Outcomes of Temporal Bone Resection for Locally Advanced Parotid Cancer

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ABSTRACT

This study was conducted to report outcomes and identify factors predictive of survival and recurrence in patients undergoing lateral temporal bone resection (LTBR) as part of an extended radical parotidectomy for parotid cancer. This is a retrospective cohort study which includes all patients undergoing LTBR for parotid cancer between 1994 and 2010 at two affiliated academic centers. Survival and recurrence rates were analyzed using the Kaplan-Meier method and Cox multivariate regression. A total of 12 patients with median follow-up duration of 30.6 months were included: 6 de novo cases and 6 patients referred after local recurrence. Actuarial locoregional control at 2 years was 73%. Most patients (11; 92%) developed disease recurrence with distant metastases the most common site of first failure (83%). Overall and disease-specific survival rates were 80% at 2 years and 22.5% at 5 years. Recurrence-free survival (RFS) was 67% at 2 years and 8.3% at 5 years. On multivariate analysis, surgical margin status was an independent predictor of RFS (hazard ratio = 3.85, $p = 0.045$). In advanced parotid cancer, LTBR with a goal of gross total resection offers good locoregional control with an acceptable complication rate. The benefits of this surgery must be balanced with the morbidity and low likelihood of long-term survival, with most patients ultimately experiencing disease recurrence and death.

KEYWORDS: Temporal bone resection, parotid cancer, outcomes

The age-adjusted annual incidence of salivary malignancy in the United States is 1.2 per 100,000, with survival rates reported at 75 to 80% at 5 years, and 65 to 70% at 10 years.^{1,2} Surgery remains the standard of care for salivary malignancy, with postoperative radiation therapy employed for high-grade tumors, advanced stage disease, nodal metastasis, and incomplete resection.³⁻⁵ Despite an overall excellent prognosis, locoregional recurrence rates are reported to be between 21 and 33% for malignant major salivary gland tumors.^{2,6}

Outcomes in patients with parotid cancer differ significantly based on a variety of factors, including histologic grade, T stage, nodal status, and the use of adjuvant radiation therapy.^{7,8} In cases of locally advanced parotid cancer, complete resection may require the performance of an extended total parotidectomy, which can include adjunct procedures such as mandibulectomy, skin resection, infratemporal fossa dissection, and skull base or temporal bone resection. Advances in surgical reconstruction have now helped facilitate these

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radical parotidectomy procedures, including skull base resection. Several authors have advocated skull base surgery for advanced parotid neoplasms, and have reported widely varying survival outcomes depending on several clinical and pathologic tumor factors.^{9–13} Certain locally advanced parotid tumors will require temporal bone resection, either due to invasion or to obtain appropriate access. To our knowledge, outcomes after temporal bone resection for parotid malignancy alone have not been reported. This study represents a larger study looking at outcomes of temporal bone resections for all malignant tumors involving the external ear from our collective institutions.

Our objectives were to systematically analyze outcomes in a cohort of patients with locally advanced parotid cancer requiring extended surgery with temporal bone resection, and to identify factors predictive of recurrence and survival.

METHODS

This study included 12 patients. After institutional review board approval, we reviewed the records of 262 patients who underwent temporal bone surgery between 1994 and 2010 at two affiliated medical centers in New York, Memorial Sloan-Kettering Cancer Center (MSKCC) and New York Presbyterian Hospital/Cornell Campus (NYPH). These years were chosen to restrict the cohort to patients undergoing contemporary techniques of imaging, surgery, reconstruction, and radiation therapy. We then identified a cohort of patients within this

population who had primary diagnosis of parotid cancer, either de novo or recurrent disease after treatment. Patient, clinical tumor, pathologic tumor, and treatment characteristics were recorded. The American Joint Committee on Cancer staging system for parotid tumors (Table 1) was used to classify tumors.¹⁴

Patient and clinical characteristics analyzed included age, gender, race, tobacco use, alcohol use, medical comorbidity, previous treatment, tumor histology, differentiation, local extension, facial nerve status, and clinical TNM classification. All patients underwent lateral temporal bone resection with resection of any remaining parotid tissue. In some cases, combinations of additional local resection such as mandibulectomy, infratemporal fossa dissection, partial auriculectomy, sacrifice of facial nerve, and neck dissection were also performed. Pathologic characteristics included tumor histology, local extension, bone-, perineural, lymphatic, and angioinvasion, depth of invasion, margin status, and pathologic TNM classification.

