in Relation to Operation Duration



4.4.8. **Obliteration of Semicircular Canals and Vestibule**

The involvement of semicircular canals and vestibule has turned out to be the only statically significant parameter coexisting in the patients with cochlear obliteration due to our data, which are analyzed according to Boschloo`s test. p-value is 0.002, odds ratio 12.36 and confidence interval 95 % between 1.49 and 102.71 (►**Graphics 11 & 12**)

Figure 14/►**Graphic 11**: Postoperative Obliteration of Semicircular Canals and Vestibule

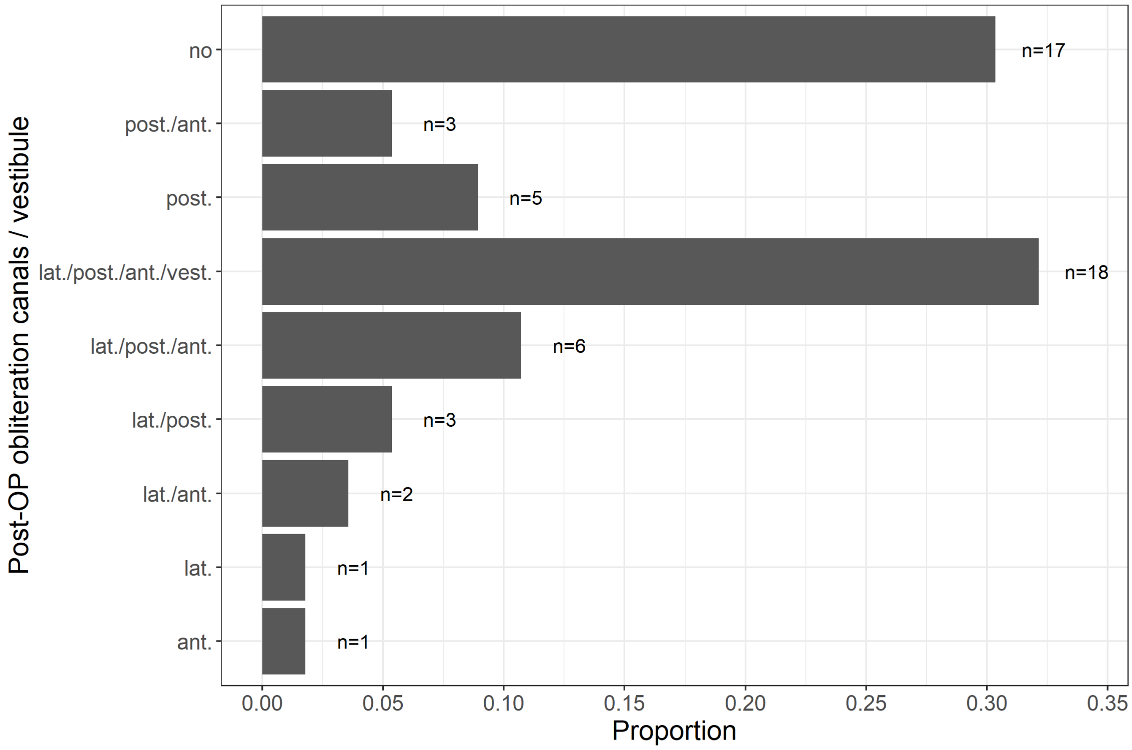
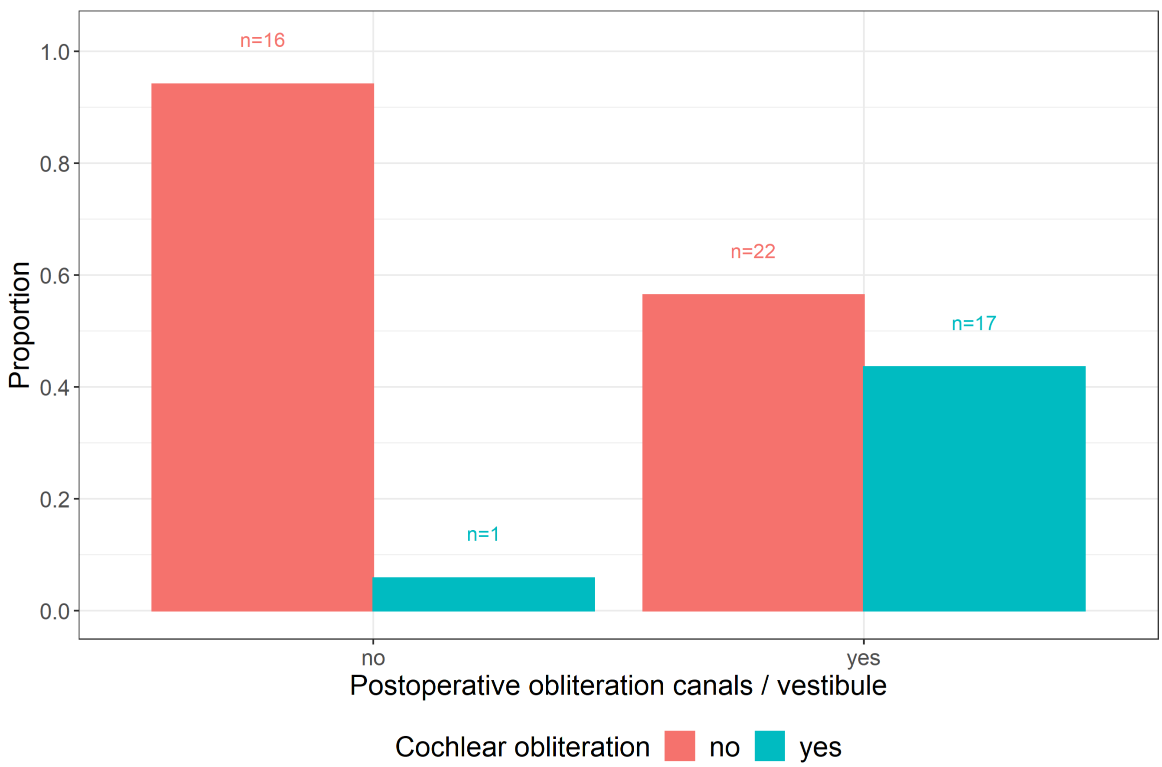


