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Title: Clinical management for T1 and T2 external auditory canal cancer

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Abstract

Objective: The purpose of this study was to clarify the impact of superficial parotidectomy and postoperative radiotherapy (PORT) for the surgical treatment of early stage squamous cell carcinoma (SCC) in external auditory canal (EAC).

Materials and Methods: Thirty-seven patients with T1 (n=14) or T2 (n=19) SCC in EAC treated between 2000 and 2016 at Kobe University Hospital were enrolled in this study. Thirty-three patients were operated with sleeve resection or lateral temporal bone resection.

Results: The 5-year overall survival and disease-specific survival rates were 95% and 100%, respectively. Surgical margin was positive in 4 patients, who were treated by PORT and have been alive without disease. Prophylactic superficial parotidectomy was simultaneously performed at the time of initial surgery in 15 patients, in whom no lymph node (LN) metastasis was observed. Among the other 22 patients, regional recurrence in parotid LN was observed in one patient, who was successfully salvaged by total parotidectomy. Potential parotid lymph node metastasis rates of T1 and T2 SCC in EAC was 0% (0/14) and 5%(1/19) respectively.

Conclusions: Complete resection without positive surgical margins is essential for the treatment of the patients with T1 and T2 ear cancers. Prophylactic superficial parotidectomy or neck dissection is not mandatory for T1 and T2 diseases, as long as precisely extent of disease is assessed preoperatively. PORT should be performed for the patients with positive surgical margins.

Key Words: external auditory canal cancer, temporal bone cancer, lateral temporal bone resection, parotidectomy, postoperative radiotherapy

Levels of evidence: 4

Introduction

Squamous cell carcinoma of the external auditory canal (EAC) is extremely rare with an annual incidence estimated at between 1 to 6 cases per million of the populations.[1] For early stages T1 and T2, as defined by the modified Pittsburgh staging system [2],sleeve resection of the external canal or *en bloc* lateral temporal bone resection (LTBR), have yielded favorable oncological and functional results and are the treatment of choice at most institutions.[3] [4] [5] According to the United Kingdom National Multidisciplinary Guidelines published in 2016,[6] LTBR is regarded as the minimum oncologic operation for T1 and T2 lesions. Prophylactic superficial or total parotidectomy is recommended for all resections. Post-operative radiotherapy (RT) or chemoradiotherapy (CRT) is recommended for most T2-T4 disease, with the exception of T1 and selected T2 without particularly peri-neural infiltration and with clear margins. However, these guidelines were based on small number reports, and the indication of parotidectomy and postoperative radiotherapy (PORT) for T1 and T2 patients is not clearly determined at present. The purpose of this study was to clarify the impact of superficial parotidectomy and postoperative radiotherapy (PORT) for the surgical treatment of early EAC cancer.

Materials and Methods

Between 2000 and 2016, 99 consecutive patients with squamous cell carcinoma arising from external auditory canal were treated at Kobe University Hospital. Among them, 37 patients with T1 or T2 tumor were enrolled in this study. All patients were pathologically diagnosed as

having squamous cell carcinoma of the external auditory canal. At the initial diagnosis, extent of disease was assessed with the aid of contrast computerized tomography (CT) scan, magnetic resonance imaging (MRI), and 18-fluoro-2-deoxyglucose positron emission tomography (FDG-PET). Diseases were staged according to the most recent version of the modified Pittsburgh classification (2000)[2].

Thirty-three patients were surgically treated with sleeve resection or lateral temporal bone resection (LTBR). The other 4 patients were treated with radiotherapy (n=3) or proton beam therapy (n=1), due to patient's refusal or to physical condition and co-existing diseases. Postoperative RT was employed in surgically treated patients only whose surgical margin was positive. Patients with close to margin (<3mm), perineural invasion, or bone invasion were only observed carefully without PORT.

We describe the indication of resection for T1 EAC cancer. Only if a tumor located in a limited area of EAC and a whole tumor was observable with appropriate surgical margins, we preformed sleeve resection. We performed LTBR, when the tumor didn't meet the above conditions.

