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REVIEW ARTICLE

The international expert consensus on management of external auditory canal carcinoma

Pei Zhou[1,2] · Rubens de Brito[3] · Yong Cui[4] · Simon Lloyd[5] · Henricus Kunst[6,7] · J. Walter Kutz[8] · Navin Mani[9] · In Seok Moon[10] · Badr Eldin Mostafa[11] · Cindy Nabuurs[6] · Sampath Chandra Prasad Rao[12] · Bingbin Xie[13] · Yibo Zhang[1,2] · Chunfu Dai[1,2]

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Abstract

Purpose The objective of this consensus is to provide otolaryngologists with appropriate strategies in the management of external auditory canal (EAC) carcinoma.

Methods In the absence of randomized controlled trials, the consensus is based on expert opinions utilizing the Rand/UCLA appropriateness method [Fitch and Aguilar in The RAND/UCLA appropriateness method user's manual, RAND Corporation, Santa Monica, CA, 2001], drawing from existing literature and clinical experience.

Results The management recommendations are structured around 12 key areas, including: definition and pathology, pathogenesis, clinical manifestations, work-up, tumor staging system, surgical management of primary tumor, surgical management of the parotid gland and the temporomandibular joint, lymph node metastasis, radiotherapy, chemotherapy, reconstruction, and follow-up.

Conclusion Management strategies for EAC carcinoma rely on tumor extension and histopathological features. Surgical removal with free surgical margins or combination with radiotherapy, chemotherapy are most often the best options. Given the rarity of the disease, prospective, randomized, multi-institutional clinical trials should be designed to enable reliable comparisons of the outcomes of EAC carcinoma treatments, thereby providing evidence-based clinical data to establish widely accepted guidelines. It emphasizes the need for a multidisciplinary team to be involved in the management of EAC carcinoma, and regular follow-up should be implemented postoperatively.

Keywords External auditory canal carcinoma · Clinical practice guidelines · Temporal bone · Expert consensus

Introduction

External auditory canal (EAC) carcinoma is a rare malignancy, representing only 0.2% of all head and neck cancers. Due to its low incidence, many otolaryngologists have limited clinical experience in managing this condition. Furthermore, the rarity of EAC carcinoma presents significant challenges for conducting randomized controlled trials. Consequently, expert consensus, informed by extensive clinical experience, is essential to provide otolaryngologists with evidence-based strategies to address the heterogeneous clinical presentations and diverse treatment modalities associated with the management of EAC carcinoma.

Definition and pathology

EAC carcinoma is a rare malignant tumor originating from the epithelium of the external auditory canal, constituting less than 1% of all head and neck cancers. It can be classified into primary and secondary types. Primary tumors originate from skin and associated glands (e.g., sebaceous glands, cerumen glands) within the EAC, while secondary tumors may arise from the adjacent structures such as the pinna or parotid gland, or from metastasis of distant tumors [2]. This consensus focuses specifically on primary EAC carcinoma.

According to the latest World Health Organization Classification of Head and Neck Tumors, the pathological types of EAC carcinoma include squamous cell carcinoma(SCC), adenoid cystic carcinoma(ACC), and basal cell carcinoma(BCC), as well as mucoepidermoid carcinoma, malignant mixed tumor, and low-grade adenocarcinomas

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[3, 4]. The incidence, biological behaviors, and prognosis of these types vary. SCC is the most common, accounting for 40% to 60% of EAC tumors, and demonstrates aggressive biological behaviors. Early-stage tumors show a favorable prognosis following aggressive treatment, whereas advanced-stage SCC often has a poor prognosis despite comprehensive treatment [5, 6]. ACC represents approximately 20 to 40% of EAC tumors and is characterized by slow growth, a tendency for recurrence, and a propensity for distant metastasis [7]. BCC accounts for 5% to 10% of EAC tumors and generally has a favorable prognosis after complete surgical resection compared to other types [8].

Key points:

1. This consensus statement addresses primary EAC carcinoma.
2. SCC is the most prevalent form of EAC carcinoma, noted for its aggressive biological behavior. ACC, while less common, exhibits slow growth and a high likelihood of recurrence and metastasis.

Pathogenesis

The etiology and pathogenesis of EAC carcinoma remain not fully understood. However, several risk factors have been identified:

1. **Chronic inflammation:** Chronic suppurative otitis media or otitis externa is associated with an increased risk of developing EAC SCC. The laterality of the disease may also be influenced by the handedness of patients who engage in habitual ear-picking, suggesting that repeated epithelial irritation may contribute to the risk of EAC SCC. [9–11]
2. **Sun exposure and radiation:** Prolonged sun exposure is a risk factor for EAC carcinoma, particularly in fair-skinned populations [12]. In Asian populations, radiotherapy for nasopharyngeal carcinoma is a significant predisposing factor for EAC SCC. The incidence of EAC SCC in patients who have undergone radiotherapy for nasopharyngeal carcinoma is approximately 0.15%, which is about 1000 times higher than in the general population [13].
3. **Genetic factors:** Whole exome sequencing (WES) has identified TP53 gene mutations in 63.6% of patients with EAC SCC [14]. Mutations in genes such as CDKN2A, NOTCH1, NOTCH2, FAT1, and FAT3 have also been observed [14]. Additionally, about 57% of ACC patients overexpress the MYB oncoprotein [15].
4. **Immunosuppression:** Solid organ transplant recipients make up most of the immunosuppressed population. The risk of developing cutaneous SCC after renal transplant is 82-fold higher compared with the non-transplanted population. Male renal transplant recipients are especially prone to developing invasive SCC in sun-exposed areas such as the scalp and outer ear [16]. Immunosuppression is reported as a consistent prognostic factor for cutaneous SCC of the head and neck [17].
5. **Other factors:** Human papillomavirus (HPV) infection in the EAC may be associated with the development of EAC carcinoma. Recurrent papillomas in the EAC may also undergo malignant transformation [18, 19].

Key points:

1. Patients with EAC carcinoma should be evaluated for a history of chronic inflammation in the EAC or middle ear, recurrent papilloma, prior radiotherapy for head and neck cancers, or use of immunosuppression medications.

Clinical manifestations

Symptoms

The clinical manifestations of EAC carcinoma are often nonspecific, which can lead to misdiagnosis, particularly when it is confused with otitis externa or otitis media, resulting in delayed treatment [20].