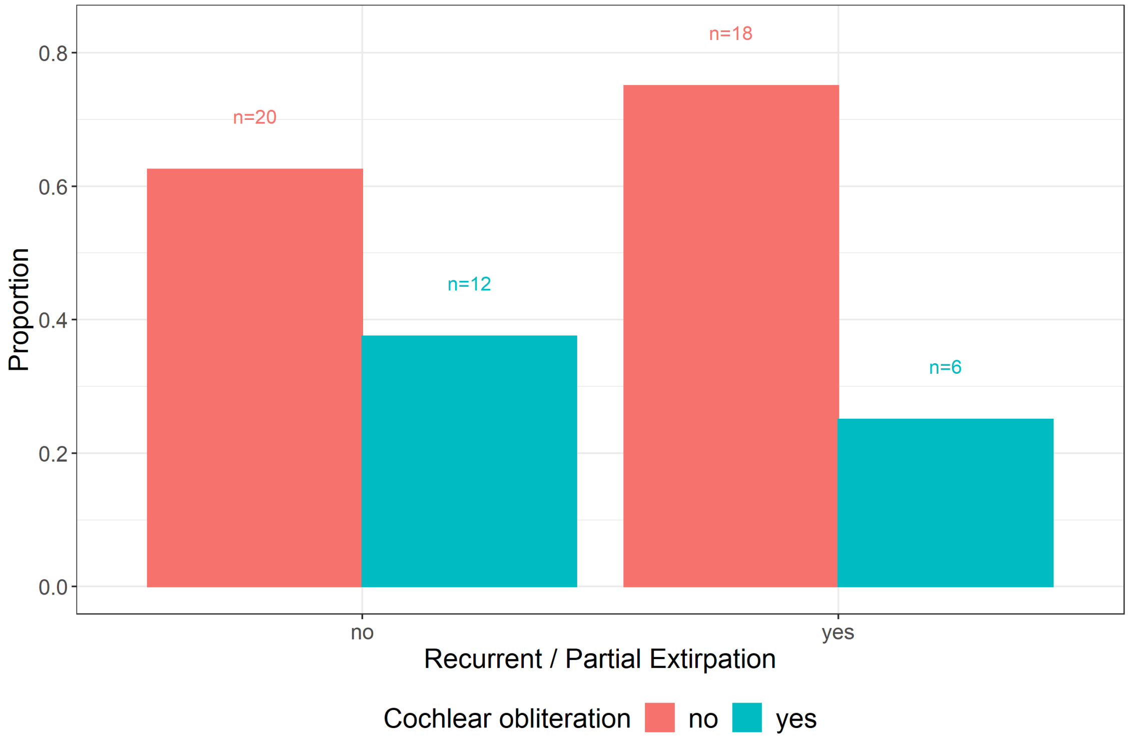
Figure 15►**Graphic 12**: Cochlear Obliteration and Concurrent Obliteration of Semicircular Canals



4.4.9. Reoperation

Revision or recurrent Operations have not accentuated the rate of cochlear obliteration due to Boschloo`s test. (p-value: 0.8; odds ratio 0.556; 95% confidence interval 0.173 to 1.788) (►**Graphic 13**)

Figure 16 / ►**Graphic 13**: Cochlear Obliteration in Relation to Reoperation



4.4.10. Duration of Follow-Up

The duration of follow-ups was determined. The results were depicted in the **graphics ►14 & 15.** A range of 1 to 78 months could be figured out.