For LTBR, the bony external auditory canal, tympanic membrane, malleus and incus were resected with extended mastoidectomy in an en bloc manner. The superficial lobe of the parotid gland was prophylactically resected in most T2 cases and the facial nerve was preserved in all cases. For T1 patients, if the tumor existed mainly in an anterior-inferior canal wall, we preferably resected a superficial lobe of parotid gland. LN metastases were not clinically observed in neck or parotid gland in any patient. Thus, no patients underwent prophylactic neck dissection.

Medical records were retrospectively reviewed to obtain information

concerning characteristics of the patients, extent of disease, surgical procedures including parotidectomy, metastasis of parotid LN, PORT, and oncological results. Kaplan-Meier plots were used to summarize time to event measured from the end of the first treatment. R software (Ver. 3.0.2. 2013. The R foundation for Statistical Computing, Vienna, Austria) was used for the statistical analysis. This study was approved by Kobe University Hospital Internal Review Board.

Results

The characteristics of the patients are summarized in Table 1. The age of the patients ranged from 38 to 94 years old with a median age of 68 years and the follow-up period ranged from 7 to 134 months (median: 60 months, average: 55.0 months). The primary diseases were classified as T1 in 17 patients and as T2 in 20 patients. Of the patients with T1 disease, 3 were treated with RT alone, 6 with sleeve resection, and 8 with LTBR. Among the patients with T2 disease, one was treated with proton beam therapy, and 19 with LTBR.

Details of the surgically treated 33 patients are summarized in Table 2. Of the 14 surgically treated patients with T1 disease, 2 patients had PORT due to positive surgical margins. Superficial parotidectomy was performed in 3 patients whose tumor located in an anterior-inferior canal wall. However, metastasis to the parotid lymph node or direct invasion to parotid gland was not observed in any patient. Among the 14 patients, one patient treated with sleeve resection with positive margin had local recurrence, but was successfully salvaged by LTBR. During the following-up period, one patient treated with RT alone

died of other disease, but other patients have been alive with no evidence of disease.

Of the 19 surgically treated patients with T2 disease, 3 patients had PORT because 2 of them had a positive surgical margin and another one was diagnosed in spindle cell variant squamous cell carcinoma without positive surgical margin. Superficial parotidectomy was performed in 12 patients. No patients had the metastasis in parotid lymph node or direct invasion to the parotid gland. Local recurrence was observed in no patient. Among the 7 patients who did not have prophylactic superficial parotidectomy, regional recurrence in the parotid LN was observed in one patient, who were successfully salvaged by total parotidectomy. Primary disease involved to anterior-inferior canal wall in this patient. Thus, we recommended simultaneous superficial parotidectomy at the time of initial surgery, but she refused parotidectomy. During the following-up period, 3 patients died of other disease and other patients have been alive with no evidence of disease.

Patients treated by RT or proton beam therapy also have been alive without disease. The 5-year overall survival rates of the patients with T1 and T2 diseases were 94% and 95%, respectively. Disease-specific survival rates of the patients with T1 and T2 diseases were 100% and 100%, respectively. Local control rates of the patients with T1 and T2 diseases were 94% and 95%, respectively (Fig. 1). Facial nerve was preserved in all patients and no permanent facial paralysis was observed.

Peri-neural invasion was observed in 3 patients with T2, and 1 patient with T1. One patient underwent PORT followed by surgical exterpation due to positive margin, but other 3 patients did not undergo

PORT. Bone invasion was observed in 18 patients out of 19 clinical T2 patients, and in 2 patients out of 14 clinical T1 patients.

Discussion

Due to its rarity and aggressive oncological behavior, standard treatment for temporal bone cancer has not been established yet. For most reported cases, treatment consisting of surgical resection and postoperative RT has been selected.[6)-10)] Especially, cure rates of the early lesions (T1 and T2) treated by en-bloc resection were near to 100%.[6)] Relatively favorable oncological results have been reported on radiotherapy alone for T1 and T2 by Murai et al[11)]. They reported that local control rate of T1 and T2 patients is 70%. Although, all the patients treated by radiotherapy have been alive without disease in our series, radiotherapy alone may not be a first-line choice of treatment for T1 and T2 disease in the patients without serious co-existing disease and/or physical condition.

