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Guidelines for Treating Temporal Bone Carcinoma Based on Long-Term Outcomes

*Andrea Bacciu, †Ignazio Alessandro Clemente, †Enrico Piccirillo, *†Silvano Ferrari, and †Mario Sanna

**Head and Neck Department, University-Hospital of Parma; and †Gruppo Otologico, Piacenza-Rome, and University of Chieti, Italy*

Objective: To describe our experience in the management of patients with squamous cell carcinoma of the temporal bone (TBSCC) and to identify factors predictive of outcome.
Study Design: Retrospective study.
Setting: Quaternary referral otology and skull base center.
Patients: A total of 45 consecutive patients with histologically confirmed TBSCC were treated surgically at our institution between 1993 and 2011. Patients were divided into 5 stage I (11.1%), 6 stage II (13.3%), 15 stage III (31.1%), and 19 stage IV tumors (42.2%) according to the University of Pittsburgh modified TNM staging system.
Interventions: Twenty-one patients underwent lateral temporal bone resection, and 24 underwent subtotal temporal bone resection. Postoperative radiotherapy was performed in 27 cases.
Results: The 5-year disease-specific survival (DSS) and recurrence-free survival (RFS) for patients with early-stage disease (Stages I and II) was 100%. The 5-year DSS and RFS rates for patients with advanced disease (Stages III and IV) were 65.1% and 59.6%, respectively. On univariate analysis, factors that had a significant effect on both DSS and RFS were advanced Pittsburgh stage, presence of facial nerve palsy, positive tumor margins, and invasion of the fallopian canal, medial wall, middle ear, mastoid, temporomandibular joint, jugular bulb, and dura. Multivariable analysis identified only dural involvement as an independent predictor for both DSS and RFS.
Conclusion: In this study, the Pittsburg staging system allowed an estimation of the prognosis. In fact, the prognosis of TBSCC was strictly correlated to tumor stage. The poor prognosis of advanced stage tumors underlines the importance of early diagnosis. Surgery with or without adjuvant radiotherapy remains the standard of care in the treatment of TBSCC. **Key Words:** Cancer—External auditory canal—Middle ear—Prognostic factors—Squamous cell carcinoma—Surgical management—Temporal bone.
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Malignant neoplasms of the temporal bone are rare, accounting for approximately 0.2% of all head and neck malignancies (1). The annual incidence is estimated to be between 1 and 6 per million population (2). Squamous cell carcinoma is the most common histologic subtype to occur in the temporal bone followed by basal cell carcinoma, adenocarcinoma, adenoid cystic carcinoma, mucoepidermoid carcinoma, ceruminoma, melanoma, and sarcoma (3–4). Currently, there is no universally accepted staging system for carcinomas of the temporal bone. In 1990, a staging system based on preoperative clinical and computed tomography findings was proposed by a group of the University of Pittsburgh (5). Since its introduction, the Pittsburgh classification has been increasingly used by authors to classify squamous cell carcinoma of the temporal bone (TBSCC). This attitude would contribute to harmonization of the international data.

The optimal management of patients with TBSCC remains a topic of debate and controversy. Surgery with or without adjuvant radiotherapy is considered the standard of care in the treatment of TBSCC. Up until the middle of the 20th century, radical mastoidectomy was the surgical treatment of choice for malignancies of the temporal bone. In 1954, Parsons and Lewis (6) proposed the en bloc subtotal temporal bone resection (STBR) as an alternative to the classical management of radical mastoidectomy. In 1960, Conley and Novack (7) described the technique of lateral temporal bone resection (LTBR). In 1984, Graham et al. (8) reported the first successful single stage total en bloc removal of the temporal bone with internal carotid artery sacrifice. In 1997, Moffat et al. (9) proposed the en bloc extended temporal bone resection with preservation of the internal carotid artery and piecemeal removal of the petrous apex. Despite the technical advances in preoperative neuroimaging and

Address correspondence and reprint requests to Andrea Bacciu, M.D., Head and Neck Department, University-Hospital of Parma, Via Gramsci, 14, 43100 Parma, Italy; E-mail: andreabacciu@yahoo.it

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cranial base microsurgery, surgery for advanced tumors is still associated with poor outcome.

The present study aims to review the management and survival of 45 patients with TBSSC seen and treated in a single center. We also present a further review of the literature including the main studies that used the Pittsburgh classification.

METHODS

A retrospective analysis of patients treated at the Gruppo Otologico between January 1993 and November 2011 with a diagnosis of primary external auditory canal and temporal bone malignancies was performed. Forty-five patients had a histologically confirmed diagnosis of TBSCC and were included in the study. All other histologic subtypes were excluded. Also excluded were tumors arising from the parotid, auricle, concha, or periauricolar skin. Institutional review board approval was obtained before commencement. The collected data were analyzed for age, sex, presenting symptoms, tumor stage, treatment, histologic features, and patient outcome. Preoperatively, all patients underwent both gadolinium-enhanced magnetic resonance imaging and high resolution computed tomography. A postoperative follow-up examination was performed at 1, 3, 6, and 12 months and then yearly. All tumors were staged according to the University of Pittsburgh modified TNM staging system (Table 1) (1,5). Overall survival, disease-specific survival (DSS) and recurrence-free survival (RFS) were analyzed. A univariate analysis was conducted in relation to DSS and RFS by the Kaplan-Meier method for the following variables: age, sex, presence of facial palsy at time of diagnosis, T stage, margin status, tumor differentiation, cervical lymph node status, and involvement of the mastoid, middle ear, fallopian canal, otic capsule, temporomandibular joint, parotid, jugular bulb, and dura. The statistically significant variables in the univariate analysis were included in a multivariable analysis. Multivariable analysis was performed using the Cox proportional hazard model. $p < 0.05$ was considered statistically significant. The data were analyzed with a statistical software program (MedCalc; Mariakerke, Belgium).