Figure 17 / ►**Graphic 14**: Postoperative Follow-Up

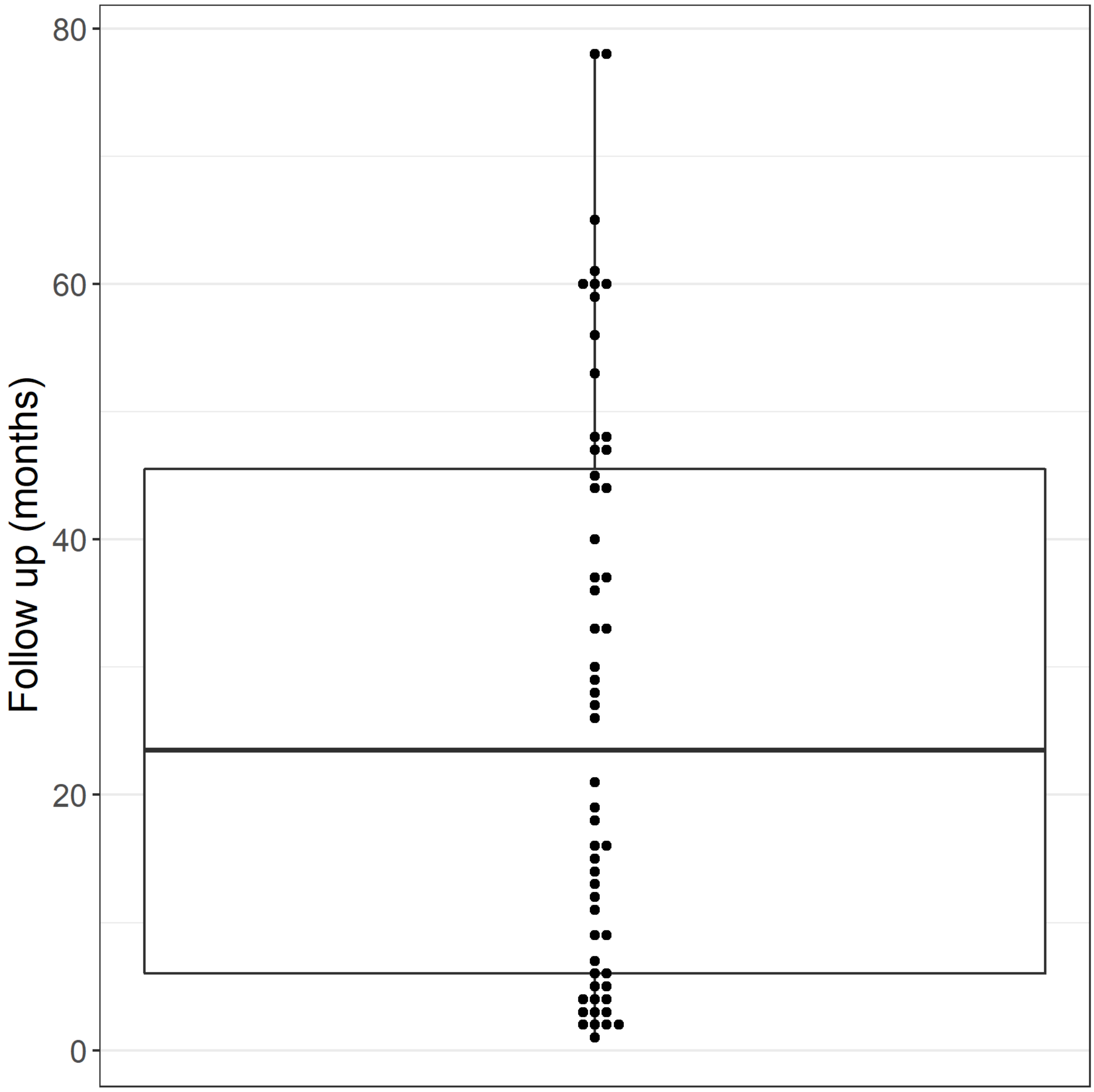
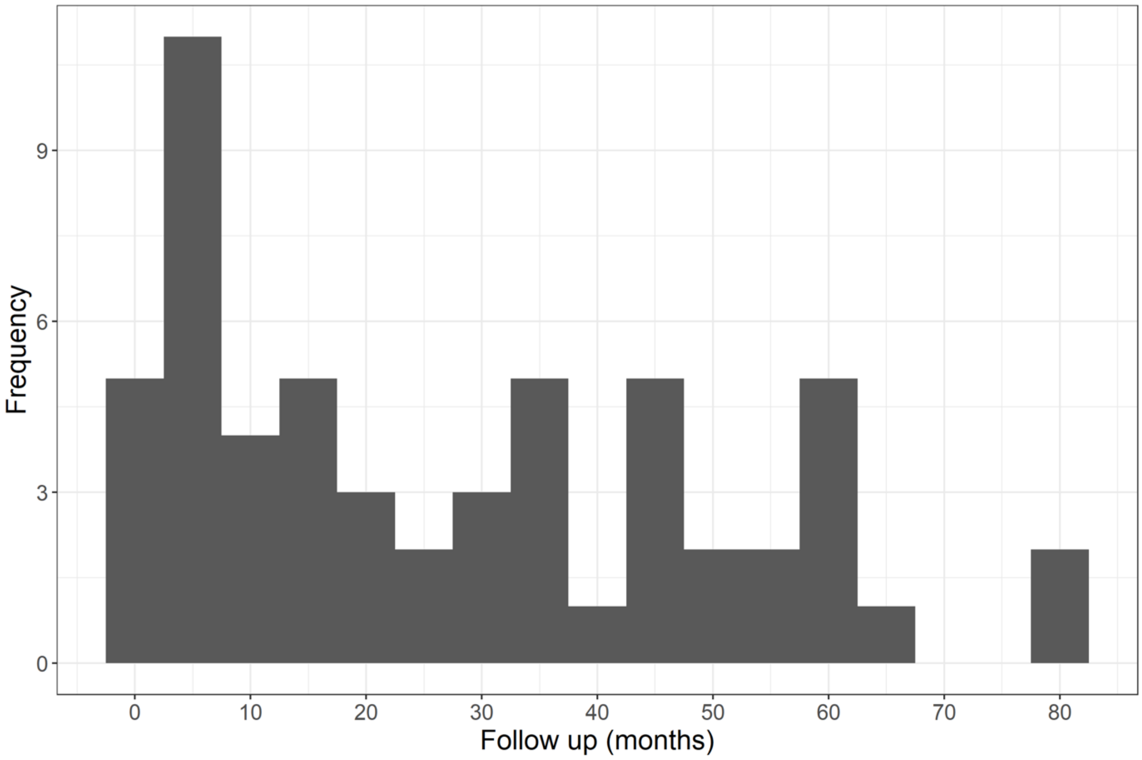