Actuarial outcomes including overall survival (OS), disease-specific survival (DSS), recurrence-free survival (RFS), and cumulative recurrence rates were calculated from the date of surgery using the Kaplan-Meier method. RFS was defined as the cumulative probability of remaining alive and free of recurrent disease. Univariate survival analysis was performed with the log-rank test. Those variables with $p < 0.20$ and/or were clinically relevant were then evaluated further with multivariable Cox proportional hazards regression, using forward entry to construct a parsimonious model based

Table 1 American Joint Committee on Cancer 7th ed TNM Staging of Salivary Gland Malignancy

T Stage	
TX	Primary tumor cannot be assessed.
T0	No evidence of primary tumor.
T1	Tumor ≤ 2 cm in greatest dimension without macroscopic extraparenchymal extension.
T2	Tumor > 2 cm but ≤ 4 cm in greatest dimension without macroscopic extraparenchymal extension.
T3	Tumor > 4 cm in greatest dimension and/or tumor having macroscopic extraparenchymal extension.
T4A	Tumor invades skin, mandible, ear canal, and/or facial nerve.
T4B	Tumor invades skull base and/or pterygoid plates and/or encases carotid artery.
N Stage	
NX	Regional nodes cannot be assessed.
N0	No regional lymph node metastasis.
N1	Metastasis in a single ipsilateral lymph node, 3 cm or less in greatest dimension.
N2A	Metastasis in a single ipsilateral lymph node, < 3 cm but ≤ 6 cm.
N2B	Metastasis in multiple ipsilateral lymph nodes, none ≥ 6 cm.
N2C	Metastasis in bilateral or contralateral lymph nodes, none ≥ 6 cm.
N3	Metastasis in a lymph node, > 6 cm.
M Stage	
MX	Distant metastasis cannot be assessed.
M0	No distant metastasis.
M1	Distant metastasis.

on likelihood ratios. Given the low n , the number of covariates used was limited to two. Statistical analysis was performed in PASW 18 (SPSS Inc., Chicago, IL).

RESULTS

Patient Characteristics

The study included 12 patients who underwent lateral temporal bone resection (LTBR) for parotid cancer between 1994 and 2010 with median follow-up duration of 30.6 months. The mean age of patients at the time of surgery was 62 years old (range, 33 to 88 years), with 8 males (67%) and 4 females (33%). Patient characteristics are presented in Table 2.

Clinical and Tumor Characteristics

Clinical tumor and invasion characteristics are presented in Table 3. Six cases had undergone previous surgery and radiation therapy for malignant parotid cancer with an average disease-free interval of 42.5 months (median 38, range 8 to 93). Histology included mucoepidermoid (three), myoepithelial (three), adenoid cystic (two), squamous cell (two), adenosquamous (one), adenocarcinoma (one), and invasive salivary duct carcinoma (one). Of note, four cases had current or past pathology indicating that the tumor arose from a pleomorphic adenoma; these were classified as listed above using the malignant component of the tumor. There were four patients (33%) who had intact facial nerve function prior to surgery, while the remainder had clinical facial nerve dysfunction either from prior surgery ($n=2$) or presumed tumor infiltration ($n=6$).

Treatment and Pathology

All patients in this series underwent LTBR. In addition, five patients had segmental mandibulectomy, one patient had marginal mandibulectomy, and two patients had infratemporal fossa dissection for tumor removal. Of 12 patients, 8 underwent free flap reconstruction with either rectus abdominus (6) or gracilis (2) myocutaneous flaps; 3 patients had regional flaps (2 pectoralis major myocutaneous flaps and 1 cervicthoracic rotation flap); and 1 patient had a primary closure with a fat graft. The patients who underwent neck dissection were 9, of which 8 were elective and 1 therapeutic. Two patients had previous neck dissections and one patient with a de novo poorly differentiated adenocarcinoma without evidence of nodal metastases did not undergo neck dissection.

Eleven patients had adjuvant radiation therapy including five patients who were re-irradiated; four with intraoperative brachytherapy; and one patient who underwent neutron beam therapy. One patient with

Table 2 Patient and Tumor Characteristics

Patient Characteristics	No.	Percentage
Total Patients	12	
Gender		
Male	8	67%
Female	4	33%
Age		
<60 y	5	42%
≥60 y	7	58%
Race		
White	6	50%
Non-white	2	17%
Unknown	4	33%
Tobacco Use		
Active	0	0%
Former	5	42%
Never	7	58%
Alcohol Use		
Regular	2	17%
Social	3	25%
Former	1	8%
Never	6	50%
Medical Comorbidity		
Present	5	42%
None	7	58%
Previous Non-Head and Neck Cancer		
Yes	4	33%
No	8	67%

recurrent tumor and pulmonary metastases at the time of surgery was not re-irradiated after LTBR. Two patients received adjuvant chemotherapy. Pathologic staging, margins, and invasion are presented in Table 4. Total gross resection was performed in 11 cases with microscopically positive margins seen in 6 patients; one patient had disease left at the carotid bulb and pterygoid muscles.