TABLE 1. *Modified Pittsburg staging system (1,5)*

Factor	Description
T status	
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 mm)
T3	Tumor eroding the osseous EAC (full thickness) with limited soft tissue involvement (<5 mm) or tumor involving 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 tumor with extensive soft tissue involvement (>5 mm), such as involvement of temporomandibular joint or styloid process; or with evidence of facial paresis
N status	
N0	No regional nodes identified
N1	Single ipsilateral regional node <3 cm in size
N2a	Single ipsilateral regional node 3–6 cm in size
N2b	Multiple ipsilateral nodes
N2c	Bilateral or contralateral nodes
N3	Node >6 cm
Overall stage	
I	T1 N0
II	T2 N0
III	T3 N0
IV	T4 N0 and T1-T4 N+

RESULTS

Clinical Data

The 45 patients with TBSCC included 25 men (55.6%) and 20 women (44.4%). The mean age of patients at the time of surgery was 61.9 ± 12.6 years (range, 36–89 yr). Twenty-four patients (53.3%) were older than 65 years, and 21 patients (46.7%) were 65 years old or younger. Twenty-six tumors (57.8%) were on the right side and 19 (42.2%) on the left side. The follow-up of the series ranged from 1 to 144 months (mean, 46.7 ± 42 mo). Table 2 shows demographic characteristics, treatment, and outcome of the investigated group.

Three patients had a history of chronic suppurative otitis media. Two patients had a positive history of previous head and neck radiation therapy because of nasopharyngeal carcinoma. Hearing loss was the predominant presenting symptom occurring in 34 patients (75.5%), followed by otorrhea (73.3%), otalgia (22.2%), and bleeding (17.7%). Eight patients (17.7%) had facial nerve palsy on initial diagnosis. Presence of external auditory canal mass was recorded in all patients. The mean length of symptoms before presentation was 7.2 ± 8. 3 months (range, 1–50 mo).

Classification of the Tumor

The tumor stage was determined postoperatively using the radiology reports, the intraoperative findings, and the surgical pathology report. Distribution of tumors according to the modified Pittsburgh staging system (1,5) was as follows: Stage I, 5 cases (11.1%); Stage II, 6 cases (13.3%); Stage III, 15 cases (31.1%); and Stage IV, 19 cases (42.2%). Four patients had metastatic cervical lymph nodes. One patient was N1 and 3 patients were N2b. Because all the metastatic nodes were in the T4 patients, for the purpose of this article, ''T'' measurement and ''Staging'' are used interchangeably.

In all patients, the tumor was present within the external auditory canal. The frequency of involvement of other structures was as follows: middle ear, 20 (44.4%), middle ear with erosion of the medial wall, 14 (31.1%); mastoid, 15 (33.3%); fallopian canal, 13 (28.8%); middle cranial fossa dura, 9 (20%); temporomandibular joint, 7 (15.5%); parotid gland, 6 (13.3%); jugular bulb, 6 (13.3%); otic capsule, 5 (11.1%); concha, 4 (8.8%); styloid process, 2 (4.4%); petrous apex, 2 (4.4%); posterior cranial fossa dura, 1 (2.2%); internal carotid artery, 1 (2.2%); and Eustachian tube, 1 (2.2%).

Treatment

All the patients underwent primary surgery with curative intent. Classic approaches to the surgical management of TBSCC include local resection, lateral temporal

TABLE 2. *Clinical data of 45 cases of squamous cell carcinoma of the temporal bone*

