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REVIEW

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Squamous cell carcinoma of the temporal bone: A current review

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Abstract

Objectives: The rarity of temporal bone squamous cell carcinoma (TBSCC) precludes a clear understanding of the disease and approach to its management. This review provides general background on the disease and discusses the current and emerging oncologic and rehabilitative management options.

Data Sources: PubMed literature review.

Methods: A review of the current literature was conducted to assess and collate up-to-date information regarding TBSCC management.

Results: TBSCC is a rare and aggressive disease arising in the ear canal, temporal bone, or extratemporal sites. Prior radiation, chronic ear disease, or habitual ear picking may contribute to primary disease development. Because the symptoms of TBSCC and benign otologic disease are similar, TBSCC diagnosis may be delayed, allowing the tumor time to spread throughout the anatomically intricate temporal bone. The extent of the disease is determined based on imaging and is usually staged with the Pittsburgh Staging System. Temporal bone resection with parotidectomy and neck dissection is the current standard of care. Survival is generally good for early disease and poor for advanced disease, but chemotherapy is emerging as a promising treatment option. Auditory rehabilitation with osseointegrated hearing aids is recommended at initial oncologic resection.

Conclusions: The knowledge of and outcomes for TBSCC have improved with time, but because of the aggressive nature of the disease and the anatomic intricacy of the temporal bone, TBSCC treatment is complex and should be delivered by a multidisciplinary team. Inter-institutional collaboration may accelerate research for this rare disease.

Level of Evidence: 5.

KEYWORDS

biomarkers, ear canal cancer, osseointegrated hearing aids, squamous cell carcinoma, temporal bone

1 | INTRODUCTION

Malignancies of the temporal bone are rare. They encompass only 0.2% of all head and neck malignancies and are found in one in every 5000 to 20 000 patients with otologic complaints.[1,2] The worldwide annual incidence is estimated to be 1.3 cases per million.[3] Further stratifying these patients, squamous cell carcinoma (SCC) represents even fewer encounters. A recent review by Gidley et al[4] demonstrated that the three most

common temporal bone tumor histologic types, including both primary temporal bone tumors and those which affect it secondarily, are SCC (39%), basal cell carcinoma (14%), and adenoid cystic carcinoma (7%). Given the paucity of temporal bone malignancies, there are few large-scale studies and meta-analyses, no clinical trials, and substantially variable institutional management practices for TBSCC. As such, optimal treatment for the disease remains elusive. The goal of this review is to provide background on TBSCC, an overview of current and emerging oncologic and rehabilitative management practices for its treatment, and management recommendations based on the existing literature.

2 | METHODS

A PubMed literature review was performed to identify publications regarding TBSCC through August 2019. Search terms included combinations of the following phrases: "temporal bone," "squamous cell carcinoma," "malignancy," "cancer," "outcomes," "radiotherapy," "chemotherapy," "osseointegrated hearing aids," and "biomarkers." Each reference section was further reviewed to identify additional publications. Only articles published in the English-language were included.

2.1 | Primary origin, epidemiology, and etiology

SCC can affect the temporal bone either primarily—within the ear canal, middle ear, or mastoid—or secondarily, from extratemporal sites. The extratemporal sites that most commonly infiltrate the temporal bone include the periauricular skin, auricular skin, parotid gland, and skull base. In a review of temporal bone malignancies, the periauricular skin and parotid gland were more common primary sites than the temporal bone itself.[5] The site of origin has important prognostic implications. Gidley et al[4] demonstrated higher overall survival (OS) and disease-free survival (DFS) rates for primary external auditory canal (EAC) tumors compared to auricular, periauricular, and parotid primary tumors affecting the temporal bone. SCC accounts for 60% to 80% of primary tumors of the temporal bone, while it makes up only around 40% of all tumors of the temporal bone.[4,5] Finally, in most studies of TBSCC, approximately 60% of the patients are men and the most common age at diagnosis is 60 to 69 years, in accordance with most other epithelial malignancies.[6,7]

