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**Skull base surgery**

# Early surgery and definitive cure in small sporadic vestibular schwannoma

## *Chirurgia precoce e guarigione definitiva nel piccolo schwannoma vestibolare sporadico*

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SUMMARY

**Objective**. To report surgical outcomes of a cohort of small sporadic vestibular schwannoma and discuss the role of early surgery.

**Methods**. Retrospective descriptive analysis of 234 consecutive patients with small vestibular schwannoma operated on with translabyrinthine or hearing preservation surgical approaches. Outcome measures were control of disease, postoperative facial nerve function, complications and hearing outcome.

**Results**. A translabyrinthine approach was performed in 59% of cases, hearing preservation surgery in 40% and transmeatal approach in 1%, respectively. Complete resection was achieved in 100% of cases. Overall, postoperative major and minor complications were 8.5% in the series, with complete recovery and no sequalae. Facial nerve function at one year postoperatively was House-Brackmann scale (HB) 1-2 in 95% of cases. The rate of hearing preservation was 70% A-B-C classes of Tokyo classification and 77% AB classes of AAOHNS classification.

**Conclusions**. Early surgery in small vestibular schwannoma is a valid option, due to good functional outcomes, low morbidity and definitive cure. Early surgery is associated with better outcomes when considered in relation to non-surgical treatments reported in the literature.

KEY WORDS: vestibular schwannoma, definitive cure, early surgery, translabyrinthine surgery, hearing preservation surgery

RIASSUNTO

***Obiettivo.*** *Presentare i risultati chirurgici di una serie di piccoli neurinomi sporadici e discutere il ruolo della chirurgia precoce nel trattamento.*

***Metodi.*** *Analisi retrospettiva e descrittiva di 234 pazienti affetti da piccolo schwannoma vestibolare operato con approccio translabirintico o chirurgia di preservazione dell'udito (HPS). I risultati sono discussi alla luce del controllo di malattia, della funzione postoperatoria del nervo facciale, dell'insorgenza di complicanze e della preservazione uditiva.*

***Risultati.*** *L'approccio translabirintico è stato eseguito nel 59% dei casi, HPS nel 40% e quello transmeatale nell'1%. La resezione completa è stata ottenuta nel 100% dei casi. Si sono osservate complicanze postoperatorie nell'8,5% dei casi, risoltesi con completa guarigione e assenza di sequele. La funzione del nervo facciale a 1 anno dall'intervento è stata I-II HB nel 95% dei casi; il tasso di conservazione dell'udito del 70% in classe A-B-C secondo la classificazione di Tokyo e del 77% in classe A-B secondo la classificazione AAO-HNS.*

***Conclusioni.*** *La chirurgia precoce nel piccolo schwannoma vestibolare si è rivelata essere un'opzione conveniente in alternativa alle terapie non chirurgiche, considerate nell'intero corso della terapia, in ragione dei risultati, della bassa morbidità e della guarigione definitiva.*

PAROLE CHIAVE: *piccolo schwannoma vestibolare, chirurgia precoce, chirurgia translabirintica, chirurgia di preservazione dell'udito, guarigione definitiva*

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## Introduction

Small vestibular schwannoma (VS) is defined as a tumour of less than or equal to 10 mm in size in the cerebello-pontine angle (CPA) and to a various extent in the internal auditory canal (IAC) [1,2]. Use of high-resolution magnetic resonance imaging (MRI) in the diagnosis of unilateral hearing loss or vestibular dysfunction has allowed small vestibular schwannoma to be diagnosed with higher frequency than in the past. The current challenge is to promote a treatment where early diagnosis allows no further functional losses, definitive cure, and least impact on the healthcare system. Observation, surgery, and radiotherapy are the therapeutic options, but their indications are a matter of ongoing debate [3-7]. The short and mid-term outcomes favour both observation and radiotherapy, but it gradually emerged that the outcome must include both the long-term [8,9] and the full course of therapy, including surgery, in failures [10-12]. As additional data on non-surgical therapies is being made available, a change in the current trends is emerging [13-15].

The aim of this study was to present a consecutive series of patients treated for small VS with a translabyrinthine (TLAB) approach or hearing preservation surgery (HPS). We also aim to offer a contribution to the debate on therapy in small vestibular schwannoma and combine our and the literature data to reappraise the role of surgery in small tumours.

## Materials and methods

*Population*

Data on 234 consecutive patients diagnosed with small (i.e., intrameatal tumours or lesions with ≤10 mm extension in the CPA) VS and treated surgically were retrieved from a prospectively maintained database and retrospectively analysed for this study. Clinical, surgical, and radiological data were obtained.