Patient/ sex	Age at diagnosis (yr)	Structures involved	FN palsy at presentation	Tumor stage	Diff	Surgical treatment	Margin status	Postoperative RT	Recurrence (mo)	Follow-up (mo)	Status
1/F	89	EAC	No	T1N0	Well	LTBR	-	No	No	26	DOC
2/M	68	EAC	No	T1N0	Well	LTBR	-	No	No	1	NED
3/F	63	EAC	No	T1N0	Mod	LTBR	+	Yes	No	69	NED
4/M	55	EAC	No	T1N0	Well	LTBR	-	No	No	114	NED
5/F	77	EAC	No	T1N0	Mod	LTBR	-	No	No	86	DOC
6/F	60	EAC	No	T2N0	Well	LTBR	-	No	No	51	NED
7/M	78	EAC	No	T2N0	Well	LTBR	-	No	No	96	NED
8/M	67	EAC	No	T2N0	Well	LTBR	-	No	No	44	NED
9/F	70	EAC	No	T2N0	Well	LTBR + SP	+	Yes	No	37	NED
10/M	40	EAC	No	T2N0	Mod	LTBR + SP	-	No	No	140	NED
11/F	59	EAC	No	T2N0	Well	LTBR	+	Yes	No	10	NED
12/F	69	EAC, ME	No	T3N0	Mod	STBR	+	Yes	No	38	NED
13/M	39	EAC	No	T3N0	Well	LTBR	+	Yes	Neck (7)	8	DOD
14/F	68	EAC	No	T3N0	Well	LTBR	-	Yes	No	99	NED
15/M	71	EAC	No	T3N0	Well	LTBR + SP	-	Yes	No	71	NED
16/F	73	EAC	No	T3N0	Mod	LTBR + SP	-	Yes	No	9	NED
17/F	59	EAC	No	T3N0	Mod	LTBR + SP	-	Yes	Neck (30)	144	NED
18/M	82	EAC, ME	No	T3N0	Mod	STBR	+	Yes	No	61	NED
19/F	78	EAC, ME, MST	No	T3N0	Well	STBR	+	Yes	No	63	NED
20/M	45	EAC	No	T3N0	Mod	LTBR + SP + ND	+	Yes	No	32	NED
21/M	66	EAC, ME	No	T3N0	Poor	STBR	-	Yes	No	38	NED
22/F	77	EAC	No	T3N0	Mod	LTBP	-	Yes	No	31	NED
23/M	79	EAC	No	T3N0	Mod	LTBR	+	Yes	No	109	NED
24/F	74	EAC, MST	No	T3N0	Mod	STBR	+	Yes	Local (11)	12	DOD
25/M	54	EAC, ME	No	T3N0	Mod	STBR + SP	+	Yes	No	37	DOC
26/F	36	EAC, ME	No	T3N0	Well	STBR + SP	-	Yes	No	33	NED
27/M	85	EAC, ME-mw, MST	No	T4N0	Well	STBR + TP	+	Yes	Local (13)	29	NED
28/M	57	EAC, ME-mw, MST, MCF, OC, JB, FC	Yes	T4N0	Well	STBR	+	Yes	Local (11)	12	DOD
29/M	75	EAC, ME-mw, MST. MCF, JB, PA	No	T4N0	Mod	STBR	+	Yes	Local (2)	3	DOD
30/M	53	EAC, ME-mw, FC, TMJ, PRT	No	T4N2b	Mod	STBR + TP + MCR + ND	-	Yes	No	139	NED
31/M	49	EAC, PRT	No	T4N0	Mod	LTBR + TP	-	Yes	No	116	NED
32/F	68	EAC, ME-mw, MST, MCF, PCF, FC	No	T4N0	Well	STBR + TP + ND	+	Yes	Local (15)	16	DOD
33/M	62	EAC, TMJ, FC	Yes	T4N0	Mod	STBR + TP + MCR	+	Yes	Local (7)	8	DOD
34/F	56	EAC, ME-mw, OC, PRT, TMJ	No	T4N1	Mod	STBR + TP + MCR + ND	+	Yes	No	105	NED
35/M	58	EAC, ME-mw, MST, MCF, FC, OC, JB, ET, TMJ, Concha	Yes	T4N0	Well	STBR + MCR + TP	+	Yes	Local (3)	24	DOD
36/M	40	EAC, ME-mw, MST, FC, MCF, TMJ	Yes	T4N0	Mod	STBR + TP + MCR	+	Yes	Local (1)	3	DOD
37/F	71	EAC, ME-mw, MST, MCF, FC, ICA, PA, TMJ, PRT	Yes	T4N0	Well	STBR + TP + MCR	+	Yes	Local (6)	7	DOD
38/F	73	EAC, ME-mw, MST, FC, SP	No	T4N0	Poor	STBR + TP + ND	+	Yes	No	68	NED
39/M	58	EAC, MST, MCF, JB	No	T4N0	Mod	STBR + TP + MCR	+	Yes	Local (2)	3	DOD
40/M	53	EAC, ME-mw, MST, FC, SP	No	T4N0	Mod	STBR + TP + ND	+	Yes	No	25	NED
41/M	42	EAC, ME-mw, MCF, FC, OC, Concha	Yes	T4N0	Mod	STBR + TP	+	Yes	Local (1)	17	DOD
42/F	61	EAC, ME-mw, MST, FC, JB, OC, PRT, Concha	Yes	T4N0	Well	STBR + ND + TP + MCR	+	Yes	No	29	NED
43/M	47	EAC, MST, FC	Yes	T4N2b	Mod	STBR + TP + ND	+	Yes	No	17	NED
44/F	61	EAC, ME-mw, MST, MCF, FC, JB, SP	No	T4N0	Mod	STBR + TP	+	Yes	No	13	NED
45/M	51	EAC, TMJ, PRT, Concha	No	T4N2b	Poor	LTBR + TP + MCR + ND	+	Yes	No	9	NED

M indicates male; F, female; FN, facial nerve; Diff, differentiation; Well, well differentiated; Mod, moderately differentiated; Poor, poorly differentiated; RT, radiation therapy; EAC, external auditory canal; ME, middle ear; ME-mw, erosion of the medial wall of the middle ear; MST, mastoid; MCF, middle cranial fossa dura; PCF, posterior cranial fossa dura; OC, otic capsule; FC, Fallopian canal; JB, jugular bulb; PA, petrous apex; PRT, parotid gland; TMJ, temporomandibular joint; ICA, internal carotid artery; SP, styloid process; ET, eustachian tube; LTBR, lateral temporal bone resection; STBR, subtotal temporal bone resection; ND, neck dissection; SP, superficial parotidectomy; TP, total parotidectomy; MCR, mandibular condyle resection; DOD, dead of disease; DOC, dead of another cause; NED, no evidence of disease.

bone resection, subtotal temporal bone resection, and total temporal bone resection. In this series, only LTBR and STBR were used. The LTBR is designed primarily for tumors of the bony and cartilaginous portions of the external auditory canal without extension into tympanic cavity and/or mastoid. The approach entails a complete canal wall up mastoidectomy with an extended facial recess opening. The external auditory canal is resected en bloc along with the tympanic membrane, the malleus, and the incus, with the medial limit defined at the level of the incudostapedial joint. The STBR extends medially and includes internal auditory canal identification, facial nerve transection, and removal of the otic capsule with preservation of the petrous apex. The inferior plane of resection is lateral to the jugular bulb and internal carotid artery. If the tumor extends into the mastoid and dural involvement is suspected, middle and posterior fossa craniotomies might be necessary to achieve adequate exposure. If the dura is found infiltrated, an incision of the dura is undertaken at an area free of infiltration, and the involved dura is elevated until free margins are reached. If the facial nerve is invaded by the tumor, the nerve should be included in the specimen. The bone medial to the facial nerve is removed by drilling out the lateral and posterior semicircular canals. The sigmoid sinus and jugular bulb are preserved unless infiltrated. The drilling is then advanced anteriorly in the region of the attic. The lower part of the tympanic bone is removed until reaching the soft tissue of the temporomandibular joint. The condyle of the mandible is resected and included in the specimen. The remaining bony attachment is fractured using a rongeur. If the tumor is found to involve the cochlea, drilling should be further advanced medially until the internal auditory canal is reached. A total temporal bone resection removes the entire temporal bone and may include carotid artery sacrifice. This approach was not used in this series.