1. **Otorrhea**: Most patients with EAC carcinoma present with otorrhea, which is frequently bloody and often occurs alongside a long history of chronic suppurative otitis media or otitis externa.
2. **Otalgia**: Tumor invasion into the periosteum and local nerves can cause severe otalgia that does not improve with antibiotics or analgesics. In cases where the tumor infiltrates the dura, otalgia may worsen. Intermittent otalgia can be an early symptom of ACC in the EAC [7, 21].
3. **Tinnitus, hearing loss, *vertigo***: Tumor obstruction of the EAC or invasion into the middle or inner ear may result in symptoms such as aural fullness, tinnitus, hearing loss, and vertigo.
4. **Others**: Advanced tumors with extensive invasion of the temporal bone and surrounding soft tissues may lead to dysfunction of the facial nerve and lower cranial nerves. This can present as facial nerve paralysis, hoarseness, or dysphagia. Involvement of the temporomandibular joint may result in trismus [21–23].

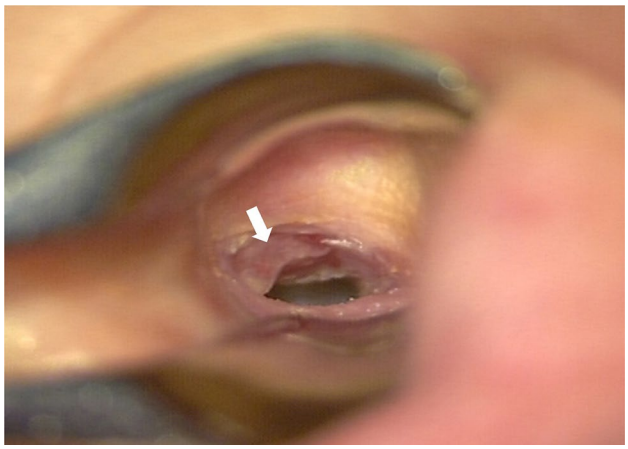

Fig. 1 A 52-year-old male presented with otalgia and ear discharge lasting for three months. Physical examination revealed granulation tissue (arrow) in the bony EAC. A biopsy of the EAC confirmed the diagnosis of SCC

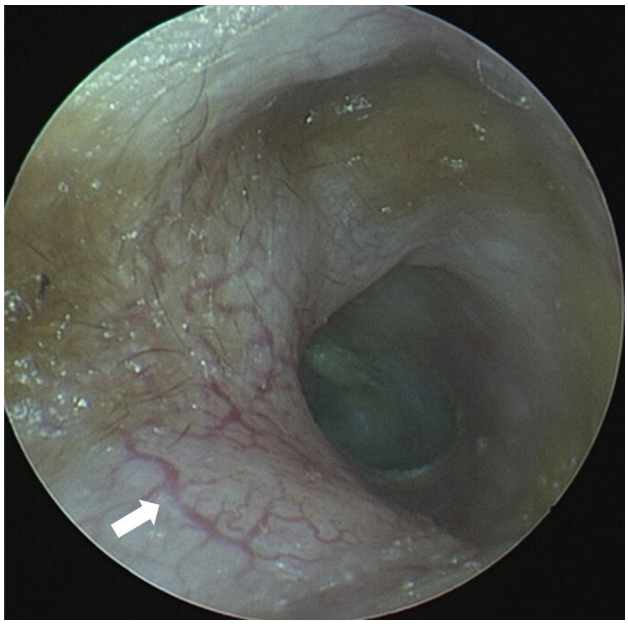

Fig. 2 A 38-year-old female presented with otalgia as the sole symptom for approximately one year. Physical examination revealed a smooth, bulged mass with surface neovascularization (arrow) in the cartilaginous EAC. Biopsy results confirmed the diagnosis of ACC in the EAC

Signs

SCC typically presents as an irregular mass with excoriation, ulceration, and granulation tissue in the bony EAC (Fig. 1); ACC often appears as a smooth nodular neoplasm with surface neovascularization in the cartilaginous EAC (Fig. 2). Occasionally, ACC may present with only otalgia, with or without redness of EAC skin. Other physical examination findings may include: facial nerve paralysis, asymmetry of soft palate elevation, vocal cord paralysis, tongue weakness, and shoulder weakness. Additionally, parotid or neck masses may be palpated, indicating metastasis to the parotid gland or cervical lymph nodes [24].

Work-up

1. **Medical history**: Document any history of chronic middle or external ear infections, previous head and neck radiotherapy, and any immunocompromised states such as organ transplant.
2. **Otoendoscope or microscope**: Use an ear endoscope or microscope to assess tumor location, size, and surface characteristics.
3. **Hearing test**: Conduct pure tone audiometry, tympanometry, and speech audiometry to evaluate hearing function.
4. **Laryngoscope**: Perform laryngoscopy if there is suspicion of lower cranial nerve involvement.
5. **Facial nerve function evaluation:** Document facial nerve function using the House-Brackmann (HB) grading system or alternative system (Sunnybrook facial grading system, Fisch facial grading system).
6. **Vestibular function evaluation**: If labyrinthine involvement is suspected, perform a caloric test, Vestibular Evoked Myogenic Potentials (VEMPs) and video Head Impulse Test (vHIT) to assess vestibular function and predict dizziness symptom following labyrinthectomy.
7. **Head and neck exam:** Evaluate the oropharynx for soft palate weakness. Examine the skin of the head and neck for additional lesions. Palpate the parotid gland and neck to check for local nodal metastasis.

Imaging

High resolution temporal bone CT

Obtain axial and coronal CT scans of the temporal bone with a recommended slice thickness of less than 1 mm. This imaging is crucial for assessing bony erosion in the EAC wall, mastoid, middle and inner ear, middle and posterior cranial fossae, fallopian canal, temporomandibular joint, internal carotid canal, and jugular foramen (Fig. 3). Additionally, include imaging of the neck and chest as part of the staging workup to evaluate for regional and distant metastases.