Patients were all operated on by the same team (A.M., E.Z., D.d'A., L.D.) between 1973 and 2021. Tumour size was the inclusion criterion: only small VS were included. Tumour size was preoperatively measured as the largest diameter (mm) in the CPA on contrast enhanced T1 sequences for extrameatal lesions, and as the maximal tumour length for intrameatal ones [2]. For diagnoses between 1980 and 1990, tumour measures were performed using contrast-enhanced CT.

Patients with neurofibromatosis type 2, intralabyrinthine VS, previously irradiated VS, and CPA/intrameatal lesions other than VS were excluded.

*Surgical procedure*

All the selected patients were surgically treated with TLAB, or transmeatal, or retrosigmoid approaches. The latter encompassed the retrolabyrinthine meatotomy, a modification of the procedure for hearing preservation purposes [16,17]. Intraoperative continuous facial nerve electromyography (EMG) monitoring was adopted with NIM-Response 3.0, Medtronic Xomed Inc. Intraoperative hearing was monitored with NIM-Eclipse, Axom Medtronic Inc.

*Outcomes*

Completeness of tumour resection, peri- and postoperative complications, facial nerve and hearing function were the main outcomes. Tumour resection was assessed intraoperatively and at 1, 3, 6, and 10 years postoperatively with contrast-enhanced MRI. We defined as postoperative major complications brain or cerebellar edema/infarction, hydrocephalus, intracranial hypertension, symptomatic dural venous sinuses thrombosis, 5$^{th}$, 6$^{th}$, 9$^{th}$-11$^{th}$ cranial nerve impairment, meningitis, nasal cerebrospinal fluid (CSF) leakage requiring revision surgery and extradural haematoma requiring evacuation. Minor complications were wound CSF leakage and nasal CSF leakage treated conservatively, and haematoma in the abdominal site of fat harvesting.

Facial nerve outcome was evaluated at discharge and 12 months after surgery. It was graded from I to VI according to the House-Brackmann (HB) scale [18]. HB Grades I and II corresponded to good facial nerve function.

In the group of patients submitted to HPS, preoperative hearing of "in-protocol" cases designated ≤ 30 db PTA, ≥ 70 SDS and normal or slightly altered auditory brainstem responses (ABR).

Hearing was measured with pure tone average (PTA) at 0.5, 1, 2 and 4 KHz, and speech discrimination score (SDS). Hearing was classified according to the American Academy Otolaryngology-Head and Neck Surgery (AAO-HNS) [19] and the Tokyo B [2] classifications. According to the Tokyo classification, in classes C, D, E, F "a better speech discrimination score class than the PTA class made the category of the patient one class better". This means that a 31-40 PTA with > 70% SDS upgrades class C to B, a 41-60 PTA with > 60% SDS upgrades class D to C.

## Results

Two hundred and thirty-four patients met the inclusion criteria and were enrolled in the study. The mean age at surgery was 52.4 years (range 10-77), and 50.8% were female. Sixty-one cases (26.0%) were diagnosed with intrameatal VS and 173 (74.0%) with extrameatal tumours (mean tumour size in the CPA 6.9 mm, range 1-10 mm). Tumour characteristics are presented in Table I. A TLAB approach was the procedure used in 138 cases (59.0%), HPS in 94 (40.0%) and transmeatal in 2 (1.0%). Cochlear implantation was performed in 11 cases (4.8%), 10 in TLAB ap-

**Table I.** Tumour characteristics.

| | N (%) | Tumour size (mm) |
|---|---|---|
| Intrameatal tumours | 61 (26) | Mean (7.63)<br>Median (8)<br>Range (3-13) |
| Extrameatal tumours | 173 (74) | Mean (6.9)<br>Median (8)<br>Range (1-10) |
| Total | 234 (100) | |

proach (simultaneous in 5 and sequential in 4), and one in HPS failure. Radiological and clinical follow-up was available for all patients. Two patients, one HPS and one TLAB, had less than 1 year follow-up and were excluded by clinical evaluation of facial nerve/hearing outcomes.

Complete gross tumour resection was achieved in 100% of cases, but three recurrences were observed over the years in patients with HPS (overall 1.3%; 3% of HPS subgroup of patients); two were operated on with a revision HPS with hearing preserved in one case, and one with a TLAB approach.