En bloc removal by LTBR was performed in 21 patients with tumors lateral to the tympanic membrane (5 T1, 6 T2, 8 T3, and 2 T4). The subtotal temporal bone resection (STBR) by using a combination of en bloc and piecemeal resection techniques was chosen in 24 cases (7 T3 and 17 T4). Eight patients (2 T2 and 6 T3) with involvement of the anterior canal wall without bony erosion had superficial parotidectomy performed. Seventeen patients with advanced disease (T4) in which the bony canal had been violated underwent total parotidectomy. Nine patients underwent mandibular condyle resection and drilling of the glenoid fossa because macroscopic infiltration of the temporomandibular joint was found during surgery. Eight patients underwent ipsilateral neck dissection because lymph node metastases were suspected on the basis of preoperative imaging findings. Lymph node metastases were confirmed histologically in 4 cases.

The auricle was resected and included in the specimen in 4 cases. The reconstruction of the surgical defects was performed using a tunnelled supraclavicular artery island flap in 2 patients, a trapezius myocutaneous flap in one patient, and a latissimus dorsi myocutaneous flap in another patient. The facial nerve was sacrificed in 13 cases due to tumor infiltration. Facial nerve grafting using the sural nerve was accomplished in 5 cases. One patient with Stage I tumor and 2 patients with T2 tumor received postoperative radiotherapy because surgical margins were found positive on histologic examination. All patients with T3 and T4 tumors received postoperative radiotherapy. The average dose of radiation was 60 Gy.

Histopathology

Nineteen of the tumors (42.2%) were well-differentiated TBSCCs, 23 (51.1%) were moderately differentiated TBSCCs, and 3 (6.7%) were poorly differentiated TBSCCs. Surgical margins were positive in 28 cases (62.2%) and negative in 17 cases. In early-stage tumors (T1-T2) and in some T3 tumors limited to the external auditory canal, an en bloc complete resection was performed including additional soft tissue margin in suspicious areas. According to Arriaga et al. (5), frozen sections were used to assure clear margins. In the presence of advanced disease, resection was accomplished in a piecemeal manner and clear surgical margins could not be obtained.

Recurrence

Overall, 13 patients (28.8%) experienced recurrence. Median time to recurrence was 8.3 months (range, 1–30 mo). All patients but one who experienced recurrence had positive surgical margins. At the time of this analysis, none of the patients with early-stage tumors (T1 and T2) had recurrence. Of the 15 patients with T3 disease, 1 patient had local recurrence, and 2 patients had neck recurrence. Of the 19 patients with T4 diseases, 7 patients had local recurrence, and 1 patient had local recurrence followed by cerebral metastases. Eleven patients who experienced recurrence died (84.6%). Mean survival time after diagnosis of recurrence was 4.2 ± 7.1 months (range, 1–21 mo).

General Survival

There were no perioperative deaths in this series.

Upon completion of follow-up, 31 patients were alive without evidence of disease. Two patients died of intercurrent disease. Eleven patients died of TBSCC (24.4%): 2 T3 and 9 T4 patients.

The 5-year overall survival, DSS and RFS rates for all patients were 67.6%, 73.7%, and 68.9%, respectively (Fig. 1).

The 5-year DSS and RFS for patients with early-stage disease (T1-T2) was 100%. The 5-year DSS for patients with T3 and T4 disease were 86.2% and 48.7%, respectively. The 5-year RFS rates for patients with T3 and T4 disease were 79% and 45.2%, respectively (Fig. 2). T4 had significantly worse DSS ($p = 0.0110$) and RFS ($p = 0.0065$) than early-stage (T1-T2) tumors. There was also a statistically significant difference in DSS ($p = 0.0326$) and RFS ($p = 0.0281$) between T4 and T3 tumors. There was no statistically significant difference in 5-year DSS ($p = 0.243$) and RFS ($p = 0.154$) between patients with T1-T2 tumors and patients with T3 tumors.