Indication of prophylactic parotidectomy and neck dissection, or PORT have not been established yet. Zhang et al[12)] reported that tumor had invaded the parotid gland directly 2/6 in T1 patients and 5/11 in T2 patients. One patient with T2 had a metastatic lymph node in superficial parotid gland. From these results, they suggested that superficial parotidectomy was necessary for patients with an early stage cancer. In response to their remarks, Homer et al[6)] recommended total parotidectomy for advanced T3 or T4 tumor. They recommended also at least a superficial parotidectomy for all resection in UK official

guidelines. In another report by Prasad et al[13], the incidence of parotid involvement is in the range of 10%-62% of cases, but they did not mention about a necessity of parotidectomy in early stages. Several surgeons performed a prophylactic superficial parotidectomy as a standard of care[14)-16)], but others did not accept this because there seems to be no survival benefit of a prophylactic parotidectomy[5), 17)]. Hosokawa et al[18)] suggested that if the tumor invaded anterior-inferior wall of canal, parotidectomy was recommended.

In our series, no T1 and T2 diseases invaded parotid gland directly, and only one patient with T2 tumor had potential parotid gland lymph node metastasis at the time of inital diagnosis. Fortunately, the recurrence tumor was successfully salvaged by superficial parotidectomy without facial nerve paralysis. In the present study, the rates of potential parotid gland lymph node metastasis in T1 and T2 were 0% (0/14) and 5% (1/19) respectively. That is significantly lower than the previous reports. The possible explanation of this discrepancy is the accuracy of the preoperative assessment of extent of disease. As mentioned above, the extents of the diseases were precisely assessed by contrast and thin-sliced CT scan, MRI, and FDG-PET in our series. The patients in the previous reports may include underdiagnosed advanced diseases. Taken together, present results suggest that prophylactic superficial

parotidectomy is not mandatory in T1 disease and in T2 disease without tumor in anterior or inferior canal wall. However, precise preoperative assessment and careful follow-up are mandatory using diagnostic imaging including high-resolution CT scan, MRI and FDG-PET.

A necessity of prophylactic neck dissection in T1 and T2 patients is also controversial. Gidley et al[16] suggested selective neck dissection (level II-III) for T1 or T2 patients. Prasad et al[13] proposed that they examined frozen section of level II lymph node, then dissected neck lymph node only when histology of frozen section showed positive metastatic cancer. However, in the present study, no neck LN metastasis was observed in any of the 37 patients not only at the time of initial diagnosis but also during the all the follow-up period. Thus, we believe that prophylactic neck dissection is not necessary for T1 and T2 patients[19], as long as precisely extent of tumor is assessed by imaging as mentioned above.

As for PORT, UK guidelines recommend post-operative (C)RT for most of T2-T4 with the exception of T1 and selected T2 without particularly peri-neural infiltration and with clear margins. In accordance with UK guidelines, many authors recommended PORT in T2 patients[2, 3, 16], especially in case with close or positive surgical margins, peri-neural invasion, or vascular invasion. Oya et al[20] reported meta-analysis of PORT

for early stage patients. Survival analysis of all patients showed no differences between the surgery-only and PORT groups. However, PORT exhibited a better prognosis than surgery alone in T1 patients. They indicated that PORT can be the standard therapy for T1 and T2 patients. In the present series, we recommended PORT only for the patients with positive surgical margins in T1 and T2. As a result, 4 patients had positive surgical margins and 3 of them underwent PORT and have been alive without recurrence during the observation period. In the present study, local recurrence occurred in only one patient treated by sleeve resection, who was successfully salvaged by LTBR. Indeed, complete resection without positive surgical margins is essential for the treatment of the patients with T1 and T2. However, PORT should be considered for patients with positive surgical margins. In our case series, we have not recommended PORT to the patients with perineural invasion, vascular invasion, or bone invasion, but almost all patients with these elements have not had local recurrence except for only one patient who was salvaged by operation.