Overall, 8.5% of cases (20 patients) experienced major (5.1%, 12 cases) and minor (3.4%, 8 cases) postoperative complications. No events such as death, intracranial haematoma, or meningitis were observed. Major complications are reported in detail in Table II. Minor complications (8 cases, 3.4% in all the series) were transient retroauricular wound swelling and abdominal haematoma at the site of fat-graft harvesting in the TLAB procedures. All patients with major and minor complications recovered completely and no sequalae were observed.

Facial nerve function at 12-months postoperatively was: grades I-II HB in 95.0% of cases (220/232), grade III in 3.9% (9/232) and grade V and VI in 0.9% (2/232) and 0.4% (1/232) of cases respectively. The cases with ≥ III° HB facial nerve included those with intraoperative loss of continuity and immediate reconstruction with graft (2%, 5 cases).

Details on facial nerve outcomes are shown in Table III. I-II HB facial nerve function did not show a significant difference between the surgical procedures (translabyrinthine *vs* HPS, p = 0.118) and the subsites of tumour extension (purely intrameatal *vs* intra-extrameatal, p = 0.233).

As for hearing outcomes, in the HPS "in protocol" cohort, postoperative class A of AAO-HNS and class AB of Tokyo designating "good" hearing were, respectively, 30.0% (20/65) and 49.0% (32/65). Class AB of AAO-HNS designating both "good" and "serviceable" hearing was 76.0% (42/62), class AB of Tokyo, inclusive of B upgraded to C (with PTA between 30 and 40 dB and > 70% SDS), designating both "good" and "socially useful" hearing, was 71.0% (44/62).

## Discussion

Over 50 years of microsurgery as well the long experience with radiotherapy and observation are expected to offer sufficient data to indicate the most appropriate treatment for small vestibular schwannoma [4,6,7]. The surgical outcome has been known for decades [20] and recently improved to the present levels [14,15]. The outcome of observation and radiotherapy took more time to assess mid- to long-term growth as it was to include the result of the full course of therapy, that is of secondary surgery in failures due to growth of the observed or radiated tumour [10-12]. This changed the balance between the three options, i.e. observation, radiotherapy and microsurgery, as follows.

1) Observation has been a widely used first-line treatment in small-medium size tumours [9,21] and was based on the assumption that most small tumours do not grow [21]. This supported the choice of wait and see protocols in small tumours, although the unpredictability of growth required continual control. A more accurate volumetric measurement of tumour size showed a 65% growth rate [22] and changed our view on the natural history of small vestibular schwannoma. Moreover, the results of surgery on small tumours are superior to those of medium-large tumours [5,14,15,20]. An

**Table II.** Major complications.

| Description | N (%*) | Surgical procedure (%‡) | Treatment | Outcome |
|---|---|---|---|---|
| Transient cerebellar oedema with hydrocephalus and partial sigmoid sinus thrombosis | 1 (0.4) | 1 HPS (1) | Transient external ventricular drain | Complete recovery |
| Nasal CSF leakage | 7 (3) | 5 HPS (5)<br>2 TLAB (1.4) | Surgical revision or/and transient lumbar drain | Complete recovery |
| Wound CSF leakage | 1 (0.4) | HPS (1) | Surgical revision and transient lumbar drain | Complete recovery |
| Late transient temporal oedema | 1 (0.4) | 1 HPS (1) | Medical treatment | Complete recovery |
| Wound extradural haematoma | 2 (1.5) | 2 HPS (2) | Surgical drain | Complete recovery |

*CSF cerebrospinal fluid; HPS hearing preservation surgery; TLAB translabirintine.*
** % of all procedures (N = 234). ‡% of the considered procedures: HPS (N = 94) or TLAB (N = 138).*

**Table III.** Postoperative facial nerve function; cases that required intraoperative reconstruction (n = 5, 2%) are included.

| Facial nerve grading (H-B) | All cases N (%) | TLAB/ Trans meatal N (%) | HPS N (%) | Extrameatal tumours N (%) | Intrameatal tumours N (%) |
|---|---|---|---|---|---|
| I | 197 (84.91) | 110 (79.14) | 87 (93.55) | 140 (81.40) | 57 (95.00) |
| II | 23 (9.91) | 19 (13.67) | 4 (4.30) | 21 (12.21) | 2 (3.33) |
| III | 9 (3.88) | 7 (5.04) | 2 (2.15) | 8 (4.65) | 1 (1.67) |
| IV | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| V | 2 (0.86) | 2 (1.44) | 0 (0) | 2 (1.16) | 0 (0) |
| VI | 1 (0.43) | 1 (0.72) | 0 (0) | 1 (0.58) | 0 (0) |
| Total | 232 (100) | 139 (100) | 93 (100) | 172 (100) | 60 (100) |