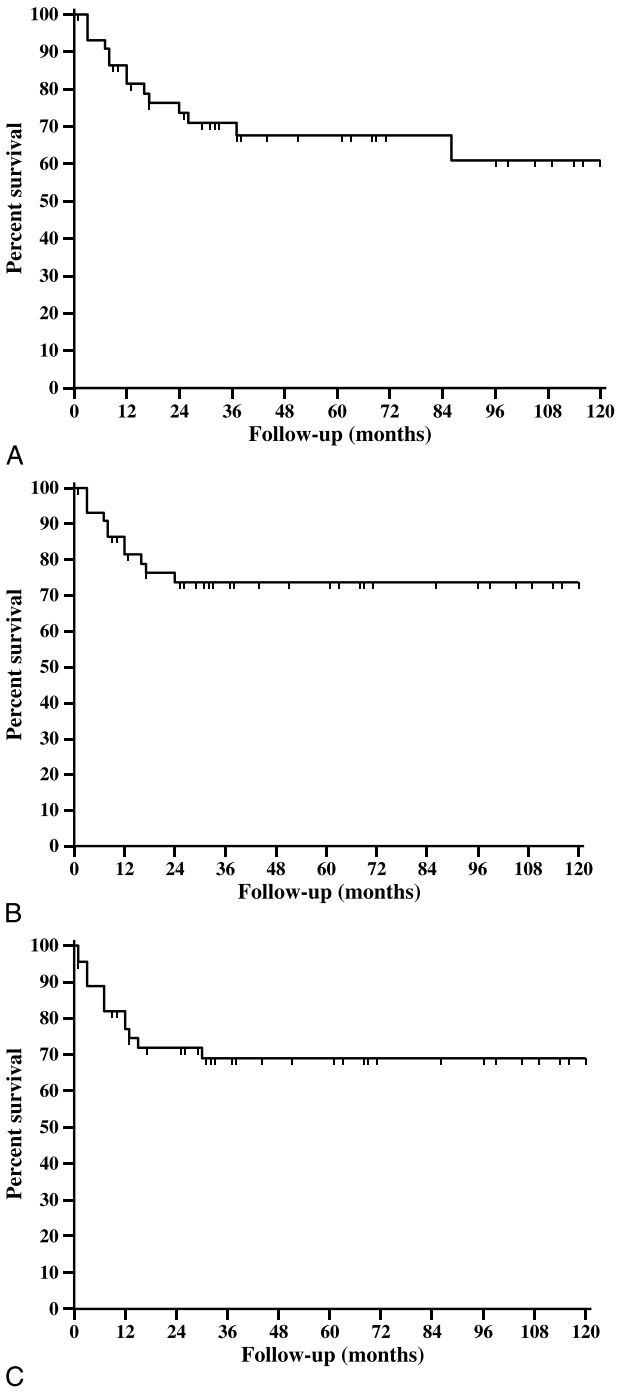

FIG. 1. Kaplan-Meier curves for overall survival (*A*), disease-specific survival (*B*), and recurrence-free survival (*C*) for study population of 45 patients with squamous cell carcinoma of the temporal bone.

The 5-year DSS rates for patients with negative surgical margins and patients with positive margins were 100% and 57.9%, respectively ($p = 0.0042$). The 5-year RFS for patients with positive surgical margins and for patients with negative surgical margins were 55.3% and 92.9%, respectively ($p = 0.0080$) (Fig. 3).

In the univariate analysis, strong adverse predictors of 5-year DSS were advanced Pittsburgh stage, presence of facial nerve palsy, positive tumor margins, fallopian canal invasion, erosion of the medial wall of the middle ear, dural invasion, mastoid invasion, jugular bulb invasion, and temporomandibular joint invasion. The following factors were not significantly associated with prognosis: sex, age, lymph node metastasis, parotid invasion, and middle ear invasion without involvement of the medial wall. Univariate analysis for RFS showed similar results (Table 3). Multivariable analysis using the Cox proportional hazards model involving the significant factors determined by univariate analysis showed that only dural involvement was an independent predictor of DSS (hazard ratio 20.23; 95% confidence interval, 5.13–79.80; $p < 0.0001$) and RFS (hazard ratio 16.36; confidence interval 95%: 4.75–56.33; $p < 0.0001$).

DISCUSSION

The rarity of the disease, the lack of a universally accepted staging system and the variety of individualized

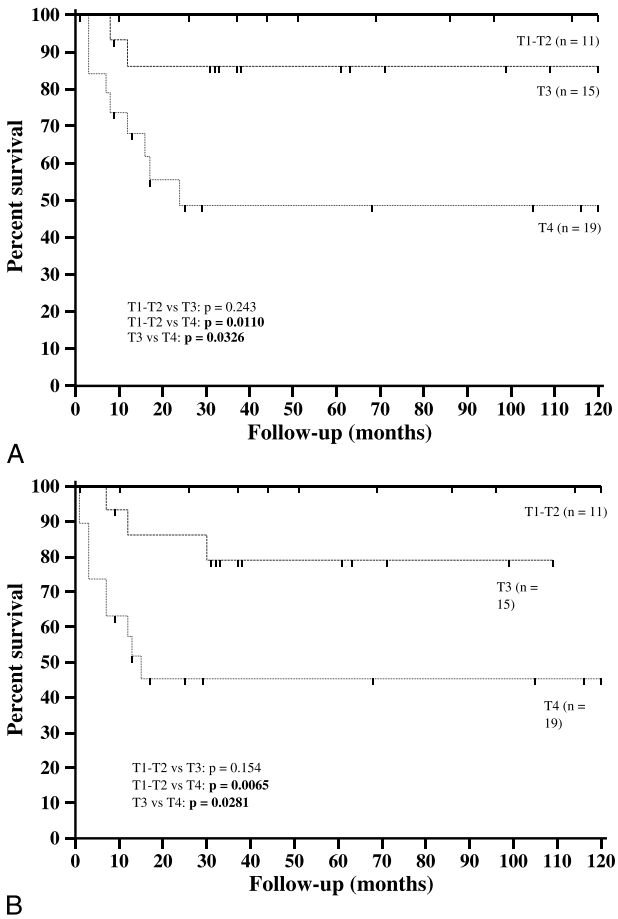

FIG. 2. Disease-specific survival (*A*) and recurrence-free survival (*B*) curves for all patients with squamous cell carcinoma of the temporal bone, according to the modified Pittsburgh staging system.