This study has some limitation due to the retrospective nature. Firstly, sample size is very small for a meaningful decision. However, the rarity of EAC cancer makes it difficult to perform well-designed analysis at a single institution. The retrospective chart review is an important method for gathering

clinical data on outcomes, aiding clinical decision-making. Secondly, selection criteria for parotidectomy is not completely constant case by case.

Conclusion

Complete resection without positive surgical margins is essential for the treatment of the patients with T1 and T2 ear cancers. Prophylactic superficial parotidectomy or neck dissection is not mandatory for T1 and T2 diseases, as long as precisely extent of disease is assessed preoperatively. PORT should be performed for the patients with positive surgical margins.

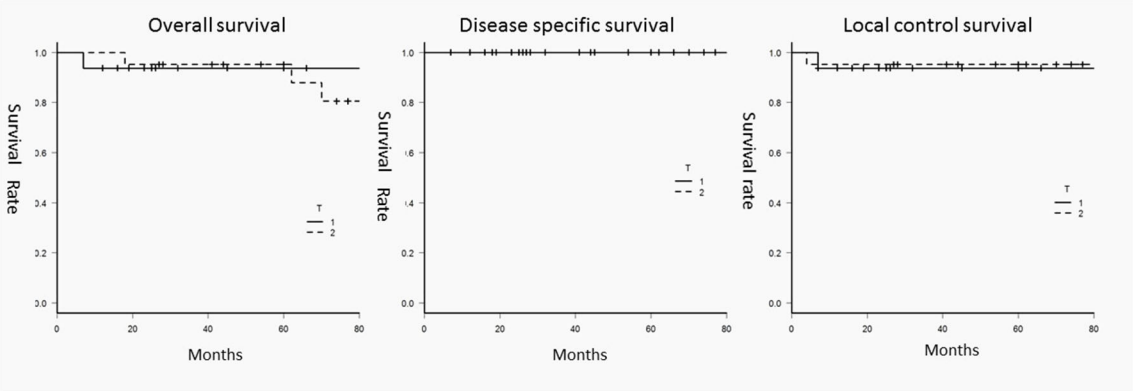
Table 1 Clinical Characteristics of 37 Patients

	No. of Patients
Sex	
Men	17
Women	20
Age: median (range)	68 (38-94)
T classification	
T1	17
T2	20
Side	
Right	18
Left	19
Treatment	
Surgery	33
Radiotherapy	3
Proton beam	1
Operation	
Sleeve resection	6
LTBR	27

Table 2. Characteristics of the Surgically Treated Patients

			Positive margin	Close to margin†	Post-ope-RT	Parotid resection	Parotid metastasis	Local recurrence
T1	(n=14)		2 (14%)	4 (28%)	2 (14%)	3 (21%)	0 (0%)	1 (7%)
	Sleeve	8	0 (0%)	3(38%)	0 (0%)	1 (13%)	0 (0%)	1 (13%)
	LTBR	6	2 (33%)	1(17%)	2 (33%)	2 (33%)	0 (0%)	0 (0%)
T2	(n=19)							
	LTBR	19	2(11%)	11(58%)	3 (16%)	12 (63%)	1 (5%)	0 (0%)
P value			1.0	0.16	1.0	0.01	1.0	0.42

†; Close to margin; <3mm



Disclosure Statement

All authors have no conflict of interest to declare related to this manuscript.

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Legends for Tables and Figure

Table 1. Clinical characteristics of 37 patients

Table 2. Characteristics of the Surgically Treated Patients
†; Close to margin; <3mm

Figure 1. Patient Survival Curves (with Kaplan-Meier estimates of overall survival rate, disease specific survival rate, and local control rate for T1 patients (solid line) and T2 patients (dotted line)).