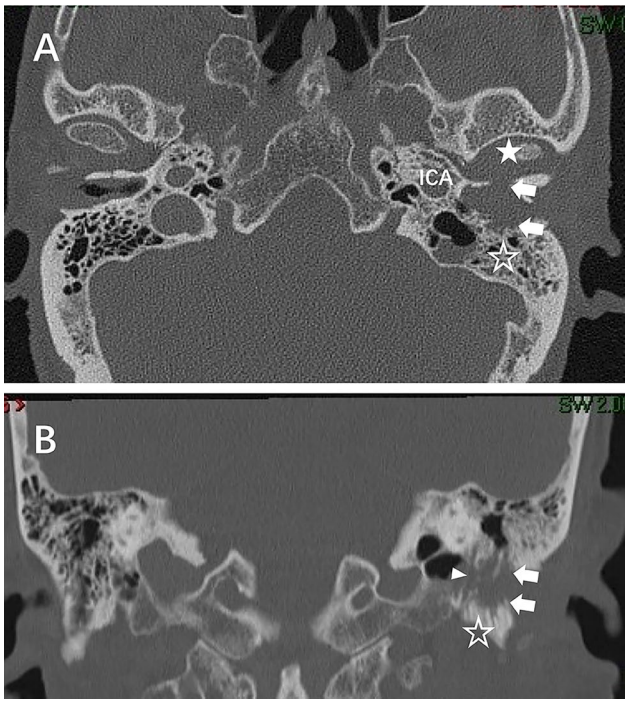

Fig. 3 **A** A patient with T4N0M0 SCC of the EAC. Temporal bone axial HRCT reveals bony erosion of both anterior and posterior walls (arrow) of the EAC. The tumor has invaded the temporomandibular joint (transparent star), mastoid (star) and facial nerve. **B** Temporal bone coronal HRCT demonstrates bony erosion of both the superior and inferior walls (arrow) of the EAC. There is invasion into the fallopian canal (triangle) and tympanic bone (transparent star). *ICA*: internal carotid artery

Temporal bone MRI with enhancement

Compared to temporal bone CT, MRI provides superior definition of tumor characteristics and better identifies soft tissue involvement. MRI is particularly useful for evaluating the dura, brain parenchyma, parotid gland, cervical lymph nodes, infratemporal fossa, and parapharyngeal space. It also helps differentiate between tumor tissue, edematous mucosa, and mastoid effusion.

T1-weighted sequences with contrast and T2-weighted sequences with fat suppression are recommended, with a slice thickness of less than 3 mm. Tumors show isointense or hypointense signal on T1-weighted Image (T1WI) sequences, isointense or slightly hyperintense signal on T2-weighted Image (T2WI) sequences, and hyperintense signal with contrast enhancement on post-contrast T1-weighted images (Fig.4) [25]. Fat suppression is particularly important for patients with a history of surgical resection to distinguish between residual tumor and fat or muscle. For patients unable to undergo MRI, contrast-enhanced temporal bone CT can be used as an alternative.

Occasionally, preoperative temporal bone imaging may underestimate the extent of a lesion. In such cases, surgeons should be prepared to adjust their approach, potentially performing more extensive or palliative surgery based on intraoperative findings.

Temporal bone magnetic resonance arteriography (MRA)/magnetic resonance venography (MRV)

Temporal bone MRA/MRV is recommended if there is a suspicion that the tumor may involve the internal carotid artery, jugular bulb, or sigmoid sinus. For patients who are unable to undergo MRI, computed tomography arteriography (CTA) is an alternative to evaluate vascular involvement.

Chest CT

For patients with ACC of the EAC, a chest CT is necessary to assess for potential pulmonary metastases.

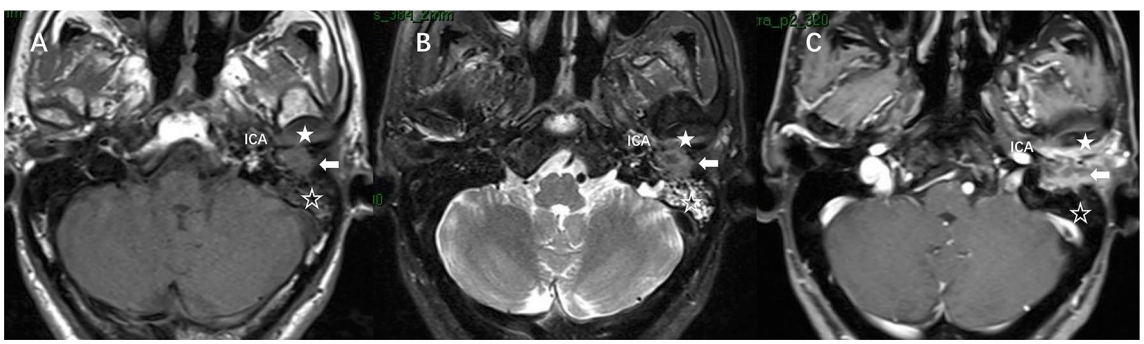

Fig. 4 A Patient with T4N0M0 SCC in the EAC. Temporal bone MRI T1WI (**A**) shows an isointensity signal (arrow) in the EAC. T2WI (**B**) shows an isointensity signal (arrow) in the EAC. T1WI with contrast (**C**) shows a hyperintensity signal (arrow) in the EAC, mastoid (star), and temporomandibular joint (asterisk). *ICA*: internal carotid artery

PET-CT

PET-CT is recommended for patients with advanced-stage tumors and/or when aggressive histopathological features are revealed to determine the presence of distant metastases.

Ultrasound-guided fine needle aspiration

Ultrasound-guided fine needle aspiration of the neck and parotid for cytology to identify clinical suspected lymph nodes could be an option to guide surgical strategy. Ultrasound may be omitted in case a performed MRI scan, showing a normal neck and parotid.

Digital Substration Angiography (DSA)

If primary surgery is planned and the tumor is close to the internal carotid artery, potentially requiring its sacrifice, a pre-operative balloon occlusion test with or without embolization may be considered. [26]

Key points:

1. Image studies (both temporal bone HRCT and MRI) should be used to define the location and extent of the tumor. These imaging modalities provide essential information for accurate diagnosis and effective management.
2. Patients with advanced-stage tumors should undergo PET-CT to assess for distant metastasis.

Biopsy and histopathological examination

The forementioned clinical findings combined with relevant medical history should raise suspicion of EAC carcinoma, prompting the need for a biopsy [20, 27].