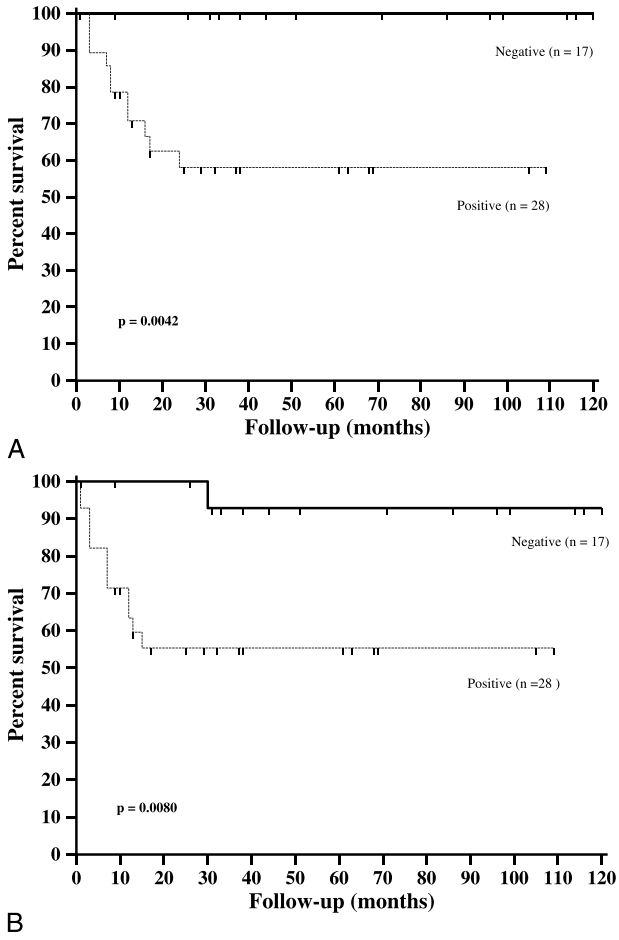

FIG. 3. Disease-specific survival (*A*) and recurrence-free survival (*B*) curves for cases with or without positive margins.

therapeutic protocols make comparison of results among different studies difficult. A summary of treatment and outcome in studies reporting 15 or more patients with TBSCC staged according to the Pittsburgh classification is reported in Table 4. The analysis of the table demonstrates the excellent prognosis of early-stage tumors (T1-T2) and the dismal outcome for patients with advanced disease (T3-T4). Although DSS rates based on staging are reported infrequently in other studies, the 5-year overall survival rates have been reported as 48% to 100% for early-stage disease (T1-T2), 21% to 80% for T3 disease, and 7% to 53% for T4 disease (3,5,10–20). In our study, the 5-year DSS rate was 100% for patients with early-stage disease (T1 and T2), 86% for T3 disease, and 48.7% for T4 disease. Our results are consistent with those reported in the literature.

Local recurrence is relatively high even after curative resection of the tumor. Recurrence remains the major cause of mortality in patients with TBSCC. The overall recurrence rate in several large series has been reported as 23% to 63.8% for advanced stage tumors and 5% to 19% for early-stage tumors (4,15). In our series, recurrent tumors occurred in 28.8% of patients. The 5-year RFS rate for patients with early-stage disease (T1 and T2) was 100%, whereas the 5-year RFS rates for patients with T3 and T4 disease were 79% and 45.2%, respectively.

Because of the rarity of these tumors, there is still no universally accepted management. The major controversy revolves around patients with advanced disease.

Although en bloc resection of the tumor with negative surgical margins is the ideal objective of surgery, this is not always possible especially with advanced lesions. We commonly use the en bloc LTBR technique in patients

TABLE 3. *Univariate analysis of factors predictive of outcome*

Variable	No. of patients	5-year DSS (%)	Log-rank test *p* value	5-year RFS (%)	Log-rank test *p* value
Sex			0.189		0.172
Male	25	65		62.2	
Female	20	82.9		76.5	
Age (yr)			0.452		0.420
≤65	24	67.6		63.9	
>65	21	79.2		74.1	
T stage			**0.0483**		**0.0273**
T1-T2	11	100		100	
T3-T4	34	65.9		59.6	
Facial palsy			**0.0002**		**<0.0001**
Yes	8	18.7		25	
No	37	80.5		79	
Margin status			**0.0042**		**0.0080**
Positive	28	57.9		55.3	
Negative	17	100		92.9	
Lymph node metastasis			0.2882		0.194
Present	4	100		100	
Absent	41	71.4		68	
Differentiation			0.8428		0.7729
Well	19	71.1		65.5	
Moderately poor	26	75.9		71.4	
Fallopian canal invasion			**0.0051**		**0.0102**
Yes	13	41.5		44.9	
No	32	86.7		79.3	
Temporomandibular joint invasion			**0.0126**		**0.0224**
Yes	7	38.1%		42.9	
No	38	80.2%		74.1	
Dural involvement			**<0.0001**		**<0.0001**
Yes	9	0		0	
No	36	91.1		84.3	
Mastoid invasion			**0.0011**		**0.0007**
Yes	15	43.8		38.9	
No	30	89.2		85.7	
Middle ear invasion			0.2185		0.1631
Yes	20	64		59.6	
No	25	82.6		77.1	
ME-mw erosion			**0.0107**		**0.0028**
Yes	14	47.6		41.7	
No	31	86		82.1	
Parotid invasion			0.6988		0.5172
Yes	6	83.3		83.3	
No	39	72.4		67	
Jugular bulb invasion			**0.0038**		**0.0059**
Yes	6	25		33.3	
No	39	80.8		75	
Otic capsule invasion			0.127		**0.0306**
Yes	5	40		40	
No	40	79		78.8	

DSS indicates disease-specific survival; RFS, recurrence-free survival; ME-mw, erosion of the medial wall of the middle ear.