Unlike other head and neck cancers, tobacco and alcohol use do not appear to strongly increase the risk of primary TBSCC.[8] Prior radiation, however, does appear to be an important risk factor. Lo et al[9] reviewed their cohort of nasopharyngeal cancer patients who had received radiation treatment and found the incidence of subsequent EAC SCC to be 0.13%. This rate is nearly 1000 times higher than in the general population. Chronic otitis media, otitis externa, and cholesteatoma have also been implicated as causes of primary TBSCC.[10] Yin et al[7] found that 12.6% of their patients with primary TBSCC had recurrent or chronic otitis externa or otitis media, and Masterson et al[11] noted that 43% of patients with primary TBSCC had chronic suppurative otitis media. Furthermore, Tsunoda et al[12] examined the relationship between habitual ear picking and SCC of the ear canal. They found that the laterality of ear canal cancer correlated with handedness in patients with habitual ear picking, thereby possibly implicating mechanical stimulation in carcinogenesis. Finally, Vikram et al[13] described two cases of middle ear SCC in patients with concomitant chronic suppurative otitis media and cholesteatoma. Other recent studies have demonstrated the presence of human papillomavirus (HPV) genetic material in TBSCC tumors, and case reports have described the malignant transformation of benign HPV papillomas, but firm conclusions have yet to be drawn.[14-16] Sun exposure is also a leading risk factor for TBSCC, as many of these tumors arise from auricular and periauricular skin. For most, however, the exact etiology remains elusive.

2.2 | Presentation and evaluation

Unfortunately, a significant overlap exists between benign and malignant otologic disease presentations. The three most common clinical findings of temporal bone malignancies are otalgia, otorrhea, and hearing loss, all of which are also commonly seen with benign diseases such as chronic otitis media or otitis externa.[17] The classic appearance of EAC SCC is an exophytic, ulcerated mass; however, because of similar symptomatology, cancer can be mistaken for inflammatory ear disease and thus allowed to grow unchecked. Eventually, findings suggestive of a more nefarious process, such as facial weakness and a parotid or neck mass, can arise.[4] Madsen et al[3] noted that symptoms of primary temporal bone tumors were present for an average of 13 months prior to presentation. It should be noted that inflammatory disease should resolve with aural cleaning, otic drops, and systemic antibiotics, but a lack of response should raise suspicion and prompt tissue sampling.

Careful otomicroscopic examination of the ear canal and tympanic membrane can aid in the diagnosis of an otologic malignancy; however, as the tumor grows, otomicroscopy can be limited by a mass preventing distal canal visualization (Figure 1). As the majority of the temporal bone is regularly inaccessible from direct visualization, imaging plays a significant role in staging and management. Computed tomography (CT) and magnetic resonance imaging (MRI) provide complementary information regarding tumor extent. CT imaging can reliably detail erosion of the canal wall, labyrinth, petrous apex, or internal carotid artery and jugular bulb walls (Figure 2). It can also provide excellent detail of the surrounding soft tissues and regional nodal basins. Contrast-enhanced MRI is especially helpful in identifying perineural disease or dural involvement.[5,18-20] Accordingly, both CT and MRI are essential for correct tumor staging. An accurate assessment of tumor spread is critical, given that a principal prognostic factor for TBSCC is the degree of local tumor extension.[20] Finally, positron emission tomography should be utilized in patients with advanced disease to identify and evaluate distant metastases.[10,17]

2.3 | Spread of disease and the Pittsburgh staging system

In theory, the bony construct of the temporal bone should provide good protection from local tumor spread, as bone is generally a good

