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ORIGINAL ARTICLE – HEAD AND NECK ONCOLOGY

Low-Grade Salivary Gland Cancers: Treatment Outcomes, Extent of Surgery and Indications for Postoperative Adjuvant Radiation Therapy

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ABSTRACT

Background. Histologic grade of tumor is one of the major prognostic predictors for patients with salivary gland cancer. Because of disease rarity, little is known about the optimal treatment modalities and outcomes in low-grade salivary gland cancers (LGSGC). We tried to identify prognostic factors, and the adequate treatment modalities and outcomes in pathologically confirmed LGSGC patients.

Methods. We retrospectively extracted the clinical and pathology data from 179 LGSGC cases from 1995 to 2013. Pathological features, such as extraparenchymal extension, perineural/nerve invasion, lymphovascular invasion/tumor emboli, and resection margin status were redefined for each case. Risk factors for recurrence, extent of surgery, and the role of postoperative radiation therapy were analyzed.

Results. Recurrence-free survival and overall survival were 89.6 and 96.6 % at 10 years, respectively. The presence of regional nodal metastasis and positive cancer cells at resection margin were significant unfavorable prognostic factors. Postoperative adjuvant radiation treatment significantly reduced recurrences, particularly in cases with pathology risk factors (perineural invasion, lymphovascular invasion, extraparenchymal extension, or cancer cells at the resection margin), node metastasis, and advanced T-stage tumors. Close surgical margin <5 mm was not a significant risk factor for recurrence, and less-than-total resection of the affected gland did not increase recurrence, if surgery could achieve a cancer cell-free surgical margin.

Conclusion. Postoperative radiation clearly benefitted patients with pathology risk factors, node metastasis, and advanced T stage in LGSGC. Meanwhile, the oncological outcomes are very good with surgery alone in cases of pT1-2N0 LGSGC without pathology risk factors.

Salivary gland cancers comprise only 3–6 % of all head and neck malignancies and represent a wide variety of pathologies due to the diverse cell types in the salivary secretory acini and ductal units.[1,2] Currently, more than 24 different tumor types of malignant salivary gland tumors have been identified, based on their cytological and architectural features.[3] These rarity of occurrence and diverse histologic features of salivary gland cancers impose significant challenges on the clinical decision of optimal management.[4,5]

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TABLE 1 Subject characteristics ($N = 179$)

Characteristics	*N*	%
Age [years; median (range)]	47 (9–83)	
Sex (male/female)	87/92	48.6/51.4
Tumor site		
Parotid gland	131	73.2
Submandibular gland	37	20.7
Sublingual gland and minor salivary gland	11	6.1
pT classification		
T1	72	40.2
T2	49	27.4
T3	50	27.9
T4	8	4.5
pN classification		
N0	161	89.9
N1	12	6.7
N2–3	6	3.4
AJCC stage		
I	69	38.5
II	43	24.0
III	52	29.1
IV	15	8.4
Pathology diagnosis		
Mucoepidermoid carcinoma, low grade	74	41.3
Adenoid cystic carcinoma, non-solid type	42	23.5
Acinic cell carcinoma	22	12.3
Adenocarcinoma, low grade	14	7.8
Basal cell adenocarcinoma	9	5.0
Epithelial-myoepithelial carcinoma	7	3.9
Carcinoma ex pleomorphic adenoma, non-invasive type	6	3.4
Myoepithelial carcinoma, low grade	3	1.7
Oncocytic carcinomas, low grade	2	1.1
Pathology risk factors		
Perineural invasion (presence/absence)	30/149	16.8/83.2
Lymphovascular invasion (presence/absence)	12/167	6.7/93.3
Extraparenchymal extension (presence/absence)	45/134	25.1/74.9
Resection margin status (positive cancer cells at resection margin/close margin <5 mm/negative margin ≥5 mm)	45/64/70	25.1/35.8/39.1
Treatment modalities		
Surgery alone	54	30.2
Surgery + adjuvant radiation	125	69.8
Extent of surgery for primary sites		
Less-than-total resection of the gland	83	46.4
Total resection of the affected gland	96	53.6
Neck dissection		
No	134	74.9
Selective or modified neck dissection	45	25.1
Clinical outcomes		
Recurrence	14	7.8
Recurrence-free period [months; median (range)]	44 (24–184)	
Disease-specific death	2	1.1
Event-free follow-up period [months; median (range)]	48 (24–184)	

AJCC American Joint Committee on Cancer

Histologic grade of tumor is one of the major prognostic predictors for patients with salivary gland cancer.[6] Patients with low- and intermediate-grade salivary gland cancer have a 5-year survival of 85–90 %, while patients with high-grade salivary gland cancer have a 5-year survival of <40 %.[6,7] Tumor size and nodal status also tend to correlate with treatment outcomes, as well as margin status at resection and the presence of extraparenchymal extension.[8] However, most of these studies were undertaken for the whole histologic subtypes of salivary gland cancer or one specific subtype.[1,9,10]