Indications for biopsy:

1. A mass or subcutaneous swelling in the EAC that does not resolve with antibiotic or anti-inflammatory therapy.
2. Suspected otitis externa that shows no significant improvement after conventional antibiotics or anti-inflammatory therapy.
3. Unexpectedly severe and persistent ear pain in the presence of ear canal inflammation
4. New onset of facial nerve palsy or dysfunction of lower cranial nerves present in patients with a history of otitis externa or otitis media.

In most cases, a biopsy can be performed via a transcanal approach. For middle ear neoplasms, a transtympanic or transmastoid biopsy may be necessary. For tumors in the parotid or infratemporal fossa, image-guided fine needle aspiration or core biopsy may be used to establish the diagnosis. Ensure imaging findings are reviewed to increase the likelihood of obtaining a representative biopsy and to avoid false-negative results. Sufficient tissue should be obtained to ensure a representative biopsy and avoid sampling necrotic tissue. If the initial biopsy is negative but malignancy is highly suspected, additional biopsies (sometimes under general anesthesia) may be necessary. Multiple biopsies may be required to establish a precise diagnosis [28]. The histopathological examination should include morphological examination, immunohistochemistry, and other molecular pathological tests. Postoperative pathologic evaluation is necessary for disclosing margin status, perineural spread and lymphovascular invasion [29].

Key points:

1. If EAC carcinoma is suspected, a prompt biopsy should be conducted. When malignancy is highly suspected, multiple biopsies may be necessary to establish a precise diagnosis.
2. Ensure that imaging is reviewed to ensure a representative biopsy and reduce the risk of a false-negative result.

Tumor staging system

Currently, there is no universally accepted staging system for external auditory canal (EAC) carcinoma by the Union for International Cancer Control (UICC) or American Joint Committee on Cancer (AJCC). The Pittsburgh University staging system, revised by Moody et al. in 2000 [30], is widely used in clinical practice. This system incorporates temporal bone CT or MRI findings, intraoperative observations, and postoperative pathology, and is noted for its higher predictive prognostic value compared to the eighth edition of AJCC T-staging criteria for head and neck tumors [31, 32]. The lymph node staging follows AJCC staging criteria for head and neck tumors, with all patients with lymph node metastasis or distant metastases (except T1N1) classified as clinical stage IV.

The modified Pittsburgh staging system has faced criticism and limitations. Recent efforts have aimed at refining the TNM staging system by subdividing T3 into T3a and T3b based on tumor depth (less than or greater than 5mm), and T4 into T4a (anterior involvement) and T4b (posterior infiltration) [33]. Lavieille et al [34] proposed further subclassifications for T4 tumors based on extension: T4a (extracranial involvement), T4b (intrapetrous bone and extradural extension), and T4c (meningeal or intradural involvement). A multicenter retrospective study suggests these subclasses might offer additional value in clinical practice [35].

Key points:

1. The modified Pittsburgh staging system correlates well with disease status and is widely accepted in clinical practice. Further refinement of the staging system is ongoing to enhance its clinical utility.

Surgical management of primary tumor

A multidisciplinary team (MDT) should decide if surgical management is appropriate based on the tumor's location, extent of invasion, metastases, and the patient's overall health. Due to the varying biological behavior of different EAC carcinoma types, the surgical approach and extent of resection should be tailored individually. In cases where the tumor encases the internal carotid artery or invades significant brain parenchyma, surgical resection might not improve prognosis and could be avoided [36].

Local canal resection (Sleeve resection)

An endaural incision made between the tragus and root of the helix provides better access and visualization of the tumor in the EAC [29]. The resection involves removing the tumor along with the surrounding skin and underlying cartilage. Using a frozen section to confirm clear surgical margins is crucial. If margins are not clear, lateral temporal bone resection may be necessary. Local canal resection should be strictly limited, even if the patient wishes to preserve ipsilateral hearing when the contralateral hearing is unserviceable.

Indications:

- Small, laterally located T1 tumors that are confined to the soft tissues, cartilaginous ear canal without involving the bony-cartilaginous junction of the EAC.
- T1 superficial BCC involving the cartilaginous EAC may be considered of local resection. For tumors affecting the bony EAC, a lateral temporal bone resection (LTBR) is necessary for adequate margins.
- Local canal resection should be reserved for tumors that do not cross medially over the bony–cartilaginous junction of the EAC.

Lateral temporal bone resection (LTBR)

LTBR introduced by Conley and Novack in 1960, involves a complete canal wall up mastoidectomy with an expanded facial recess opening [37]. The procedure entails en bloc resection of the external auditory canal, tympanic membrane, and malleus, with the medial boundary defined by the stapes suprastructure and the facial nerve (Fig. 5) [38].