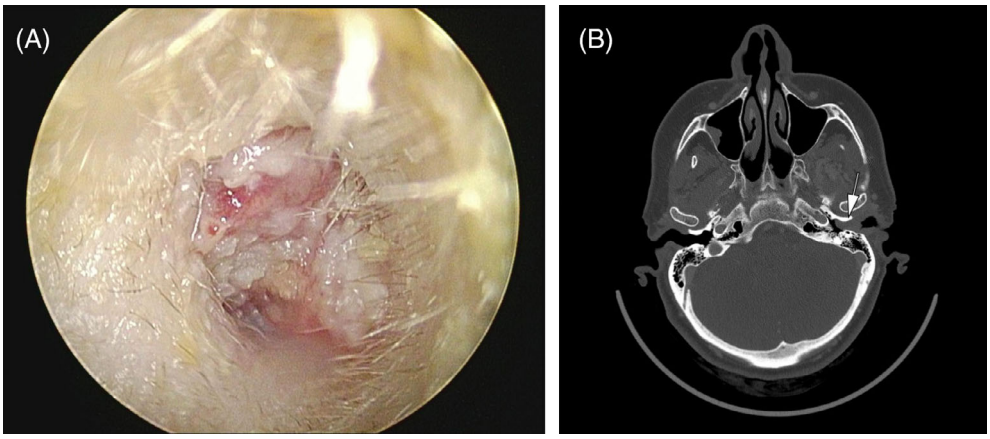

FIGURE 1 This 59-year-old woman presented with a one-year history of left ear blockage. A, Otoendoscopic view of left ear canal shows squamous cell carcinoma completely obstructing the canal. B, Axial computed tomography scan shows the tumor confined to the external ear canal without any bony destruction (arrow). No parotid invasion or cervical lymphadenopathy was present. The tumor was clinically staged in the Pittsburgh staging system as T1N0, but the final pathologic examination showed invasion into the bone of the ear canal. Thus, the patient's tumor was staged as pT2N0, and she received postoperative radiotherapy. At the time this review was written, she had survived 3 years after treatment with no evidence of recurrence

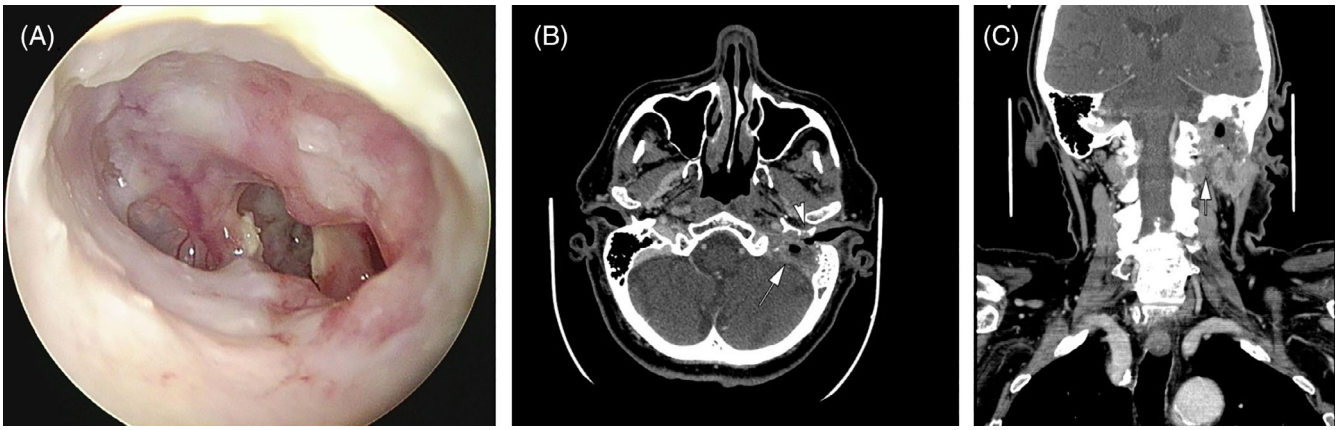

FIGURE 2 This 82-year-old man presented with a 4-month history of left facial paralysis, hearing loss, otorrhea, hoarseness, and weight loss. A, Otoendoscopic view of the left ear canal shows squamous cell carcinoma involving the middle ear. B, Axial computed tomography scan shows destruction of the posterior temporal bone and obstruction of the sigmoid sinus (arrow). The scan also revealed that the tumor was destroying the bony ear canal (arrowhead). C, Coronal computed tomography scan shows the extent of disease in the upper neck and paraspinous muscles (arrow). The patient was given palliative treatment and died 2 months later