*TLAB: translabyrintine; HPS: hearing preservation surgery.*

argument against the observational strategy is that growth during observation leads to surgery on a larger tumour and worse facial nerve outcomes [13]. Facial nerve outcomes were compared based on initial treatment strategy, so that patients operated on at diagnosis with primary surgery were compared with patients allocated to conservative management and operated on after established tumour growth. The conclusion was that surgical treatment was to be administered as soon as growth was established irrespective of tumour size. This radically changed the authors' previous indication to wait and see protocols. The recent literature [14,15] points to the fact that 1 cm in the CPA is the critical size allowing good preservation of the facial nerve. Allocating a 1 cm tumour to observation involves a higher risk of impaired facial function in the case of delayed surgery. The benefits of early surgery on small (< 1 cm) *vs* medium-sized tumours (between 1 and 2 cm) was also evident in our experience[15] when facial nerve outcomes were compared between the two groups wherein surgery on small tumours offered excellent rates of functional preservation. Our conclusion was that early surgery on a small, growing tumour was a viable alternative to observation.

2) Radiotherapy (RT) is an active treatment alternative to surgery. The use of RT irrespective of tumour growth, with the goal of preventing growth in a potentially non-growing tumour, was the commonest therapy until the recent, infrequent switch to radiate the tumour after growth is observed [23]. Lerner [12] reported on the outcomes of primary radiotherapy on the facial and other cranial nerves in small-medium size tumours; the 5.3% rate of short-term facial paresis evolved to persistent facial impairment in 4% of cases. Intrameatal tumours with extension to the fundus appeared to be at higher risk for post-treatment facial paresis, as the most fragile labyrinthine tract was exposed to radiation, not differently from the cochlea. The effects of temporary tumour enlargement after radiotherapy in intrameatal tumours were also reported [24] but the issue on radiation outcomes other than growth in a small, growing tumour has hardly been investigated. Comparing surgery and RT with the currently available data shows that both therapies have suboptimal results with small differences in rates. The key point is that data on facial nerve preservation and other complications after primary radiotherapy do not include the outcome of secondary surgery in failures. Poor outcomes both on facial nerve function (66% of facial nerve impairment) and incomplete resection [11] have been reported. Preservation of facial nerve is considered a burden of salvage surgery in irradiated patients [10-12], whereas the importance of definitive cure of the disease to our knowledge has never been discussed in literature. Tumour control was the term used for non-surgical treatments.

3) Microsurgery, in our experience, allowed preservation of I-II HB facial nerve function in 95% of cases, and HB > 3 in 5% including cases with nerve graft due to intraoperative loss of continuity (Tab. III). These results support the role of primary surgery in small growing tumors, as recently reported in the literature [14,15]. If such results are compared with the facial nerve outcomes after failed observation or radiotherapy, in which the poor facial nerve outcome after salvage surgery adds up to the loss due to the primary treatment, early proactive surgery [14,15] appears to be a preferable alternative to the non-surgical therapies.

TLAB and retrosigmoid approach with retrolabyrinthine meatotomy were the microsurgical procedures, apart from the few transmeatal approaches. Indications for TL or HPS were based on hearing, age/surgical risk and the patient's desire. The cases with at least 30 PTA and 70% word recognition score (WRS), with normal or slightly abnormal ABR, were submitted to HPS [16]. Cases with poorer hearing were observed and after assessing growth were submitted to TLAB surgery, but two cases to the transmeatal approach. As for surgical complications, the TL group presented an uneventful postoperative course with quick recovery in all but one case (0.7% of TLAB cases and 0.4% of the entire series), where a vasogenic temporal oedema occurred, evolving to complete recovery. In the HPS group, two ex-