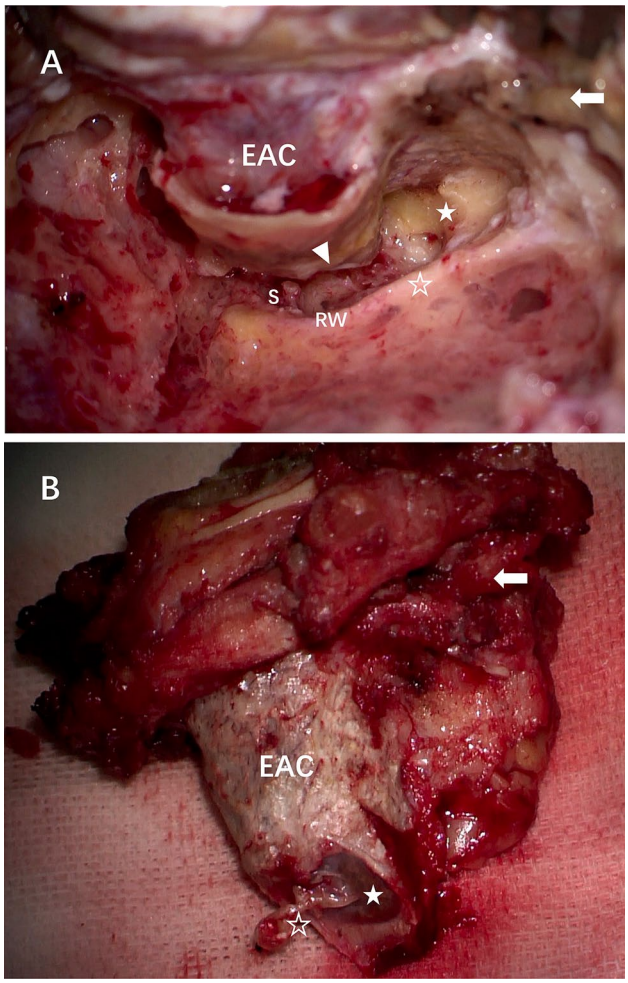

Fig. 5 **A** A patient with T2 ACC in the EAC underwent LTBR. The procedure included a canal wall up mastoidectomy with facial nerve skeletonization. An extended facial recess was performed between the facial nerve (transparent star) and the annulus (triangle), with removal of the tympanic bone (star) between the facial nerve and the parotid gland (arrow). The anterior wall of the EAC was fractured. **B** A Patient with T2 ACC in the EAC had an en bloc LTBR with partial parotidectomy. The specimen comprised the cartilaginous and bony EAC, partial parotid gland (arrow), tympanic membrane (star), and malleus (transparent star). The tumor was confined to the EAC. *EAC*: external auditory canal. *S*: stapes. *RW*: round window

Indications:

- T1 tumors in the bony ear canal and T2 tumors.
- Advanced tumors with extensive lateral soft tissue infiltration but without involvement of the medial wall of the middle ear.

Subtotal temporal bone resection (STBR)

Proposed by Parsons and Lewis in 1954 [39], STBR is an alternative to radical mastoidectomy. It involves a lateral

temporal bone resection followed by piecemeal removal extending medially to identify and potentially resect the internal auditory canal (IAC), facial nerve, and otic capsule while preserving the petrous apex [38]. The surgical morbidity of STBR typically includes facial nerve palsy, profound hearing loss, and imbalance, while the carotid artery, sigmoid sinus, and jugular bulb are preserved.

Indication:

- Tumors infiltrating the medial wall of the middle ear.

Total temporal bone resection (TTBR)

First reported by Graham et al. in 1984 [40], TTBR involves a single-stage total en bloc removal of the temporal bone, including sacrifice of the internal carotid artery. The morbidities associated with potential injuries to the cavernous sinus, internal carotid artery, and deficits involving cranial nerves III, IV, V, and VI. TTBR is now rarely used due to high morbidity and uncertain survival benefit [38].

Extended temporal bone resection (ETBR)

Moffat et al. [12] proposed the en bloc ETBR with preservation of the internal carotid artery and piecemeal removal of the petrous apex in 1997. The authors proposed an auriculectomy, condylectomy, superficial parotidectomy, and neck dissection in early-stage tumors, followed by postoperative radiotherapy [41].

The essential elements of ETBR are: (1) facial nerve sacrifice; (2) posterior and middle fossa craniotomy; (3) labyrinthectomy; (4) transection of internal auditory canal; (5) resection of petrous apex; (6) exposure of intrapetrous portion of the carotid; and (7) parotidectomy (partial or total as needed).

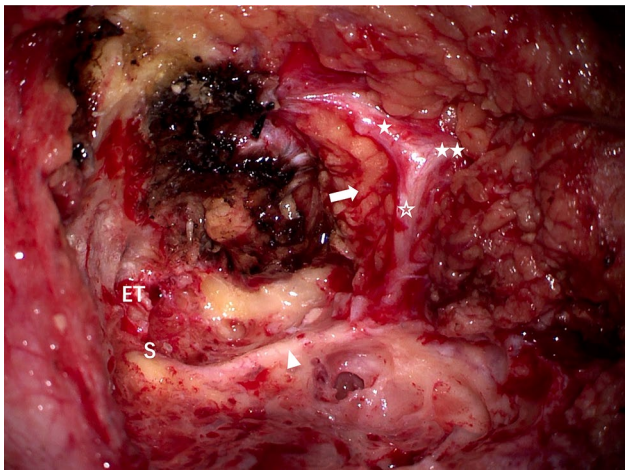

Fig. 7 Patient with T2 ACC in the EAC underwent en bloc lateral temporal bone resection with partial parotidectomy. The surgical cavity is depicted showing: the vertical facial nerve (triangle), main trunk of the facial nerve (transparent star) within the parotid gland (arrow), temporal buccal branch (star), and the cervical facial branch of facial nerve (double stars). *S*: stapes. *ET*: eustachian tube

In addition, dural involvement can be resected and repaired, with frozen section used to ensure negative margins. Involvement of the jugular bulb and sigmoid sinus requires removal of these structures and packing of the inferior petrous sinus [42]. Figs. 6, 7, 8.

Key points:

1. Achieving clear surgical margins is crucial.
2. Surgeons should be prepared to perform a LTBR when managing EAC carcinoma.

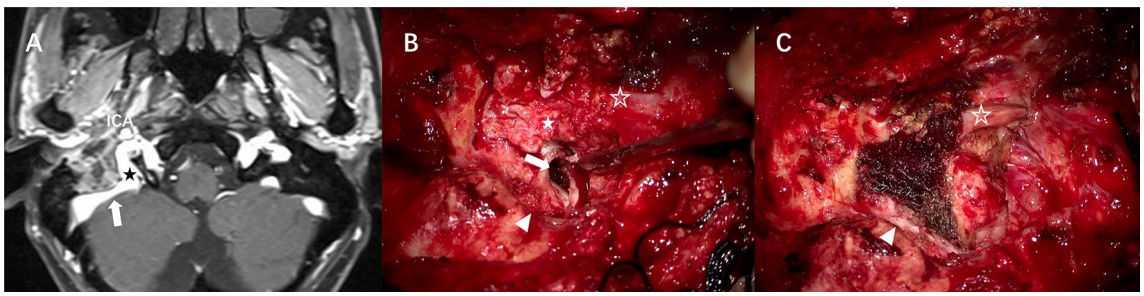

Fig. 6 **A** A male patient with T4N0M0 SCC in the EAC. The tumor has invaded the sigmoid sinus (arrow) and the jugular bulb (star). **B** The sigmoid sinus was packed, and the internal jugular vein was ligated (transparent star). An incision (arrow) into the sigmoid sinus was made, and the inferior petrous sinus (triangle) was packed with Surgicel. **C** After packing the inferior petrous sinus, the jugular bulb and sigmoid sinus were removed. The medial wall (triangle) covered by Surgicel was preserved. *ICA*: internal carotid artery