Three patients had major complications including one patient with postoperative respiratory distress requiring tracheotomy ($n=1$), one patient had developed postoperative hematoma and compromise of the free flap which was successfully salvaged with hematoma evacuation, and one patient had postoperative myocardial infarction, seizure, and deep vein thrombosis. There were no instances of cerebrospinal fluid leak, major vessel injury, or damage to nonfacial cranial nerves. The facial nerve was sacrificed in 10 cases (83%) and spared in two patients. In three cases, the facial nerve was reconstructed, either with primary neurorrhaphy ($n=1$) or nerve graft ($n=2$). Four patients underwent interval placement of gold-weight or tarsorrhaphy. Postoperatively, one patient had normal facial nerve function (House-Brackman 1/6), and one patient who had

Table 3 Clinical Tumor Characteristics

Tumor Characteristics	No.	Percentage
Recurrence		
Yes (previous surgery + radiotherapy)	6	50%
No	6	50%
Histology		
Mucoepidermoid	3	25%
Myoepithelial	3	25%
Adenoid cystic	2	17%
Squamous/adenosquamous	2	17%
Adeno	1	8%
Salivary duct carcinoma	1	8%
Differentiation/Grade		
Poorly diff/high grade	9	75%
Low or intermediate grade	3	25%
Expleomorphic Adenoma		
Yes	4	33%
No	8	67%
Clinical Extension	10	83%
EAC	3	25%
Temporal bone	5	42%
EAC/temporal bone	6	50%
Skin	4	33%
Infratemporal fossa	2	17%
Jugular foramen	1	8%
Mandible	0	0%
CN VII	8	67%
Preop Facial Nerve Status		
Intact	4	33%
Not intact	8	67%
cT Stage		
rT2	2	17%
T4A	3	25%
T4B	3	25%
rT4A	2	17%
rT4B	2	17%
cN Stage		
N0	0	0%
N1	0	0%
N2	1	8%
N3	0	0%
cM Stage		
M0	0	0%
M1	1	8%

CN, cranial nerve; EAC, external auditory canal.

primary facial nerve reanastomosis demonstrated normal tone at rest (House-Brackmann 4/6).

Recurrence and Survival Analysis

At 2 years, OS was 80%, DSS was 80%, and RFS was 67%. Five-year OS and DSS were 22.5% and 5 year RFS was 8.3% (Fig. 1).

Table 4 Details of Treatment and Pathology

Characteristics	No.	Percentage
Total Patients	12	
Treatment		
Surgery alone	1	8.3%
Surgery + RT	9	75.0%
Surgery + CRT	2	16.7%
Extent of Surgery		
LTBR	12	100.0%
Partial mandibulectomy	7	58.3%
Partial auriculectomy	1	8.3%
Infratemporal fossa dissection	2	16.7%
Facial nerve sacrifice	10	83.3%
Neck Dissection		
Elective neck dissection	7	58.3%
Therapeutic neck dissection	1	8.3%
Previous neck dissection	3	25.0%
Reconstruction		
Free flap	8	66.7%
Rotational flap	3	25.0%
Primary/fat graft	1	8.3%
Facial nerve reconstruction	3	25.0%
Postoperative Complications		
Yes	3	25.0%
No	9	75.0%
Postoperative Facial Nerve Function		
Intact or tone	2	16.7%
Nonfunctional	10	83.3%
pT Stage		
rT3	1	8.3%
T4A	3	25.0%
rT4A	4	33.3%
T4B	3	25.0%
rT4b	1	8.3%
pN Stage		
N0	10	83.3%
Parotid nodes +	2	16.7%
N2B	1	8.3%
M Stage		
M +	1	8.3%
Invasion		
Skin	5	41.7%
Bone/skull base	4	33.3%
Neural	6	50.0%
Lymphoid	3	25.0%
Vascular	5	41.7%
Facial nerve	8	66.7%
Margins		
Positive	7	58.3%
Negative	5	41.7%

CT, chemotherapy; LTBR, lateral temporal bone resection; RT, radiotherapy.