tumor barrier; however, there are many natural pathways within the temporal bone that allow easy spread of disease. Leonetti et al[21] originally described five patterns of spread: (a) superior through the thin tegmen tympani into the middle cranial fossa, (b) anterior through the fissures of Santorini and foramen of Huschke into the glenoid fossa and infratemporal fossa, (c) inferior through the hypotympanum and jugular foramen, (d) posterior into the mastoid air cells, and (e) medial into the middle ear and carotid canal. Gidley et al[22] reported that TBSCC extended anterior to the EAC in 63% of cases and involved the jugular foramen in 23%, the carotid artery in 11%, the infratemporal fossa in 11%, and the temporomandibular joint (TMJ) in 4%. Furthermore, once tumors invade the middle ear, the air cell system allows the unimpeded spread of disease. For this reason, tumors of the middle ear and mastoid are much harder to control than tumors confined to the bony ear canal. This was demonstrated by Madsen et al,[3] who found lower rates for 5-year locoregional control, disease-specific survival (DSS), and OS for tumors with middle ear involvement compared to those confined to the EAC. Fittingly, the tympanic membrane has been previously described as the "Ohngren's line for temporal bone cancers."[23]

Although the American Joint Committee on Cancer (AJCC) has a staging system for most head and neck malignancies, it lacks one for primary temporal bone malignancies. For primary tumors of other sites that invade the temporal bone, the AJCC staging system for that site is used, such as for parotid tumors and periauricular skin cancers. For primary temporal bone malignancies, however, the most widely

used staging system is the Pittsburgh staging system (PSS), which was originally published by Arriaga et al[20] in 1990. Although the PSS is based on data from patients with SCC, it is currently used to stage other tumor histologic types as well. It utilizes the familiar tumor-node-metastasis (TNM) format and uses CT findings of bony EAC destruction, surrounding soft tissue infiltration, and medial bony temporal structure involvement to place patients in equitable treatment and prognostic groups. The TNM system can be converted into the four-stage system used for other head and neck cancers in standard fashion, with the exception that any temporal bone malignancy with lymph node involvement is automatically considered stage IV.[20] This conversion system reflects the better prognosis for tumors limited to the EAC (T1 or T2 disease) and the poorer prognosis for tumors involving the middle ear or mastoid (certain T3 or T4 disease).[3] Moody et al[1] added tumors with facial nerve involvement to the T4 category given the poor outcomes of their patients with facial paresis. Since 2000, there have been suggested variations to the PSS, but none have been widely adopted in the literature.[24,25] The amended PSS published by Moody et al remains the system most widely referenced in the current literature, as numerous studies have since confirmed its correlation with prognosis (Table 1).[3,22,26-28]

TABLE 1 Modified Pittsburgh staging system as published by Moody et al.[1] Reprinted with permission from *Temporal Bone Cancer*[23]

T classification	
T1	Tumor limited to the EAC without bony erosion or evidence of soft tissue involvement
T2	Tumor limited to the EAC with bone erosion (not full thickness) or limited soft tissue involvement (<0.5 cm)
T3	Tumor eroding through the osseous EAC (full thickness) with limited soft tissue involvement (<0.5 cm), or tumor involvement in the middle ear and/or mastoid
T4	Tumor eroding the cochlea, petrous apex, medial wall of the middle ear, carotid canal, jugular foramen, or dura; or with extensive soft tissue involvement (>0.5 cm), such as involvement of the TMJ or styloid process; or evidence of facial paresis
N classification	
N0	No regional nodes involved
N1	Single metastatic regional node <3 cm in size
N2a	Single ipsilateral metastatic node 3-6 cm in size
N2b	Multiple ipsilateral metastatic lymph nodes
N2c	Contralateral metastatic lymph node
N3	Metastatic lymph node >6 cm in size
Overall stage	
I	T1N0
II	T2N0
III	T3N0
IV	T4N0 and any T N+

Abbreviations: EAC, external auditory canal; N, node; T, tumor; TMJ, temporomandibular joint.