TABLE 4. *Review of the literature*

Study	No. of cases	Staging used	Stage	Treatment	Surgical approach	Overall survival	Disease-specific survival
Arriaga et al. (5)	39	PSS-1990	T1, 4 T2, 1 T3, 19 T4, 15	39 S	2 RM 23 LTBR 6 STBR 8 TTBR	T1-T2,100% T3, 50% T4, 15%	NA
Austin et al. (10)	22	PSS-1990	T1, 8 T2, 4 T3, 6 T4, 4	11 S 9 S + RT 2 RT	7 LR 7 LTBR 4 STBR 2 TTBR	NA	T1-T2, 66% T3, 50% T4, 50%
Zhang et al. (11)	33	PSS-1990	T1, 2 T2, 1 T3, 17 T4, 13	2 S 20 S + RT 11 RT	3 LR 19 LTBR 1 STBR	NA	T1-T2, 100% T3, 68.8% T4, 19.6%
Gillepsie et al. (12)	15	PSS-1990	T1, 4 T2, 4 T3, 4 T4, 3	6 S 9 S + RT	3 LR 8 LTBR 4 STBR	T1-T2, 100% T3, 25% T4, 0%	NA
Moffat et al. (13)	39	PSS-1990	T2, 2 T3, 6 T4, 31	37 S + RT	4 LTBR 33 ETBR	T2, 100% T3, 50% T4, 30%	NA
Nakagawa et al. (14)	25	PSS-1990	T1, 1 T2, 3 T3, 5 T4, 16	4 S 8 S + C + RT 9 C 3 RT 1 none	7 LTBR 5 STBR	T1-2, 100% T3, 80% T4, 35%	NA
Yin et al. (15)	95	PSS-1990	T1, 22 T2, 17 T3, 18 T4, 38	17 S 28 S + RT 21 S + RT + C 1 S + C 16 RT 12 RT + C	17 LR 36 LTBR 8 STBR	T1-T2, 100% T3, 67.2% T4, 29.5%	NA
Moore et al. (16)	20	PSS-1990	NA	NA	20 LTBR	T1-T2, 100% T3-T4,53%	NA
Ogawa et al. (17)	87	PSS-1990	T1, 14 T2, 29 T3, 20 T4, 24	53 S + RT 34 RT	NA	NA	T1, 83% T2, 65% T3, 55% T4, 27%
Kunst et al. (18)	28	PSS-2000	T1, 12 T2, 2 T3, 4 T4, 10	5 S 23 S + RT	12 LR 11 LTBR 2 STBR 3 TTBR	T1-T2, 85% T3-T4, 46%	NA
Ito et al. (19)	16	PSS-2000	T1,3 T2,2 T3,3 T4,8	2 S 11 S + RT 3 RT	2 LR 10 LTBR 1 STBR	NA	T1-T2, 80% T3-T4, 45%
Gidley et al. (3)	71	PSS-2000	T1, 20 T2, 14 T3, 2 T4, 35	31 S 23 S + RT 1 S + RT + C 9 RT 2 RT+C 1 C 4 palliative care 1 Biopsy	7 RM 18 LR 19 LTBR 6 STBR 5 TTBR	T1-T2, 48% T3-T4, 28%	NA
Chi et al. (20)	72	PSS-2000	T1, 15 T2, 3 T3, 19 T4, 35	6 S 66 S + RT	8 LR 29 LTBR 35 STBR	T1, 100% T2, 67% T3, 21% T4, 14%	NA
Our study	45	PSS-2000	T1, 5 T2, 6 T3, 15 T4, 19	8 S 37 S + RT	21 LTBR 24 STBR	NA	T1-T2, 100% T3, 86.2% T4, 48.7%

PSS-1990; University of Pittsburgh staging system proposed by Arriaga et al. (5); PSS-2000; modified University of Pittsburgh staging system as suggested by Moody et al. (1).

S indicates surgery; RT, radiotherapy; C, chemotherapy; RM, radical mastoidectomy; LR, local resection; LTBR, lateral temporal bone resection; STBR, subtotal temporal bone resection; TTBR, total temporal bone resection; ETBR, extended temporal bone resection; NA, not available.

with T1 and T2 tumors as well as in T3 tumors if the disease is limited to the external auditory canal. For T3 tumors extending behind the tympanic membrane we prefer to use the STBR.

The management of more advanced tumors (T4) is particularly challenging as a result of the complex anatomic location, the nearby major neurovascular structures, and the proximity of intracranial structures. In early studies, the surgical attempt to remove these lesions was associated with high rates of morbidity and mortality (7,21). The improvement in neuroimaging techniques along with the advances in skull base microsurgery has made total temporal bone resection (TTBR) realistic. Although recent studies reported an improvement in terms of surgical morbidity and survival in patients who have undergone TTBR (9,10,13), this procedure is still associated with significant postoperative deficits. As previously reported by several authors, the surgical morbidity of STBR is usually limited to a facial nerve palsy, and loss of hearing and balance, whereas additional morbidities of TTBR include potential damage to the cavernous sinus and internal carotid artery and postoperative deficits involving the IIIrd, IVth, Vth, and VIth cranial nerves (20,22,23). In agreement with other authors (1,2,10,11,16,24,25), we believe TTBR is unjustified because of the increased risk of morbidity and no proven survival benefit.

Subtotal temporal bone resection performed by a combination of en bloc and piecemeal resection techniques followed by postoperative radiotherapy may be a reasonable choice in patients with T4 tumors (16,20,23,24).

Prasad and Janecka (26), in their review of the English literature, reported that patients with carcinomatous invasion of the petrous apex, internal auditory canal, dura, and brain had a poor estimated survival rate, although TTBR or dural excision was used. Palliative LTBR or STBR plus radiation may be the best choice in these patients to reduce morbidity from disease improving quality of life.

Although no consensus exists regarding optimal management for advanced TBSCC, surgery combined with adjuvant radiotherapy is considered by many to be the mainstay of treatment because it improves survival rates and local control (10,11,14,15,17,27,28).

A number of studies demonstrated an improvement in survival rate for patients with positive surgical margins who underwent resection, followed by radiotherapy compared with patients who underwent surgical resection alone (1,5,10,11,13,16,18,24,29,30). Testa et al. (27) reported 5-year survival of 29% in patients who underwent radiotherapy alone and 63% in patients who underwent a combination of surgery and radiotherapy. Austin et al. (10) reported that, regardless of stage, those patients who received en bloc resection, without adjuvant radiotherapy had a survival rate of 75%, and those who received en bloc resections plus adjuvant radiotherapy had a survival rate of 100%. In contrast, those patients who received local or incomplete resections had a survival rate of 21% without adjuvant radiotherapy and 66% when adjuvant radiotherapy was administered. These authors recommend the use of adjuvant radiotherapy for all patients with advanced disease (Stages III and IV). Zhang et al. (11) reported 69% estimated survival rate in their Stage III patients who underwent surgery followed by radiotherapy. The indications for postoperative radiotherapy in en bloc resected early lesions (T1 and T2) remain controversial. Our results seem to suggest that postoperative radiotherapy is not necessary in early-stage tumors (T1-T2) when resection margins are negative. This opinion is shared by others (1,18).