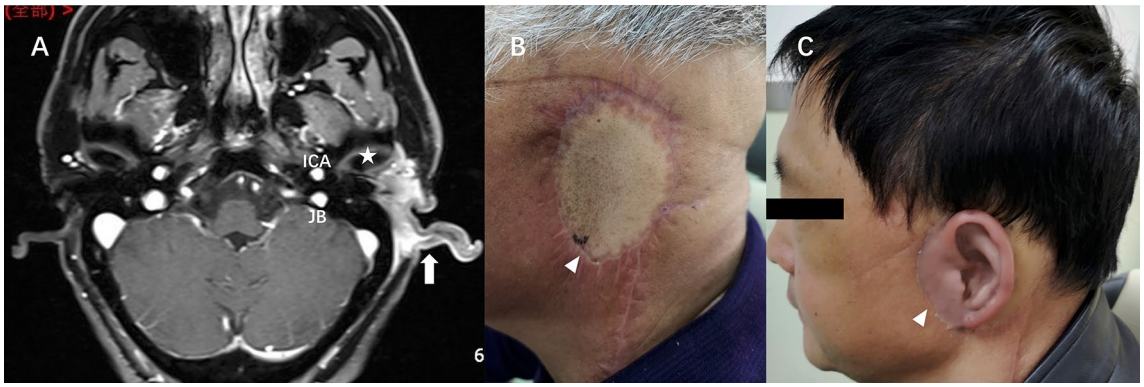

Fig. 8 **A** A 52-year-old male with T4N0M0 ACC involving the temoporomandibular joint (star) and auricle (arrow). **B** Following LTBR, partial parotidectomy and auriculectomy, the defect was repaired with a supraclavicular insular flap (triangle). **C** An artificial auricle (triangle) was created and attached to the reconstructive flap. *ICA*: internal carotid artery. *JB*: jugular bulb

Surgical management of the parotid gland and the temporomandibular joint

Due to the anatomical predisposition of EAC carcinoma to invade the parotid gland via various pathways, including fissures of Santorini and foramen of Huschke, partial or total parotidectomy is often recommended. The rate of parotid metastases in SCC patients is 28%-33%, and direct invasion in ACC patients is 57.6%, regardless of the tumor stage [43, 44]. For TMJ involvement, a partial mandibulectomy ranging from condylectomy to resection extending from the mandibular notch to the angle may be necessary. Preservation of the inferior alveolar nerve should be prioritized. Routine TMJ resection is not required with LTBR [26].

Key points:

1. Partial parotidectomy is recommended for T1-2 tumors with anterior or inferior wall involvement of the EAC.
2. Total parotidectomy with facial nerve sacrifice should be considered for T3-4 tumors with evidence of parotid gland invasion or facial nerve involvement within the parotid gland, particularly in differentiated tumors with no multiple metastases.
3. TMJ resection is performed after LTBR if the TMJ is invaded by the tumor.

Lymph node metastasis

Cervical lymph node metastasis and the role of a neck dissection

Cervical lymph node metastasis in EAC carcinoma ranges from 10% to 23%, with regions II and III most commonly affected [12, 45, 46]. Cervical lymph node dissection is recommended for SCC patients with advanced tumors (T3, T4) or if imaging indicates lymph node metastasis. In N+ patients with SCC of the EAC, dissection should include levels II, III, parotid lymph nodes, and level Va depending on the radiological findings [47]. It is controversial whether to perform prophylactic cervical lymph node dissection for early-stage patients without signs of metastases. A preoperative ultrasound with fine needle aspiration cytology of the neck and parotid glands can be diagnostic when nodal metastasis is suspected. If suspicious enlarged cervical lymph nodes are identified intraoperatively, it is recommended to perform a frozen section, and proceed with neck dissection only if the results are positive for metastasis [48].

Parotid lymph node metastasis

The parotid gland is abundantly supplied by lymph nodes, with lymphatic drainage from the facial skin and scalp being particularly important. Despite this, parotid lymph node metastasis is relatively uncommon, especially in ACC. Previous studies found parotid node involvement in only advanced-stage SCC, and no nodal involvement in any stage of ACC [27, 43]. The characteristics of ACC are known to be indolent growth, local recurrence, perineural invasion rather than nodal involvement, and late distant metastasis, mostly to the lung, even in the early stages. Effective management of parotid node metastasis is crucial in advanced-stage SCC [43].

Key points:

1. Routine neck dissection is not recommended for N0 necks in early-stage (T1, T2) tumors.
2. Routine elective neck dissection (II-III neck dissection) is recommended for T3 and T4 SCC or if imaging suggests lymph node involvement.

3. Neck dissection is generally not recommended for ACC unless there is confirmed lymph node involvement on imaging.

Radiotherapy

Definitive radiotherapy

Definitive radiotherapy for early-stage tumors

Hearing preservation is a significant advantage of definitive radiotherapy. Previous studies demonstrate that overall survival (OS) rate achieved in 83% to 100% of patients with T1 tumors following radiotherapy alone [49–51]. However, surgical management (local resection or LTBR) yields a 100% 5-year OS rate for T1 tumors [9]. Morita et al [52] found that patients with T1-2 tumors who underwent surgical management had a higher 5-year OS rate of 100%, compared to 81.3% for those treated with radiotherapy alone. This indicates that while radiotherapy can be effective, the choice of single-modality radiotherapy for early-stage tumors remains controversial.

Definitive radiotherapy for advanced stage tumors

Few studies suggest that radiotherapy alone yields comparable outcomes to combined surgery and radiotherapy for advanced-stage tumors [53, 54]. Most clinicians recommend radical surgery followed by postoperative radiotherapy as the preferred approach for advanced-stage tumors.

Indication of definitive radiotherapy:

- Patients with unresectable tumors, distant metastases or poor general health who may not tolerate surgical intervention.

Total doses between 68-70 Gy are recommended for definitive radiotherapy. In cases where the tumor is inoperable, radiotherapy alone often correlates with poorer survival rates. Some experts advocate for higher total doses, ranging from 65 to 75 Gy [55].

Adjuvant radiotherapy

Indications for preoperative radiotherapy

In patients with advanced (T4) EAC carcinoma, especially when the tumor involves neurovascular structures in the lateral skull base, where complete resection may not be possible, preoperative radiotherapy can be administered to reduce the volume of tumor. This approach may facilitate to achieve total resection and minimize the risk of neurovascular damage.