2.4 | Management of the temporal bone

The standard of care for the oncologic management of TBSCC is surgery.[26] There are three options for resection: lateral temporal bone resection (LTBR), subtotal temporal bone resection (STBR), and total temporal bone resection (TTBR). All of these procedures take advantage of the anatomy of the temporal bone in establishing tumor-free margins and can be performed either *en bloc* or in piecemeal fashion.

LTBR is the most widely used approach for otologic oncologic surgery. Predominately performed *en bloc*, it is the removal of the ear canal lateral to the facial nerve and stapes. Specifically, the EAC, tympanic membrane, malleus, and incus are removed, preserving the inner ear. As such, LTBR is typically used for cancer that has not invaded the middle ear or mastoid. Because LTBR involves disruption of the natural sound conduction mechanism, patients can expect maximal conductive hearing loss post-operatively. Recently, Ghavami et al[29] proposed a modified LTBR with the goal of preserving conductive hearing in TBSCC patients with very limited bony canal involvement. They performed a standard LTBR but preserved the tympanic membrane and ossicles and reconstructed the remaining EAC with a split-thickness skin graft. The mean post-operative air-bone gap was 9 dB, significantly less than expected after a true LTBR.[30] However, the generalizability of these results is limited by the fact that the study only included five patients with a mean post-operative follow-up of 29 months.

STBR can be performed when disease extends past the tympanic membrane into the middle ear or mastoid. At its core, this procedure is a LTBR with additional removal of the bony labyrinth; thus, it sacrifices sensorineural hearing and, often, facial nerve function.[24] However, a landmark study by Prasad and Janecka[31] demonstrated a survival benefit in patients with disease extending into the middle ear who underwent STBR rather than LTBR. Furthermore, STBR can be executed *en bloc* or piecemeal. To date, there is no literature demonstrating improved outcomes with *en bloc* vs piecemeal resection, but some still advocate for a "no touch" *en bloc* procedure to obtain negative margins.[32,33] Given the substantial exposure of STBR and the proximity of neurovascular structures, such as the jugular bulb and internal carotid artery, many surgeons elect to perform STBR in a piecemeal fashion to reduce morbidity.[17,22]

TTBR is a STBR with additional removal of the petrous apex and internal auditory canal. It may be considered when malignancy spreads into or medial to the bony labyrinth. Both *en bloc* and piecemeal excisions have been described. *En bloc* TTBR involves resection of the internal carotid artery, cranial nerves VI through XII, and surrounding structures.[34] Given the morbidity associated with this procedure and the lack of a proven survival benefit when compared with less aggressive resections, many authors believe that TTBR is not justified, and it is rarely performed today.[31,32] A surgical alternative to TTBR is STBR with selective piecemeal excision beyond STBR's normal boundaries.[19,32] Regardless of approach, patients with T4 tumors generally have a dismal prognosis when treated with TTBR and radiotherapy.[1] In these advanced cases, chemotherapy has recently gained attention as an attractive substitute for surgery and radiotherapy.

All three types of temporal bone resection permit adequate exposure for dural resection. The extent of dural resection is based on margin status and is repaired with a dural substitute.[35] Resection of the internal carotid artery is also an option, but it can add significant morbidity and has not been shown to improve survival.[31,36] Absolute contraindications to curative surgery are poor health, cavernous sinus involvement, unresectable neck disease, and distant metastases.[5] Relative contraindications include carotid artery and lower cranial nerve involvement.[37]

One last resection option described in the literature is a local canal resection (LCR), also termed a "sleeve resection." This procedure generally involves removal of the skin from the bony ear canal and reconstruction of the EAC with a split-thickness skin graft. The attractiveness of this approach is preservation of hearing and lower risk to neurovascular structures; however, by its very nature, the method is not oncologically sound because the bony ear canal skin is very thin and there is no way to remove a tumor with an adequate deep margin. Not surprisingly, LCR has been linked to high recurrence rates for SCC of the bony EAC. Austin et al[38] reported that 60% of patients with T1 disease developed local recurrence when treated with LCR alone. Zhang et al[39] compared LCR to LTBR plus superficial parotidectomy in their population of patients with T1 or T2 disease and noted a positive margin rate of 54% and a local recurrence rate of 46% with LCR, compared with no positive margins or local recurrences in the LTBR group. Therefore, cancer within the bony EAC or abutting the bony-cartilaginous junction should be resected with a LTBR. On the other hand, if the lesion is located completely within the cartilaginous portion of the EAC, wide local excision is appropriate as adequate deep margins can be obtained.