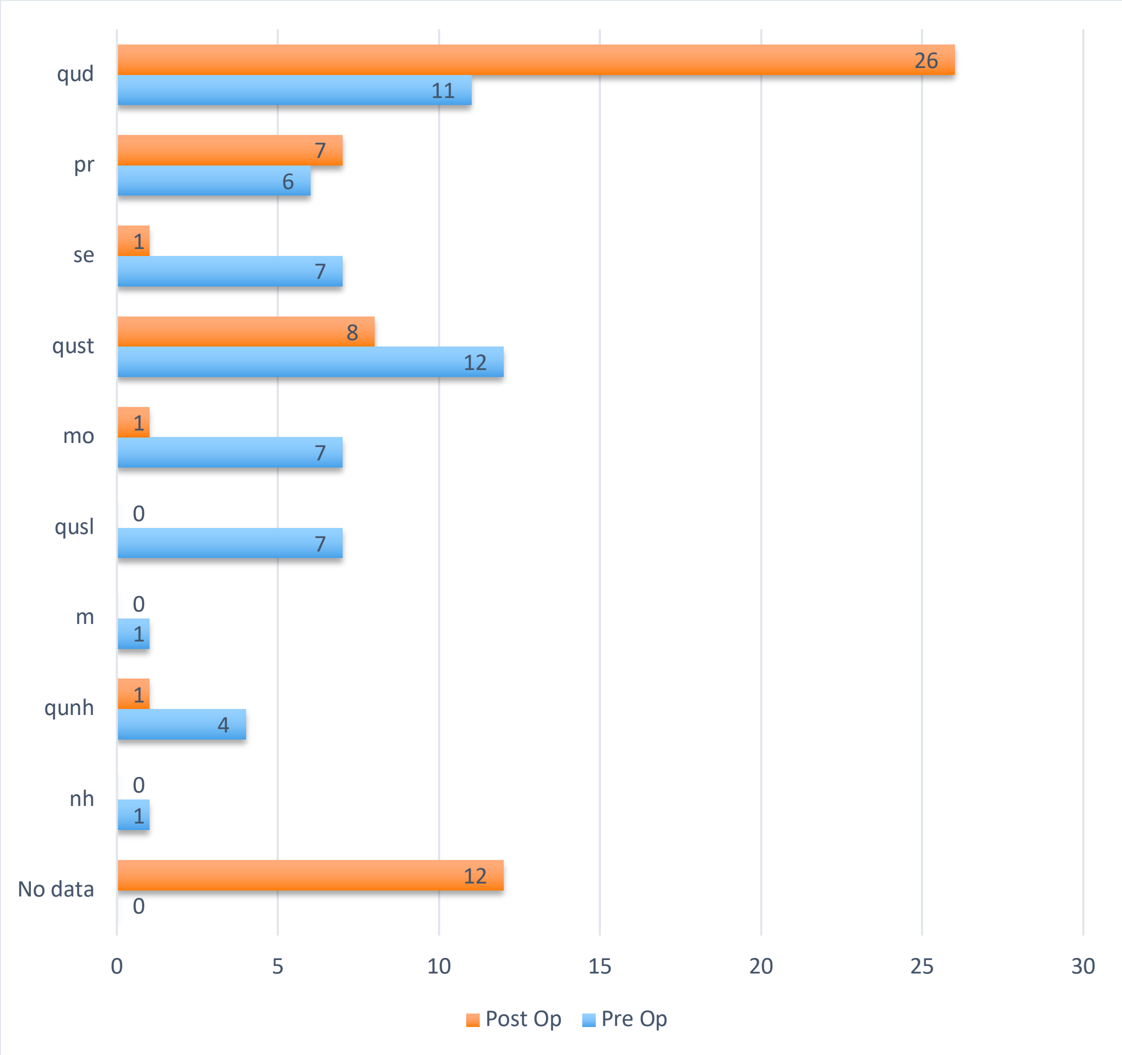
Figure 18/ ►**Graphic 15**: Distribution of Follow-Up Intervals (months)



4.4.11. Postoperative Hearing

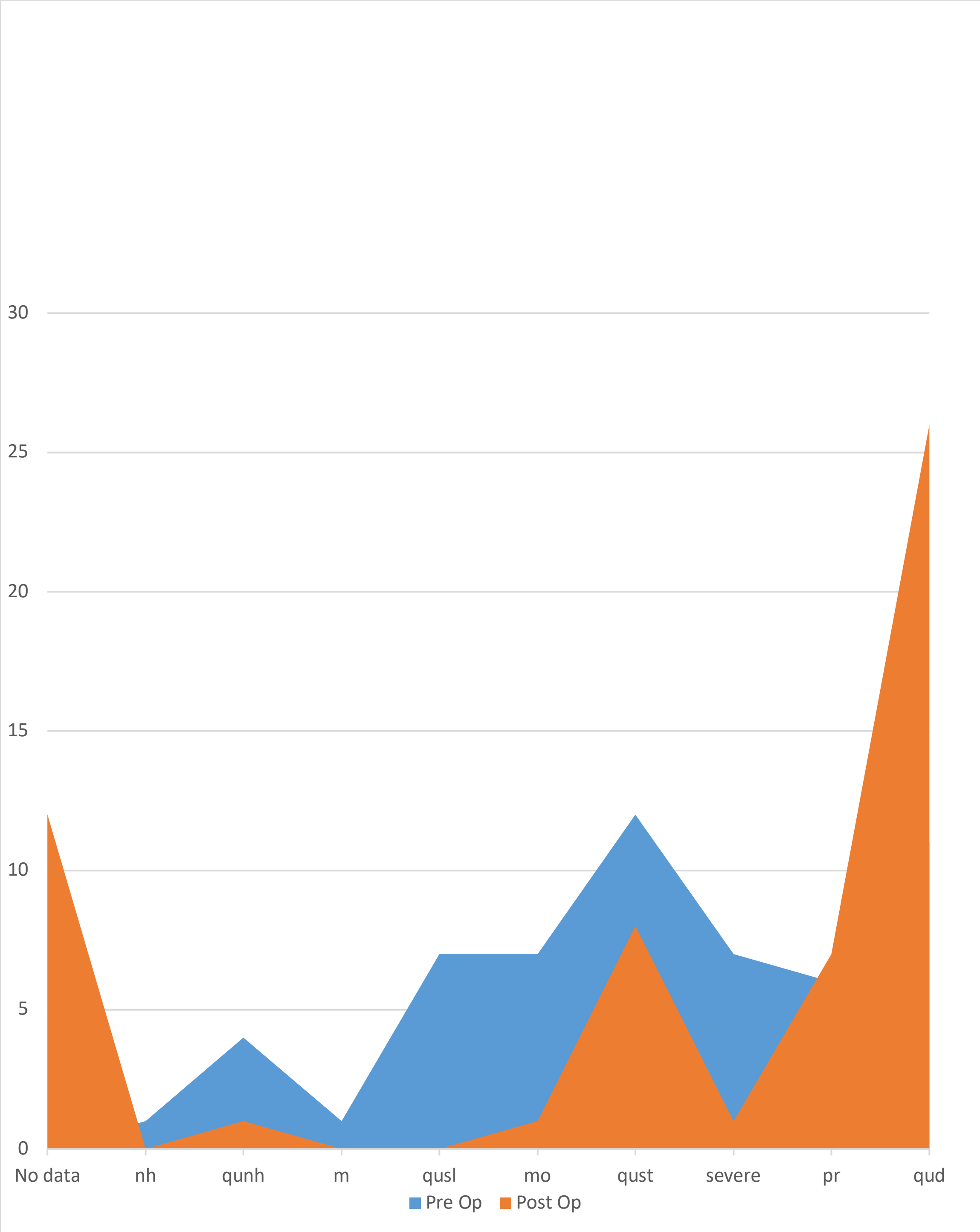
Finally, the deterioration of hearing capability is depicted comparing the pre- and postoperative hearing based on a modified ASHA hearing-classification. Since audiometric exams did not exist for all patients´ population postoperatively, we were obliged to modify this classification to include even those patients into the statistic, whose postoperative hearing capabilities were assessed exclusively by means of clinical evaluations. (►**Graphics 16 & 17**)