Indications of postoperative radiotherapy

Postoperative radiotherapy is recommended for all SCC patients with T3 and T4 tumors, particularly if the tumor has invaded neurovascular structures or the dura, if surgical margins are positive or less than 0.5 cm, or if the pathological exam reveals perineural infiltration or extranodal spread [30, 41, 56, 57]. Radiotherapy should commence within 2-6 weeks postoperatively.

Recommended doses are 50-60 Gy for patients who had preoperative radiotherapy, 60-66 Gy for those with complete resection, and 66-70 Gy for cases with positive margins or residual tumor. [58]

Key points:

1. The use of single-modality radiotherapy for early-stage tumors remains controversial.
2. For advanced-stage tumors, a comprehensive approach combining radical surgery with postoperative radiotherapy is generally preferred.
3. Postoperative radiotherapy is not recommended for early-stage tumors with clear surgical margins.

Chemotherapy

Currently, there is limited evidence to support the use of chemotherapy as a significant survival benefit for patients with early-stage EAC carcinoma, and chemotherapy alone is rarely utilized in this context [21]. However, preoperative concurrent chemoradiotherapy is beneficial for T3 and T4 stage SCC, as it can assist in achieving negative surgical margins and improving overall survival rates [59–62]. For some patients with unresectable tumors, concurrent chemoradiotherapy combined with other treatment modalities may offer better prognostic outcomes [59, 60, 62].

The most commonly used chemotherapeutic agents for the treatment of SCC or ACC include cisplatin, carboplatin, 5-fluorouracil, docetaxel, cyclophosphamide, doxorubicin and mitomycin. The traditional chemotherapy regimen is cisplatin combined with 5-fluorouracil (PF regimen). More recent regimens include the addition of docetaxel to form the cisplatin, 5-fluorouracil, and docetaxel (TPF regimen). [59–62]

There is limited research on precise targeted therapy for EAC carcinoma. However, some case reports have shown that cetuximab combined with radiotherapy can effectively

treat advanced temporal bone SCC [63, 64]. Targeted therapy with bevacizumab and pemetrexed was reported to be effective in a 58-year-old patient with CTNNB1 and VEGFR-2 mutant temporal bone SCC [65]. Additionally, programmed death receptor-1 (PD-1) inhibitor immunotherapy, such as cemiplimab, has demonstrated potential as a novel strategy for managing EAC carcinoma [66]. Cemiplimab has shown clinical efficacy and an acceptable safety profile in patients with cutaneous SCC, particularly those unsuitable for surgical excision [67–69]. However, its specific role in EAC carcinoma requires further investigation.

Key points:

- Chemotherapy and precise targeted therapy are recommended for patients with advanced tumors (T3, T4), including those with unresectable tumors, distant metastases, or postoperative recurrence.

Reconstruction

To improve patients' quality of life postoperatively, efforts should be made to reconstruct and restore ear and facial nerve function following the complete resection of the tumor. Key aspects of reconstruction include packing of the surgical cavity, restoration of facial nerve function, repair of dural defects to prevent cerebrospinal fluid leakage, repair of skin defects, and reconstruction of the auricle.

Facial nerve reconstruction

If the tumor infiltrates the facial nerve (FN), resection of the nerve may be necessary to achieve clear surgical margins, as confirmed by frozen section analysis. In such cases, functional reconstruction of the facial nerve should be considered. FN repair is usually performed using either the great auricular nerve, sural nerve cable graft, or through V-VII or XII-VII anastomosis [70]. Reconstruction is recommended for all patients with facial nerve palsy lasting less than 12 months, even if postoperative radiotherapy is planned [71]. If complete surgical resection of the tumor is not possible but the facial nerve is not preoperatively compromised, preservation of the nerve may be feasible.

If facial nerve reconstruction is not possible or fails to restore function, alternative approaches include static procedures such as fascia lata sling for oral commissure/cheek suspension, or dynamic procedures such as a gracilis free flap, V-VII jump on the buccal branche or lengthened temporalis myoplasty (e.g. Labbé type I or II), if the deep temporal nerve and artery are preserved. Oculoplastic interventions (e.g., gold weight, canthoplasty) can be performed either during the initial tumor resection or at a later stage [26].

Hearing restoration

All patients who undergo lateral temporal bone resection will experience at least moderate conductive hearing loss. This can be managed with an osseointegrated bone-anchored hearing aid (BAHA). For those with profound hearing loss, either a BAHA or a bilateral contralateral routing of signals (CROS) aid can be used [26]. Attempts to reconstruct the external auditory canal (EAC) using split-thickness or full-thickness skin grafts combined with tympanoplasty after LTBR have shown favorable results in early-stage patients. However, complications such as chronic granulation, persistent otorrhea, and tympanic membrane lateralization may occur [72, 73]. Patients have reported satisfaction with the placement of a floating mass transducer (FMT) of a Vibrant Soundbridge (VSB) onto the round window membrane after subtotal petrosectomy with complete fat obliteration of the middle ear [74]. While middle ear and cochlear implants can affect MRI quality, they may be considered after five years of disease-free survival in EAC SCC patients. In case of a single-sided-deafness, hearing aids with CROS or bilateral CROS, as well as a cochlear implant may also result in an acceptable hearing rehabilitation [75, 76]. In patients with cochlear implant, tumor monitoring may be performed via high-resolution temporal bone CT scans.

Defect surgical cavity packing

In patients who have undergone LTBR or STBR, managing the surgical cavity is crucial to prevent complications and promote healing. Abdomen fat graft is often used due to its availability and effectiveness, particularly in cases where cerebrospinal fluid (CSF) leakage is present. A temporalis muscle flap or sternocleidomastoid muscle flap may be applied in some cases, where there is significant inflammation or when tumors have been treated with radiotherapy [77]. Alternatively, if the defect is adequately closed with a temporalis muscle flap, a small split thickness skin graft may be applied to cover the meatal defect [29].

Skin defect repair

Depending on the size of skin defect and patient's general condition, various flaps can be chosen for repair. For relatively small defects (less than 50 cm^2), or in cases with poor vascularity of the recipient area or the patient's general condition, local or pedicle skin flaps are preferred. Larger

defects may require free flap reconstruction or distant pedicle insular flaps with more tissue. Commonly used local flaps include the platysma myocutancous flap and the rotating faciocervical flap. Examples of pedicled insular flaps include the supraclavicular insular flap, sub-chin insular flap, trapezius flap, and latissimus dorsi flap. Free flap options include the anterolateral thigh flap, radial free flap of the forearm, and rectus abdominis flap [78, 79].