2.5 | Management of extratemporal structures

Temporal bone resection can be combined with parotidectomy and neck dissection for adequate staging and control of extratemporal disease. Given the pathways of the temporal bone—such as the fissures of Santorini—and the lymphatic drainage from the EAC, most authors consider the parotid at high risk for tumor invasion or intraparotid lymph node metastasis. Proven direct or lymphatic spread to the gland necessitates parotidectomy, but elective parotidectomy is controversial. Morris et al[40] reported that 25% of patients with T2 through T4 EAC SCC had pathologic evidence of direct parotid invasion and 42% had parotid nodal metastases. However, the literature contains discrepancies regarding the isolation of early ear canal disease. Zhang et al[39] noted direct parotid invasion in 33% and 45% of patients with T1 or T2 SCC, respectively, but parotid lymphatic disease in 0% and 9%, respectively. In contrast, Shinomiya et al[41] recently reported no direct parotid invasion among patients with T1 or T2 disease and parotid lymphatic disease in 0% and 5%, respectively. Unfortunately, the literature contains no outcome data based solely on the addition of elective parotidectomy. As such, some authors support superficial parotidectomy in all cases of EAC SCC, whereas others state that it is not mandatory in T1 and T2 cases in which the tumor does not involve the anteroinferior canal wall.[40-43] Deep lobe management is also controversial; some authors advocate inspection at the time of surgery and others advocate total parotidectomy for all T3 and T4 tumors.[40,44]

Given its proximity to the parotid and EAC, the TMJ is also vulnerable to invasion. Most authors advocate for mandibular condylectomy in patients with T3 or T4 EAC SCC, but the procedure is controversial in patients with early disease.[45] Masterson et al[11] resected the TMJ in eight patients with T2 disease and did not identify any malignant spread to the TMJ. However, Hosokawa et al[42] demonstrated tumor extension into the soft tissue around the TMJ in all patients with T2 disease with anteroinferior bony EAC erosion >2 mm on preoperative CT scan. As such, they recommended condylectomy in this subset of patients. In contrast, Moffat et al[45] recommended routine resection in all T1 and T2 cases because of the TMJ's proximity to the margin of resection. No outcome data based solely on the addition of condylectomy exist.

Although TBSCC was historically considered to have a low rate of cervical metastasis, Rinaldo et al[46] reviewed the literature and noted a 17.7% rate of cervical involvement among 491 cases representing all T stages. Morris et al[40] later estimated that the clinically occult cervical metastasis rate for primary TBSCC is 12.5% across all T stages. In T1 and T2 disease, Shinomiya et al[41] decided not to perform elective neck dissections at time of initial resection and found no recurrences in the neck over a 5-year period. Others argue that neck dissection is not necessarily a therapeutic tool, but serves as a staging tool for determining the need for adjuvant therapy or allows for the exposure of vessels for microvascular free tissue transfer.[22] Most authors undertaking elective neck dissections advocate for dissections of levels II and III, as these are the most commonly affected, but others still recommend completing levels Ib through V.[4,22,44] Because there is no outcome data for elective neck dissection, some authors choose to perform it in all cases and others only in advanced disease.[22,28,44,45]

In light of the low incidence of TBSCC, proper randomized trials are lacking and the extent of resection still varies widely between authors and institutions. Resection protocols based on PSS T stages do not exist. In general, at The University of Texas MD Anderson Cancer Center, T1 and T2 tumors, which are confined to the ear canal, are treated with *en bloc* LTBR, and elective parotidectomy and level II lymph node dissection are used for adequate staging. T3 tumors, which at minimum involve the middle ear, are treated with piecemeal STBR, parotidectomy, and levels II and III neck dissection. T4 tumors are treated similarly to T3 tumors, but piecemeal TTBR is performed when tumors involve the petrous apex. Mandibulectomies, zygoma resections, and dural resections are performed if there is direct involvement of these structures.