tradural haematomas (2.1% of the HPS) were treated with surgical evacuation, and one case of transient hydrocephalus for cerebellar oedema was successfully treated with temporary ventricular drain. Recurrence from residual tumour in HPS treated with revision surgery occurred in the first 50 cases, and it did not with the last meatotomy technique that provided control of the distal extent of the tumour [17]. No case in the series presented permanent sequalae after these major complications. To our knowledge, the reported rates of permanent complications in a small-medium sized tumour after primary radiotherapy involved hydrocephalus requiring ventriculo-peritoneal drain in 4-6% of cases and permanent multiple cranial nerves dysfunction (cochlear, facial, trigeminal, lower cranial nerves) in 24.5% of cases, in 2% of cases permanent > 3 HB facial nerve loss of function [12]. If the mentioned upfront postsurgical complications are compared with the complications of first-line radiotherapy and especially of secondary surgery [10-12], the balance appears to point to a more favourable outcome of primary surgery. In the group of HPS patients, serviceable hearing preservation was successful in 71% and 76% of the "in-protocol" cases, according to the two classification systems [2,19]. The rate decreased to 23% in the "off-protocol cases" in both classifications. This is likely to support the principle that HPS is expected to provide better long-term hearing results than conservative therapies, such as 23% of preserved A-B AAOHNS class at 10 years in observation [9], and 34% in radiotherapy [8]. Within this perspective, HPS seems to comply with the statement "the only reason for active treatment (surgery or radiotherapy) is attempted hearing preservation" [9] and seems to be a realistic goal. In the other cases of small tumours, when HPS is deemed to have an unsuccessful outcome, observation remains the choice and, if growth is assessed, a prompt shift to TL surgery is recommended. Cochlear implant (CI) rehabilitation is considered in the case of preserved cochlear nerve [25] in early TL and failed HPS cases, whereas hearing aid rehabilitation can be an option in preserved-hearing cases. In clinical practice, when should surgery be performed for a small tumour? If hearing is the goal, growth is disregarded and HPS is advised at the shortest time after diagnosis with the already mentioned hearing parameters. When hearing is not preservable and growth is assessed, translabyrinthine surgery is advised when tumour gets close to 8-9 mm in size. The main weakness of the paradigm 10 mm size-observation-early surgery lies in the retrospective nature of this study. The prospective, non-randomised study under way cannot change this limitation. Other weak points are that surgery itself is an invasive therapy, the questionable issues [7] of observing a first diagnosis 10 mm tumour which has already reached the threshold size for surgery, and the case of spontaneous stop of growth beyond the 10 mm limit.

The strong point seems to be that the role of definitive cure of the disease, which has so far been disregarded when balancing conservative therapies like observation and radiotherapy *vs* surgery, can only be assigned to surgery.

## Conclusions

Small vestibular schwannoma is a completely different disease from a larger size tumour, and being the most diagnosed it requires effort to determine the best management. This goal is possible due to the several years of experience with the three current therapies: observation, surgery and radiotherapy. While surgery can obtain a definitive outcome in one year, morbidities and success/failure, observation and radiotherapy need a longer duration of follow-up. A non-surgical therapy can be soundly evaluated, if the result includes the full course of therapy in terms of long-term outcomes and the effects of secondary therapy on failures, in particular salvage surgery. The worse facial nerve results after delayed surgery in failed observation or secondary surgery in failed radiotherapy represents the price that non-surgical therapies pay in small VS. Surgery appears to be superior in terms of definitive cure with quick recovery to normal life and no or minimal further losses or complications. The decisive aspect of outcome in favour of surgery is that in growing tumours non-surgical therapies fail, requiring secondary surgery with poorer results than in an early-treated smaller tumour. The 10 mm critical size is conventionally set for a small tumour, which hardly contacts the brain stem and allows the least surgical trauma. The two surgical therapies, TLAB and HPS are different considering aim, execution, and burden on the patient. TLAB surgery disregards hearing unfit for preservation and affords a definitive cure with the lowest rates of complications and no sequelae.

When hearing is the goal, HPS is an option requiring both the patient's and surgeon's choice. Both TLAB and HPS for small tumours appear to be close to achieving the goals of definitive cure of the disease and functional preservation or rehabilitation.

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*Conflict of interest statement*

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### *Author contributions*

EZ: surgery; conceptualization; methodology; investigation; data curation; original draft; writing-review and editing; supervision. SC: methodology; investigation; data curation; original draft; writing-review and editing. GT: surgery; methodology; original draft; writing-review and editing; supervision. DC: surgery; conceptualisation; methodology; data curation; writing-review and editing; supervision. LD: surgery; conceptualization; supervision. Dd'A: surgery; conceptualization; supervision. AM: surgery; conceptualization; methodology; writing - review and editing; supervision.

### *Ethical consideration*

The study was conducted in accordance with the principles of the Helsinki Declaration and the data were collected, grouped, and examined in agreement with Italian privacy and data laws. Before undergoing surgery, 220/234 patients included in the study signed an informed consent. The remaining 14 patients agreed retrospectively agreed for personal data to be treated anonymously, in accordance with the in-house rules for retrospective studies of the Otolaryngology Section at Padova University (Italy).

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