Key points:

1. Facial nerve function reconstruction should involve either active procedures or static procedures.
2. Hearing restoration options include BAHA, BI-CROS hearing aids, and, in certain circumstances, middle ear implants or cochlear implants.
3. Various flaps, including local flaps, pedicled insular flaps, and free flaps, can be selected for repairing skin defects following the surgical removal of the auricle and surrounding skin. The choice depends on the size of the skin defect and the surgeon's preference.

Recurrence, metastasis, and prognosis

A recent meta-analysis revealed recurrence rate of 33.2% in patients with EAC carcinoma with a median time to recurrence of 13.0 months, and a median survival time of 28.0 months [80]. Surgical removal is recommended if the recurrence lesion is resectable; otherwise, radiotherapy or chemotherapy may be considered.

The prognosis of EAC carcinoma is generally related to the clinical stage and pathological diagnosis [52]. Surgical resection with clear margins achieves a five-year survival rate of 90%-100% for early-stage patients (T1, T2) [81], but only 35.8%-72.5% for advanced-stage patients(T3, T4) [22, 45, 82]. Surgical resection combined with preoperative or postoperative radiotherapy may result in better outcomes compared to single-modality treatment in advanced cases [41, 49, 62, 82, 83].

The possible prognostic indicators for EAC carcinoma include T stage, lymph node metastasis, facial nerve involvement, dura infiltration, positive surgical margins, and postoperative recurrence [22, 41, 56, 57, 80, 84–86]. There is limited evidence suggesting that biomarkers such as laminin 5-g2 and p53 have a significant impact on patient survival.

Due to the indolent nature of ACC, patients with ACC often show favorable overall survival rates even when distant metastases (commonly in the lungs, liver, and bones) occur. The cumulative survival rates of lung metastases were 66.8% at 5 years and 40.5% at 10 years [87]. A disease-free interval (DFI) greater than 36 months and completeness of resection are the best prognostic indicators, and surgical management of lung metastasis should be considered as a therapeutic option to achieve local control of disease [87].

Key points:

1. The most important prognostic indicators for EAC carcinoma include T stage, lymph node metastasis, facial nerve involvement, dura infiltration, positive surgical margins and postoperative recurrence.
2. Lung metastasis is common in patients with ACC.

Follow-up

Postoperative imaging and surveillance are crucial for monitoring and managing EAC carcinoma. Initial imaging should be performed approximately 12 weeks after the completion of definitive treatment to establish a baseline scan. Temporal bone MRI with contrast and/or PET-CT is recommended for post-treatment surveillance, as most tumor recurrences may not be detectable through clinical examination alone, particularly if blind sac closure or a free flap has been employed. Postoperative high resolution temporal bone CT scans in bony windows may also be informative if revision surgery is considered. A regular follow-up schedule is advised: every 3 months in the first year post-treatment, then every 6 months in the second year. For patients with SCC of the EAC, a follow-up period of 5 years is recommended. For patients with ACC of the EAC, a chest CT is recommended every 6 months during the first 3 years, transitioning to annual scans thereafter [88].

Key points:

1. Regular follow-up with temporal bone MRI with contrast is recommended postoperatively.
2. A low-dose chest CT should be ordered in patients with ACC in the EAC as part of the surveillance protocol.

Conclusions

Management strategies for EAC carcinoma rely on tumor extension and histopathological features. Surgical removal with free surgical margins or combination with radiotherapy, chemotherapy are most often the best options. Given the rarity of the disease, prospective, randomized, multi-institutional clinical trials should be designed to enable reliable comparisons of the outcomes of EAC carcinoma treatments, thereby providing evidence-based clinical data to establish widely accepted guidelines. It emphasizes the need for a multidisciplinary team to be involved in the management

of EAC carcinoma, and regular follow-up should be implemented postoperatively.

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Authors and Affiliations

Pei Zhou[1,2] · Rubens de Brito[3] · Yong Cui[4] · Simon Lloyd[5] · Henricus Kunst[6,7] · J. Walter Kutz[8] · Navin Mani[9] · In Seok Moon[10] · Badr Eldin Mostafa[11] · Cindy Nabuurs[6] · Sampath Chandra Prasad Rao[12] · Bingbin Xie[13] · Yibo Zhang[1,2] · Chunfu Dai[1,2]

✉ Chunfu Dai
cfdai66@126.com

1 Department of Otology and Skull Base Surgery, Eye Ear Nose and Throat Hospital, Fudan University, 83 Fenyang Road, Shanghai 200031, China

2 Key Laboratory of Hearing Medicine, Eye Ear Nose and Throat Hospital, Ministry of Health, Fudan University, 83 Fenyang Road, Shanghai 200031, China

3 Department of Otorhinolaryngology, University of São Paulo School of Medicine, São Paulo, Brazil

4 Department of Otolaryngology-Head and Neck Surgery, Guangdong Provincial People's Hospital (Guangdong Academy of Medical Sciences), Southern Medical University, Guangzhou, China

5 University Department of Otolaryngology Head and Neck Surgery, Peter Mount House, Manchester Royal Infirmary, Manchester, UK

6 Department of Otorhinolaryngology, Hearing and Genes, Radboud University Medical Center, Nijmegen, The Netherlands

7 Department of Otorhinolaryngology, Dutch Academic Alliance Skull Base Pathology, Maastricht University Medical Center, Maastricht, The Netherlands

8 Department of Otolaryngology-Head and Neck Surgery, University of Texas Southwestern Medical Center, Dallas, TX, USA

9 Department of Otolaryngology, Manchester University Hospitals NHS Foundation Trust, Manchester, UK

10 Department of Otorhinolaryngology, Yonsei University College of Medicine, Seoul, Korea

11 Department of Otorhinolaryngology Head and Neck Surgery, Faculty of Medicine, Ain-Shams University, Cairo, Egypt

12 Department of Otolaryngology, Kasturba Medical College, Manipal University, Head & Neck Surgery, Mangalore, Karnataka, India

13 Department of Otolaryngology Head and Neck Surgery, the Second Affiliated Hospital of Nanchang University, Nanchang, China