2.6 | Reconstruction

Reconstruction of temporal defects is critical to appropriate healing and prevention of complications. For most LTBR defects, a temporalis muscle flap suffices.[47] The temporalis muscle depends on the deep temporal artery for its blood supply. If this artery is damaged, then an

alternate means of reconstruction is required. For larger defects, such as STBR defects or those resulting from auriculectomy and condylectomy, a microvascular free flap may be required.[17] In such cases, the anterolateral thigh is the most common source because it provides bulk and sufficient skin coverage.[44]

If the facial nerve is sacrificed in a patient with normal preoperative facial function, immediate nerve grafting is recommended.[44] Facial function after nerve grafting does not appear to be affected by postoperative radiotherapy.[48] For patients with pre-existing facial paralysis, static fascial slings, gold weight implants, and canthoplasties can be employed.[44]

2.7 | Outcomes, prognosis, and recurrence

Overall, survival rates are generally high for patients with T1 or T2 primary TBSCC and poor for patients with T3 or T4 disease. Moody et al[1] noted that the 2-year OS rates were 100%, 80%, 50%, and 7% for T1, T2, T3, and T4 tumors, respectively. In the literature, the 5-year DFS and DSS rates for combined T1 and T2 tumors range from 67% to 100% and from 92% to 100%, respectively; and the 5-year DFS and DSS rates for combined T3 and T4 tumors range from 41% to 59% and from 48% to 65%, respectively.[26,43] Despite the low survival rates in patients with advanced disease, the rates appear to be improving over time, with the latest meta-analysis demonstrating that the 5-year OS rates for T3 and T4 tumors were 72.5% and 35.8%, respectively.[49]

Other studies have identified prognostic factors for survival. Masterson et al[11] found that nodal involvement, poorly differentiated histology, and carotid involvement were indicators of poor DSS rates in patients with TBSCC, while Omura et al[50] found the same result for positive margins, stage T4, dural invasion, and TMJ invasion. Studies with multivariate analyses have shown that tumor stage, nodal involvement, and dura involvement are prognostic for DFS in patients with TBSCC.[26,28,51,52] A univariate analysis study by Bacciu et al[26] demonstrated that positive margins, advanced PSS stage, bony invasion of the temporal structures, and facial palsy had significant effects on DFS and DSS. Therefore, it is not surprising that the vast majority of TBSCC recurrences are local.[40]

2.8 | Role of radiotherapy and chemotherapy

Radiotherapy for TBSCC is most commonly given in the adjuvant postoperative setting. Indications for postoperative radiotherapy include lymph node metastasis, perineural invasion, positive margins, recurrent tumors, and bone invasion.[1,8,22,39,45] Most authors agree that radiotherapy is not a substitute for obtaining negative margins.[20] Multiple studies have also demonstrated improved survival rates with adjuvant radiotherapy as opposed to surgery alone for T2 and higher tumors, since T2 tumors by definition have bone invasion.[1,22,38,53,54] Little benefit of postoperative radiotherapy has been seen for patients with completely resected T1 tumors.[54] This difference highlights the need for proper staging.

The role of definitive radiotherapy for early tumors remains controversial. Its attractiveness lies in the preservation of conductive hearing. Morita et al[55] examined patients with T1 or T2 TBSCC and found improved OS with surgery and adjuvant vs definitive radiotherapy. When stratifying T1 and T2 tumors between these modalities, Ogawa et al[51] saw an improved 5-year DFS rate for T1 and reduced DFS rate for T2 in the definitive radiotherapy group. They concluded that definitive radiotherapy may be considered for T1 tumors but not for T2 tumors. Despite this, some authors believe that radiotherapy alone is insufficient for any stage of TBSCC.[32,38]