Figure 18 / **Graphic 16:** Pre-& Postoperative Hearing



►**Graphic 16:** Comparison between pre- and postoperative hearing. nh: normal hearing; qunh: quantitively inexactly defined normal hearing; m: mild hearing deterioration; qusl: quantitatively inexactly defined slight hearing deterioration; mo: moderate hearing deterioration; qust: quantitatively inexactly defined strong hearing deterioration; se. severe; pr: profound hearing deterioration; qud: quantitatively inexactly defined deaf

Figure 19 / **Graphic 17:** Pre- & Postoperative Hearing

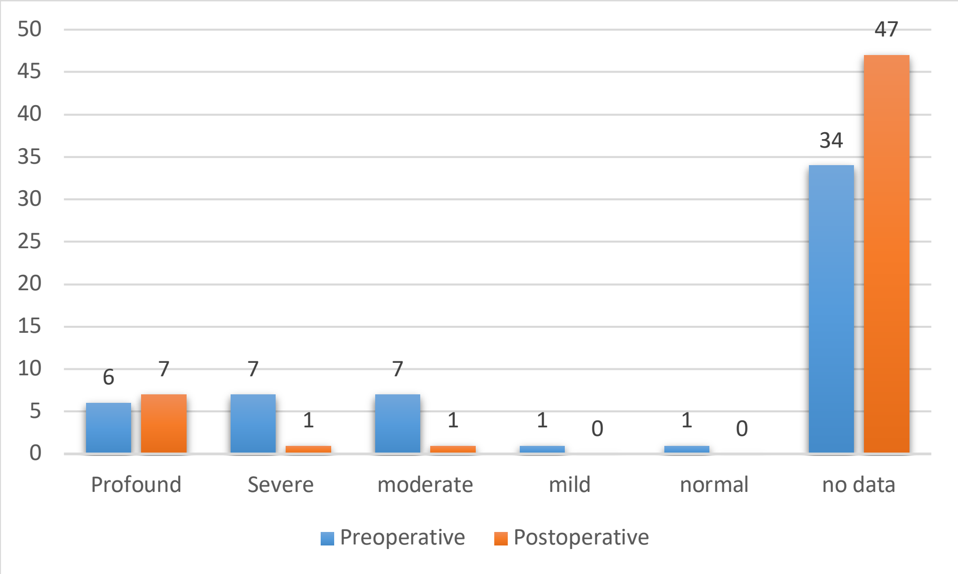


►**Graphic 17:** Comparisons of pre- and postoperative hearing capability according to a modified ASHA classification, nh: normal hearing; qunh: quantitively inexactly defined normal hearing; m: mild; mo: moderate; qusl: quantitively inexactly defined slight; mo: moderate; qust: quantitatively inexactly defined strong; pr: profound; qud: quantitively inexactly defined deaf

According to our data, a statistically significant conclusion could not be drawn due to the lack of pre- and postoperative audiograms in 60% and 84% of the patient populations, respectively.

(►**Graphic** 18)

Figure 20 / ►***Graphic 18***: Pre-& Postoperative Hearing According to Perioperative Audiogram



5. DISCUSSION

5.1. Patients´Collective and Study Design

This monocentric retrospective study primarily investigates the possible correlation between retrosigmoid approaches and postoperative cochlear obliteration in patients with vestibular schwannoma. Since postoperative hearing loss is not infrequently inevitable after such operations, the success of hearing restoration through CI-implantation depends heavily on an intact cochlea.[7] The aim of this study is the assessment of cochlear obliteration after retrosigmoid approaches as a basis for future randomized prospective studies. 56 patients (33 females, 23 males, median age: 53 years) were included in the study. In addition to cochlear obliteration many other characteristics like age, gender, tumor location, tumor diameter, operation duration, length of follow-ups, reoperations, obliteration of other parts of bony labyrinth and finally postoperative hearing status were also figured out.