Figure 1 Overall survival (OS), disease-specific survival (DSS), and recurrence free survival (RFS) curves.

Eleven patients (92%) developed a recurrence at a median time of 12 months after surgery; patterns are presented in Figs. 2 and 3. In 83% of patients recurrence was observed within 2 years. All cases of locoregional recurrence ($n=3$) occurred by 16 months, resulting in a 2-year actuarial rate of locoregional recurrence of 27%. The majority of failures (83%) occurred at distant sites. One patient referred to after recurrence of a high-grade myoepithelial carcinoma who had undergone prior pulmonary wedge resection of metastases underwent LTBR for palliation of local symptoms including full thickness skin involvement.

On univariate analysis, surgical margin status was the only factor significantly associated with RFS ($p=0.03$) (Fig. 4). There were no associations between survival or recurrence and preoperative facial nerve function, locally recurrent disease, clinical tumor extension site, histological subtype, pathologic invasion, T stage, and nodal status (Table 5). Patients who underwent LTBR for recurrent parotid cancer following

Median Time to First Recurrence = 12 months

Figure 2 Patterns of recurrence.

Figure 3 Cumulative incidence of cancer recurrence.

surgery and radiation at outside institutions had poorer outcomes than those who underwent LTBR for de novo tumors (5-year DSS 0 vs 80%); however, this difference was not statistically significant ($p=0.48$) on univariate analysis. On multivariate analysis, negative surgical margins was significantly associated with RFS ($p=0.046$, hazard ratio [HR] 3.85, 1/95% confidence interval [CI] 1.02–18.2) (Table 6).

DISCUSSION

In this study, we report survival and recurrence outcomes of patients undergoing LTBR as part of extended radical parotidectomy for recurrent or de novo locally advanced parotid cancer. While survival at 2 years was 80%, long-term outcome in these patients was poor. Overall locoregional control rate was (75%); however, recurrence was common (92%), usually at distant sites. As a result,

Figure 4 Survival curve for margin status on univariate analysis of recurrence free survival ($p=0.03$).

Table 5 Variables Predictive of Survival and Local Recurrence (Univariate Analysis)

		DSS	OS	RFS
Variable	<i>n</i>	<i>p</i>	<i>p</i>	<i>p</i>
Patient Characteristics				
Gender		0.96	0.97	0.77
Male	8			
Female	4			
Age		0.99	0.99	0.68
<60 y	5			
≥60 y	7			
Tobacco		0.7	0.7	0.88
Never	7			
Yes	5			
Alcohol		0.15	0.15	0.86
Never	6			
Yes	6			
Medical Comorbidity		0.09	0.09	0.06
Yes	5			
No	7			
Previous Non-Head and Neck Cancer		0.04	0.04	0.26
Yes	4			
No	8			
Clinical Tumor Characteristics				
Local Recurrence		0.48	0.48	0.81
Yes	6			
No	6			
Preoperative Cranial Nerve VII Intact		0.54	0.54	0.92
Yes	4			
No	8			
Clinical Extension	10			
External auditory canal/temporal bone	6	0.95	0.95	0.59
Skin	4	0.20	0.20	0.64
Cranial nerve VII	8	0.54	0.54	0.92
cT Status				
All T2	2	0.69	0.69	0.21
All T4A	5			
All T4B	5			
Pathologic Characteristics				
Histology		0.58	0.58	0.70
Adenocarcinoma	2			
Mucoepidermoid carcinoma	3			
Myoepithelial carcinoma	3			
Squamous cell carcinoma	2			
Other	2			
Differentiation/Grade		0.41	0.41	0.32
Poorly differentiated/high grade	9			
Low or intermediate grade	3			
Expleomorphic Adenoma		0.08	0.08	0.19
Yes	4			
No	8			
Pathologic Invasion				
Skin	5	0.50	0.50	0.51
Bone/skull base	4	0.67	0.67	0.32
Neural	6	0.15	0.15	0.86
Lymphoid	3	0.83	0.83	0.52

Table 5 (Continued)

Variable	n	DSS	OS	RFS
		p	p	p
Vascular	5	0.46	0.46	0.72
Facial nerve	9			
Margins		0.15	0.15	0.03
Positive or close	7			
Negative	5			
pT Stage				
All 3	1	0.80	0.80	0.17
All 4A	7			
All 4B	4			
pN Stage		0.83	0.83	0.52
Any nodes	3			
Treatment Characteristics				
Brachytherapy				
Yes	4	0.77	0.77	0.63
No	8			

survival at 5 years was only 22.5%. These data suggest that, when necessitated by extent of local disease and aggressive histology, the inclusion of LTBR as an adjunctive procedure in extended radical parotidectomy achieves reasonable rates of locoregional control and is able to palliate local symptoms.