Chemotherapy is an emerging modality in the treatment of TBSCC. Historically used only for advanced tumors in the adjuvant setting, its use as an induction agent is promising. Nakagawa et al[18] showed that preoperative chemoradiation therapy (CRT) was helpful in obtaining tumor-free margins in T3 and T4 tumors. In a later meta-analysis, Takenaka et al[49] evaluated CRT as a definitive therapeutic option and in the pre- and postoperative settings for T3 and T4 SCC. They found on multivariate analysis that preoperative CRT was associated with improved OS rate, but postoperative CRT did not affect OS. Finally, they noted that definitive CRT and the standard of care (surgery and adjuvant radiotherapy) had equivalent OS rates. In more recent studies, authors have found definitive CRT to have at least equivalent, if not improved, survival rates over surgery with adjuvant radiotherapy for T3 and T4 tumors.[56-58] Because definitive CRT has been demonstrated to be efficacious and safe, some authors have extended definitive CRT to stage II disease, as well.[59] Nearly all modern investigations utilize a regimen of 5-fluorouracil, docetaxel, and cisplatin; however, a recent case report demonstrated dramatic TBSCC response after treatment with bevacizumab and pemetrexed.[49,56-58,60] In addition, immunotherapy is emerging as an important arm of cancer therapy, especially for advanced cutaneous SCC of the head and neck, yet only case reports have been published on its use for ear canal cancer.[61-63]

2.9 | Auditory rehabilitation

Hearing loss after treatment for TBSCC can be sensorineural, conductive, or mixed. Maximum conductive hearing loss is expected after an LTBR, whereas complete sensorineural hearing loss is seen after resection of the otic capsule in an STBR or TTBR. If the inner ear is spared, patients can still develop sensorineural hearing loss from chemotherapy and radiotherapy ototoxicity. Radiotherapy has deleterious effects on the cochlea at about 40 Gray.[64] Osseointegrated hearing aids (OIHAs) are the mainstay of auditory rehabilitation following surgical treatment of temporal bone cancer, but these are not necessarily free of complications. Post-implant complications include local inflammation, infection, granulation tissue, skin overgrowth, bone exposure, and implant extrusion.[65] Complication rates do not appear to be different in otologic oncology patients compared to the general population with OIHAs.[65,66] Nader et al[65] evaluated OIHA implantation in temporal bone cancer patients and determined that, to decrease complication rates, the ideal timing of implantation is at initial oncologic resection and prior to radiotherapy, if possible. The authors also

recommend waiting 6 months prior to loading with the processor. Finally, there have been reports of promising results from conductive hearing restoration surgery, such as tympanoplasty, performed at the time of initial oncologic resection.[64]

2.10 | Biomarkers

As patients with advanced TBSCC face poor outcomes, various biomarkers have been investigated to improve prognostication and surveillance. MASPIN (MAmmary Serine Protease INhibitor) is a tumor suppressor gene found to have increased levels of cytoplasmic expression in patients without TBSCC recurrence.[67] Marioni et al[68] also displayed a significantly increased recurrence rate and shorter DFS in TBSCC that had increased expression of endoglin (CD105), a proliferation-associated protein expressed in angiogenic endothelial cells. Finally, expression of epidermal growth factor receptor has recently been associated with poor survival outcomes.[69] These biomarkers may provide avenues to identify patients at high risk for recurrence. Other biomarkers have also been studied but have not been found to correlate statistically with survival.[70-73]

3 | CONCLUSION

Although SCC is the most common malignancy of the temporal bone, it is seen only rarely in clinical practice. This has limited the ability to perform randomized trials and agree upon a management strategy. Because of the aggressive nature of the tumor, the typically late stage at presentation, and the anatomic peculiarities of the temporal bone, TBSCC treatment is complex and should be delivered by a multidisciplinary team. LTBR remains at the heart of treatment for ear canal tumors, and postoperative radiotherapy is typically given to patients with tumors at stage T2 and higher. Novel surveillance and treatment strategies are emerging for advanced tumors, but multi-institutional research collaboration efforts may prove most beneficial in defining a management algorithm for TBSCC.

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CONFLICT OF INTEREST

The authors declare no potential conflict of interest.

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