5.2. General Considerations

Vestibular schwannomas can sometimes widen the osseous internal acoustic canal, within which the tumor is located, without necessarily compromising the facial nerve function. A similar phenomenon is frequently observed in neurinomas of the spinal root nerves. In our series, cochlear obliteration was detected preoperatively only in one case. Thus, explanations other than schwannoma for the pathogenesis of postoperative cochlear obliteration appear to be plausible. There are a few studies focusing on possible associations between VS operations and cochlear ossification or obliteration. We hypothesize that the surgical approach plays a key role in pathogenesis of CO potentially through mechanical, vascular, and thermal injuries.

5.2.1. Hearing Restoration

Apart from the existing consensus on the necessity of hearing-rehabilitative surgeries following VS operations[18], the selection of an appropriate hearing restoration procedure depends on several factors including the integrity of cochlear nerve and the patency of cochlea[6]. Despite "continuously improving results in ABI implantations, CI is still a better technique for restoration of hearing after VS-Operation, if the auditory nerve is preserved and if the cochlea is patent".[3] (Hedjrat, 2017) The positive results in hearing restoration through ABI after surgery of NFII-associated VSs in recent years have been attributed to "patient, surgical and device factors".[2] (Behr, 2014) Apart from positive developments in device technologies and in surgical techniques the length of deafness is also a deciding factor.[2] Neither patients' age nor the size of tumor could significantly affect the result.[2]

5.2.2. Cochlear Obliteration as an Obstacle to Subsequent CI- Implantation

In the literature, the counterproductive effect of an obliterated or ossified cochlea on the outcome of CI-implantation have already been discussed controversially. Although few authors did not exclude CI implantation in an ossified cochlea,[19] many have found the CI-implantation in presence of cochlear obliteration, if not impossible, at least highly challenging.[7] There exist some contradicting opinions concerning the effect of surgical approaches on cochlea, too. Klenzner et al. considered CI as "an effective solution to restore hearing in patients with SSD (single-sided Deafness) following translabyrinthine access to the skull base".[18] (Klenzner, 2019) On the contrary, West et al. found translabyrinthine approaches to be more susceptible to cause cochlear change postoperatively.[6]
"Beutner et al. succeeded to demonstrate how early the cochlear changes could happen, even as early as 3 months, after translabyrinthine approaches".[20] (Beutner, 2015) In another study, early postoperatively cochlear obliteration improves in later MRI exams in some of patients undergoing a surgical resection of VS.[21]

5.3. Possible Explanations for Postoperative Cochlear Obliteration in The Literature

5.3.1. Hypoxia and Hemorrhage in The Inner Ear

Many studies have focused on the pathophysiological effect of hypoxia on cochlear as a possible etiological explanation for postoperative cochlear obliteration. However, there is some disagreement among the authors regarding the onset and persistence of hypoxia´s adverse effects. Huibert Frans van Waegeningh et al. divided sensorineural hearing loss after VS removal into "retrocochlear or cochlear types".[7] (Huibert Frans van Waegeningh, 2020) "Cochlear type of sensorineural hearing loss could be caused by compromised cochlear microcirculation and cochlear hypoxia or by ototoxic signaling proteins that are released by the schwannoma itself".[7] (Huibert Frans van Waegeningh, 2020) "Surgically induced hemorrhages could in turn lead to hyalinization and atrophy of the stria.[7] (Huibert Frans van Waegeningh, 2020) Belal et al. concluded in his study from 1982 that "patients with profound postoperative deafness showed severe degenerative changes and ossification in the membranous labyrinth”.[22] (Belal, 1982) These adverse effects were attributed to the occlusion of internal auditory artery during or after surgery.[22]

“Fibrosis or ossification of the inner ear can arise from vascular compromise and inflammatory processes such as middle ear infection, meningitis, labyrinthitis, and sepsis”.[20] (C. Beutner, 2015) “Vascular occlusions were found to play an important role in the pathogenesis of cochlear obliteration even after inflammation”.[20] (Beutner, 2015) “Experimental occlusion of the labyrinthine artery in animals resulted in progressive fibrosis and osteogenesis”.[20] (C. Beutner, 2015) “Therefore, the neo-ossification does not only occur soon after surgically related injuries of the cochlea during translabyrinthine approaches and labyrinthectomie, but also after the middle fossa approaches”.[20] (Beutner, 2015)

5.3.2. Onset of cochlear obliteration: A Matter of Controversy

As mentioned above, there is growing consensus about the detrimental effects of surgical approaches on the cochlea, which can hinder subsequent hearing restoration. The next question is when these adverse effects occur and what the optimal time for a hearing restoration surgery might be. The onset of cochlear alterations has been discussed controversially in the literature. Warren III et al found in 30 % of patients underlying VS removal through subtemporal approaches delayed secondary hearing deteriorations over 5 years indicating that these alterations happen as an ongoing process.[10] There is ongoing controversy regarding the mechanisms responsible for both acute and delayed hearing deterioration. As previously mentioned, vascular compromise is among the most widely accepted explanations. Several operation-related factors have been proposed as causes of postoperative hearing loss, including “vascular compromise and physical trauma”.[10] (Warren, 2006) “It is known that sacrificing this arterial supply in the tumor dissection will lead to hearing loss “.[10] (Warren, 2006). “Hearing loss not only occurs suddenly during the course of an operation in translabyrinthine procedures attributed to surgical traumas, but a decrease in hearing is also observed over the time in majority of patients after a middle fossa or retrosigmoid approach with initial hearing preservation”.[20] (Beutner, 2015) West et al. demonstrated more frequent cochlear signal changes on postoperative MRI in translabyrinthine approaches compared to retrolabyrinthine ones (62% versus 11% respectively).[6] They attributed these MRI signal changes to compromised vascular supply.[6] According to Fiona C E Hill et al such changes appear to occur early after the translabyrinthine approaches..[23] They concluded that the CI “should ideally be performed either simultaneously with translabyrinthine surgery or as an early second-stage procedure to maximize the chance of successful electrode insertion”.[23] (Fiona C E Hill, 2018) Therefore, the implantation of a placeholder has been suggested by the authors.