Some authors propose radiotherapy as a primary treatment for early-stage tumors reporting results equivalent to those obtained with surgery. Hashi et al. (29) reported 100% disease control in 8 patients with T1 disease treated with radiotherapy alone. Ogawa et al. (17) reported that the 5-year disease-free rate in 10 T1 patients treated with radiotherapy was 83% and concluded that radiotherapy alone is a viable treatment modality for T1 stage tumors. A few studies reported that radiotherapy alone gives comparable results to combined surgery also in advanced stage tumors (15,31). However, valid statistical comparisons between radiotherapy and surgery are difficult to make because of the small number of cases in the literature.

The role of chemotherapy in the management of TBSCC remains to be defined. However, there is some evidence that it may be of benefit in patients with T4 tumors, residual disease, and in metastatic disease (14,18).

Although many investigators have used univariate analysis to identified factors associated with overall survival, DSS, and RFS, only a few studies have used multivariable analysis to further assess independent risk factors (4,14,17). Numerous studies, have reported the importance of T stage in predicting survival and locoregional recurrence (3,17,27,32). In this series the univariate analysis suggested that advanced T stage (T3-T4) may be an important adverse prognostic factor for both DSS and RFS. In the multivariable analysis this study failed to find independent prognostic significance for advanced T stage. Nakagawa et al. (14) published similar results and found that advanced T stage (T4) was an adverse prognostic factor in the univariate analysis but was not an independent factor in the multivariable analysis. It should be noted that several studies failed to find significant difference in overall survival between early-stage tumors (T1-T2) and advanced tumors (T3-T4) (16,19). Morris et al. (4) found that advanced T classification (T3-T4) was not significantly predictive of 5-year DSS in both univariate and multivariable analyses; advanced T classification was a predictor of RFS in univariate analysis and was also independently associated with recurrence outcomes. Preoperative facial nerve palsy has also been quoted as a prognostic indicator for survival. Recently, Higgins and Moody Antonio (33) conducted a systemic review of published studies to determine the impact of facial palsy on survival outcomes. They selected 21 studies containing information on 348 subjects with TBSCC and found that the overall survival and DSS for

subjects presenting with facial palsy were significantly worse than for subjects without facial palsy.

It is well accepted that patients who had complete resection of their disease with negative margins have a better prognosis than patients with positive margins (4,5,15,16,20,22). Our findings show that the 5-year DSS and RFS rates for patients with negative surgical margins were 100% and 92.9%, respectively, whereas they were 57.9% and 55.3%, respectively, for patients with positive margins. Margin status was found to be a predictor for both DSS and RFS in the univariate analysis.

In the study by Chi et al. (20), the 5-year survival rates for 20 cases with negative margins and 18 cases with positive margins were 40% and 22%, respectively ($p < 0.05$). Ogawa et al. (17) reported 5-year disease-free survival rates of 83%, 55%, and 38% in patients with negative, positive, and macroscopic residual disease, respectively ($p = 0.007$). Morris et al. (4) reported a 5-year DSS of 90.5% in patients with negative margins and 29.4% in patients with positive margins and demonstrated in a multivariable analysis that margin status was an independent predictor of survival outcome.

The prognostic importance of regional lymph node involvement has also been widely reviewed (4,14). In the series reported by Morris et al. (4), the 5-year DSS was 80.8% in node negative patients, and 18.8% in node positive patients ($p < 0.0001$). In the review of 25 patients with TBSCC, Nakagawa et al. (14) found that the 5-year estimated survival with regional lymph node involvement was 70%; on the contrary, a positive lymph node involvement significantly decreased the estimated survival to 19%. Both studies reported that nodal metastasis represents an independent risk factor. In our study, lymph node metastases surprisingly did not adversely affected survival, which is contrary to previous reports and may merely reflect the small number of patients with positive nodes. Histologic differentiation of the tumor seems to be an important prognostic factor. Chi et al. (20) reported that the 5-year survival rates for well-differentiated, moderately differentiated, and poorly differentiated SCC were 37.5%, 35.3%, and 0%, respectively. Because of the small number of poorly differentiated tumors in our series, statistical analysis was not performed.

Extratemporal spread of the disease to the mandible or parotid gland, dura, and brain involvement have been reported as negative prognostic factors (4). Parotid gland and mandible invasion were also found to be factors independently associated with overall survival, DSS, and RFS in the multivariable analysis. Previous studies reported that middle ear involvement represents a significant negative prognostic factor (4,32). In the present study, middle ear involvement was found to be a predictor of both DSS and RFS only when erosion of the medial wall was present. Other predictors of 5-year DSS and RFS were fallopian canal invasion, dural invasion, mastoid invasion, jugular bulb invasion, and temporomandibular joint invasion. We found dural involvement to be a strong and independent prognostic factor for survival among patients with TBSCC. The results of this study confirm the validity and reliability of the Pittsburgh staging system in predicting survival. We suggest to consider the Pittsburgh classification as the standard staging system for TBSCC in order to compare treatment and outcomes among different institutions.

CONCLUSION

Squamous cell carcinomas of the temporal bone are rare and are associated with favourable survival when diagnosed at an early stage. In our study, positive surgical margins, fallopian canal invasion, dural invasion, mastoid invasion, jugular bulb invasion, and temporomandibular joint invasion had significant detrimental prognostic implications. Total tumor removal with negative surgical margins should be attempted whenever possible. New radiotherapy and chemotherapy protocols should be explored in order to achieve higher survival rates.

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