Long-term outcomes are less encouraging, as most patients in our series succumbed to recurrent disease at distant sites. While our sample size was limited by the rarity of locally advanced parotid cancer requiring LTBR, these data may be helpful in informing clinical decision-making when such extended surgery is being considered.

On multivariate analysis, surgical margin status was significantly associated with RFS ($p=0.046$, HR 3.85, 95% CI 1.02–18.2). The association between margin status and outcomes has been shown in numerous studies on salivary malignancy, including a study by Reddy and Marks that indicated that the effectiveness of radiation therapy is directly related to the volume of tumor present at the time of radiation^{8,15}.

In our cohort, patients who presented to our institutions for local recurrence following surgery and radiation had poorer outcomes than those with de novo tumors (5-year DSS 0 versus 80%); however, this

difference was not statistically significant ($p=0.48$) due to limited sample size. These results are in contrast to a recent series of 12 patients undergoing aggressive definitive surgery, including skull base surgery, for locally recurrent parotid cancer, in which 5-year DSS rate was 64%¹⁶; the difference is likely due to variation in extent of disease, stage of disease, and histologies represented.

Local, regional, and distant recurrence rates in this study were 17, 17, and 83%, respectively. While local and regional failure rates were comparable to those reported by Spiro et al in de novo salivary cancers, the rate of distant failure in this study was much higher (83 versus 19%), perhaps indicating the biologic aggressiveness and tumor burden of parotid cancers invading the temporal bone.² Local recurrence, which occurred at 5 and 15 months in two patients, is particularly devastating in this cohort given the extent of surgery undertaken and associated morbidity and potential effects on quality of life. One of these patients underwent extensive surgery for acinic cell carcinoma with focal dedifferentiation to high-grade adenocarcinoma. Despite negative surgical margins and postoperative radiotherapy, the patient experienced a local recurrence. A second patient with a

Table 6 Variables Predictive of Survival (Multivariate Analysis)

	DSS		OS		RFS		
	HR	p value	HR	p value	HR	p value	95% CI for HR
Covariates							
Neural invasion	3.7	0.24	3.7	0.24	4.3	0.89	0.31 to 3.18
Margin status	2.9	0.26	2.9	0.26	3.8	0.046	1.0 to 18.2

DSS, disease-specific survival; HR, hazard ratio; OS, overall survival; RFS, recurrence-free survival.

recurrent high-grade mucoepidermoid carcinoma had microscopically positive margins and had postoperative neutron-beam therapy with concurrent chemotherapy delayed nearly 5 months until delivery of her baby; this patient developed local recurrence. However, in the majority of cases, surgery was successful in achieving locoregional control.

While this retrospective analysis cannot demonstrate that such surgery prolongs life, in these patients, surgery was able to effectively palliate the devastating local symptoms of advanced parotid cancer, with 8 of 10 patients alive at 2 years and a locoregional control rate of 75%.

A limitation of this study was small sample size, thereby limiting our ability to identify factors that may be subtle predictors of outcome. However, to the best of our knowledge, this study represents the only reported data on outcomes after LTBR for parotid malignancy. Nevertheless, it is hoped that these preliminary findings may be useful in helping to inform clinical decision-making in these challenging cases. LTBR as part of an extended radical parotidectomy results in significant disfigurement, maximal conductive hearing loss on the affected side, and facial paralysis; these are important factors to consider given poor long-term outcomes. Interestingly, quality of life studies have shown that these three factors do not correlate with quality of life perceptions of patients undergoing parotid and temporal bone surgery for cancer.¹⁷ In fact, neither objective disfigurement and dysfunction values nor clinicians' assessments necessarily correlate with patient perception of the treatment outcome. Therefore, clinician assessment of quality of life alone is not a reason to avoid this surgery. Given the low rates of long-term survival despite effective locoregional control, it is critical that patients be informed of the incidence of death from disease, the impact on quality of life, and the potential for palliation local disease before embarking upon extended parotid and skull base surgery.

CONCLUSION

In patients with advanced parotid cancer, undergoing LTBR resulted in 2-year OS and DSS of 80% with a low complication rate and low rate of locoregional recurrence (25%). However, the benefits of this surgery must be balanced with an understanding of the universally poor outcome in terms of very high overall recurrence rates, particularly in distant sites, and low 5-year survival rates.

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