On the contrary, Bejjen et al. concluded that there were “no significant differences between early (0–3 months) and late (>3 months) scanning” in patients with meningitis and hearing loss, “showing that radiological imaging soon after meningitis allowed early diagnosis” of cochlear obliteration.[24] (Beijen, 2009) Some other authors had again contradictory opinions concerning “the onset of cochlear obliteration that could occur until several years after VS surgery. However, signs of perilymphatic alterations are commonly observed during the early stages. The absence of these signs appears to predict a long-term patent cochlea. The onset of obliteration occurred within 2-7 months in post translabyrinthine patients”.[7] (Huibert Frans van Waegeningh, 2020) Hassepass et al. carried out a similar study focusing on the effects of CI in rehabilitation of hearing and in reducing tinnitus “in patients with single sided deafness after the translabyrinthine approaches” to vestibular schwannoma.[25] (Hassepass, 2016) Although the number of patients, in whom the CI-implantation was carried out, was critically low, they found CI beneficial and should preferably carried out simultaneously with primary tumor removing operation because of “the risks of intracochlear placeholder insertion and the inherent limitations for ongoing MRI investigation of VS recurrence”.[25] (Hassepass, 2016)

These diverse and partially contradictory findings promoted us to evaluate cochlear changes in our patient cohort following retrosigmoid approaches. Our aim was a statistical analysis of cochlear obliteration after such approaches.

5.4. Results

5.4.1. Cochlear Obliteration

38 patients (68%) showed no obliteration after the retrosigmoid operations in our study. Cochlear obliteration occurred in 18 Patients (32%); therefore, this possibility should be considered when planning a surgery via a suboccipital retrosigmoid approach. Cochlear obliterations was significantly more frequent in cases with concurrent obliteration of the semicircular canals and vestibule (►**Graphic 11**). Even higher rates of obliteration were detected in semicircular canals, a finding that has been reported in another study.[7] Since translabyrinthine approaches are logically more invasive to the labyrinthine structures, they are expected to result in greater cochlear obliteration compared to retrosigmoid approaches. This estimation is supported by comparisons with findings from other studies. (►**Table 7**)

Table 7: Rates of postoperative cochlear obliteration reported in other studies

Study	Approach	Number of patients	Postoperative cochlear obliteration
West et al.[6]	translabyrinthine	74	62 %
Van Waegeningh HF et al.[7]	translabyrinthine	25	84 %
Van Waegeningh HF et al.[7]	retrosigmoid	55	20 %
Buenter et al.[20]	translabyrinthine	26	55,5%
Y Feng et al.[21]	retrosigmoid	20	30 %
Y Feng et al.[21]	translabyrinthine	20	50 %
Y Feng et al.[21]	middle fossa	20	5 %
Delgado-Vargas B et al.[26]	translabyrinthine	41	78 %

5.5. Study Variables

According to our data, there were no statistically significant differences between patients with and without cochlear obliteration in term of age, tumor diameter, operation duration, recurrent operations, or the length of follow-up.

However, a borderline p-value of 0.09 suggests that female patients may be more frequently prone to cochlear obliteration.

5.5.1. Duration of The Follow-Up

The median follow-up duration was of 23.5 months, with no statistically significant difference observed between patients with and without cochlear obliteration. Specifically, the median follow-up interval in cochlear obliteration group was 26 months, compared to 29.5 months in the group without obliteration (►**Table 5**). As only the most recent postoperative MRIs were evaluated, our study could not address the timing or progression of postoperative cochlear obliteration.

5.5.2. Impact of Mechanical Trauma in The Pathogenesis of Cochlear Obliteration

Posterior semicircular canals were obliterated nearly five times more frequently than the other canals in the subgroup with cochlear obliteration in our study (►**Graphics 11 & 12**). The reason for this heightened susceptibility of semicircular canals, particularly the posterior one, remains unclear. A notably high rate of co-occurrence between posterior semicircular canal and cochlear obliteration was observed. One possible explanation lies in the mechanics of retrosigmoid approach. Drilling of the posterior lip of internal acoustic meatus is an inherent part of this technique. Vibrational trauma generated during drilling may play a significant role. Additionally, the posterior semicircular canal lies directly lateral to the posterior lip of the meatus, making it particularly vulnerable to mechanical and/or thermal injury during bone removal in this region. In our opinion, the frequent involvement of the posterior semicircular canal supports the hypothesis of possible correlation between cochlear obliteration and localized surgical trauma. Due to its anatomical proximity to the internal acoustic canal, the posterior semicircular canal appears to be more susceptible to approach-related injuries than the other labyrinthine structures during retrosigmoid procedures.

In contrast, neither tumor size nor operation duration was significantly associated with an increased incidence of cochlear obliteration in our study (►**Graphic 10**). Surprisingly, even recurrent operations showed no statistically significant effect on the rate of cochlear obliteration. (►**Graphic 13**) In case of reoperation, the internal acoustic canal had already been opened during the primary procedure, potentially reducing the need for extensive redrilling. Therefore, we assume that additional mechanical trauma may not necessarily occur during reoperations. Importantly, there was no selection bias related to reoperations, as all patients included in the study exhibited no preoperative cochlear obliteration. Nevertheless, these findings can challenge the notion that mechanical trauma alone accounts for approach-related cochlear obliteration and highlight the need for a more precise reassessment of roles of tumor size and reoperation in the pathogenesis of cochlear obliteration.

Mechanical trauma is undoubtedly of critical importance in preserving the facial nerve. However, its role in the development of the labyrinthine injury has been underestimated and, based on our findings, warrants greater emphasis. Factors such as the bone drilling, the use of irrigation during drilling, the application of bone wax, and precise volumetric assessment of tumor size may all influence the extent of labyrinthine trauma and should be investigated further. In our cohort, tumors with both intra- & extrameatal extensions were predominant in both subpopulations. Due to low number of cases with exclusively intrameatal tumors, no statistically significant conclusion can be drawn regarding the relationship between tumor location and cochlear obliteration (►**Graphic 5**).

5.5.3. Hearing Vulnerability

Finally, we compared pre- and postoperative hearing outcomes. According to our data, postoperative hearing deterioration occurred in 44% of patients. In an additional 21% of cases, postoperative comparisons could not be performed due to the absence of precise audiometric assessments. Nevertheless, these findings highlight the vulnerability of cochlear nerve during vestibular schwannoma (VS) surgery. In other words, hearing improvement is not a realistic goal of VS surgery and should not be considered a primary objective of the procedure. (►**Graphic 16 & 17**) It is important to note that this conclusion is based primarily on clinical estimations rather than standardized postoperative audiometric assessments. As a result, no statistically significant implications can be drawn from our data.

5.6. Conclusion

In this retrospective study, 32 % patients, who underwent suboccipital retrosigmoid for vestibular schwannoma (VS) exhibited some degree of cochlear obliteration.[3] Factors, such as age, reoperation, tumor diameter and duration of the operations were not found to significantly influence the rate of cochlear obliteration.[3] Nevertheless, “cochlear obliteration was more common in females” in the studied population.[3] (Hedjrat, 2017) (P-value: 0.09; odds ratio: 2.34 with 95% confidence interval (CI) between 0.696 and 7.864) The obliteration of semicircular canals and vestibule was the only variable significantly associated with increased rate of cochlear obliteration (p-value: 0.002; odds ratio: 12.36 and confidence interval 95 % between 1.49 and 102.71). Therefore, the potential for cochlear obliteration should be carefully considered when planning surgical resection of VS via the suboccipital retrosigmoid approach. Cochlear obliteration was significantly more frequent in cases exhibiting concurrent obliteration of semicircular canals and vestibule (►**Graphic 11**). Notably, even higher rates of obliteration were observed in semicircular canals. A similar finding has been reported in a previous study.[7] The underlying reason for the increased susceptibility of the semicircular canals to obliteration remains unclear and warrants further investigation. The Posterior semicircular canal lies directly lateral to the posterior lip of the meatus and is particularly vulnerable to mechanical and/or thermal injury during drilling the posterior bony lip. In our study, the posterior semicircular canals were obliterated approximately 5 times more frequently than the other semicircular canals and vestibule in patients with cochlear obliteration (►**Graphics 11 & 12**). In our opinion, this co-occurrence of posterior semicircular canal involvement and the cochlear obliteration supports the hypothesis of possible correlation between cochlear obliteration and labyrinthine trauma. Due to the proximity of the posterior semicircular canal to the internal acoustic canal, it is likely more susceptible to approach-related injuries than the other labyrinthine structures during retrosigmoid procedures. Since the translabyrinthine approaches are inherently more invasive to the labyrinthine structures, they are expected to result in higher likelihood of cochlear obliteration than retrosigmoid ones. (►**Table 7**) Nevertheless, the assessment of tumor size and reoperation showed no significance in generation of cochlear obliteration.

Although “a relatively high rate of cochlear obliteration” following the retrosigmoid approaches has been recognized in this study, “retrosigmoid approaches are still safer” than translabyrinthine ones concerning the rate of cochlear obliteration and consequently the chance hearing restoration.[3] (Hedjrat, 2017) Translabyrinthine approaches are well-known for not being hearing protective.[27,28] The objective of this study was to search for the frequency of cochlear obliteration which has turned out to be surprisingly high after retrosigmoid approaches. Nevertheless, this rate is still lower than those with translabyrinthine approaches (►**Table 7**). Even if the cochlear nerve is preserved during the operation, the long-term safety of hearing preservation after retrosigmoid approaches cannot be taken for granted. Therefore, regular postoperative clinical exams of such patients are advisable. They enable physicians to recognize and to treat patients´ hearing deterioration in time. Our study was not a prospective, controlled, and randomized one. Retrospective studies could be principally afflicted with a selection bias. Although retrosigmoid approaches remain more hearing protective comparing to translabyrinthine ones,[20,27,28] this study should perhaps draw attention to consider the revision of the belief that retrosigmoid approaches would be safe concerning postoperative cochlear obliteration. It remains still to clarify which factors contribute to initiate and to maintain the postoperative obliterating process in inner ear. Should cochlear obliteration occur after a retrosigmoid approach, when would be the optimal time for a CI-Implantation? All these questions could be subject to future randomized controlled studies.

5.7. Study Limitation

- Due to the retrospective method, a selection bias cannot be ruled out.

- Volumetric assessments of the tumors could have probably provided a more thorough estimation of the tumor size comparing to one-dimensional ones.

- The pre- and postoperative CT scans could not be carried out routinely because of the retrospective method of the study and from the ethical consideration regarding the radiation exposure. Hence, the differentiating between cochlear fibrosis und ossification was not possible. A cochlear ossification would be logically more challenging in case of a CI-implantation; therefore, the differentiation could be of importance for further hearing restoration.

- Lack of speech audiometric exams as a parameter for the assessment of neural auditory function.

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7. Appendix

7.1. Figures & Tables

8. PUBLICATION OF RESULTS

A.R. Hedjrat, K. Schwager, E. Hofmann, R. Behr Postoperative Cochlear Obliteration after Retrosigmoid Approach in Patients with Vestibular Schwann*oma*, J. of neurosurgery B, 2015 September; *DOI https://doi.org/10.1055/s-0037-1608649. ISSN 2193-6331.*