Surgery and radiation therapy (RT) are essential in the management of salivary gland cancer.[11] Postoperative RT can reduce local failure[11–13] and has been increasingly used for cases with high-risk features, high-grade histology, advanced T stage (T3 or T4), the presence of extraparenchymal extension, close or positive surgical margins, lymph node involvement, and perineural invasion.[14] However, there is a lack of consensus regarding the indication of postoperative RT in patients with low-grade salivary gland cancers (LGSGC), as well as the extent of surgery.

This study aimed to reveal prognostic factors affecting recurrence and outcomes, and to suggest the optimal selection of managements (surgical extent and postoperative RT) in patients with pathologically confirmed LGSGC.

MATERIALS AND METHODS

The protocol of this retrospective study was approved by the Institutional Review Board before enrollment, and written informed consent was waived.

Study Subjects

We gathered the study population from 485 patients diagnosed as having salivary gland cancer at our institute from January 1995 to December 2013. The inclusion

TABLE 2 Univariate and multivariate analysis of clinical and pathological variables for recurrence-free survival

Variables	Univariate			Multivariate		
	HR	95 % CI	*p* value	HR	95 % CI	*p* value
Age (1-year increased)	0.998	0.964–1.033	0.895			
Sex (male/female)	0.901	0.316–2.571	0.846			
Primary site						
Parotid gland	Ref					
Submandibular gland	0.980	0.270–3.562	0.975			
Sublingual and minor salivary gland	1.496	0.191–11.711	0.701			
Disease extent						
T3–4/T1–2	1.224	0.409–3.657	0.718			
N1–3/N0	4.575	1.42–14.675	0.011	6.492	1.480–28.471	0.013
Stage III–IV/I–II	1.849	0.647–5.279	0.251			
Pathology diagnosis						
Mucoepidermoid carcinoma, low grade	Ref					
Adenoid cystic carcinoma, non-solid type	1.816	0.454–7.263	0.399			
Others	1.918	0.541–6.803	0.313			
Pathology risk factors						
Perineural invasion (Y/N)	1.516	0.423–5.442	0.523			
Lymphovascular invasion (Y/N)	6.868	2.145–21.988	0.001	3.288	0.909–11.894	0.070
Extraparenchymal extension (Y/N)	1.830	0.612–5.471	0.279			
Resection margin						
Negative margin ≥5 mm	Ref			Ref		
Close margin <5 mm	3.379	0.762–18.747	0.104	4.486	0.855–23.524	0.076
Positive cancer cells at resection margin	5.126	1.034–25.419	0.045	14.639	2.429–88.238	0.003
Treatment modalities						
Surgery with radiation/surgery alone	0.420	0.147–1.197	0.105	0.129	0.038–0.442	0.001
Surgical extent						
Total resection/less-than-total resection	1.085	0.377–3.129	0.767			
Neck dissection/no neck dissection	0.557	0.125–2.488	0.443			

HR hazard ratio, *CI* confidence interval, *Ref* reference value, *Y* yes, *N* no

criteria were patients who had (i) only LGSGC by surgical pathology; (ii) completed with recommended treatment; (iii) no previous treatments to their LGSGC; and (iv) >2 years of follow-up from the end of definitive treatment. Patients diagnosed as metastatic tumors to salivary gland from other malignancies or recurred tumors, and those with a previous history of head and neck cancer or irradiation to the head and neck area were excluded. Finally, 205 patients were included in this study, but 26 were further excluded because of incomplete clinical and pathological information ($N = 179$ in these analyses). All patients had initially undergone curative surgery of primary tumors with or without neck dissection. Based on the surgical pathology reports, each tumor was reassigned to a pathological tumor-node-metastasis (pTNM) stage using the 7th American Joint Committee on Cancer staging manual.[15]

Pathology Diagnosis

To confirm the diagnosis of LGSGC, a senior pathologist (YHK) with over 10 years of experience in pathological diagnosis of salivary gland tumors reviewed the pathology slides and reports. Pathological features, such as extraparenchymal extension, perineural/nerve invasion, lymphovascular invasion/tumor emboli, and resection margin status were redefined for each case. In cases with node-positive disease, the number of metastatic nodes was also recorded.

Low-grade mucoepidermoid carcinomas were diagnosed mainly qualitatively based on the pathologic features, and intermediate- or high-grade subtypes were excluded from the analysis.[16,17] With regard to adenoid cystic carcinomas, tumors without solid component were only included in this

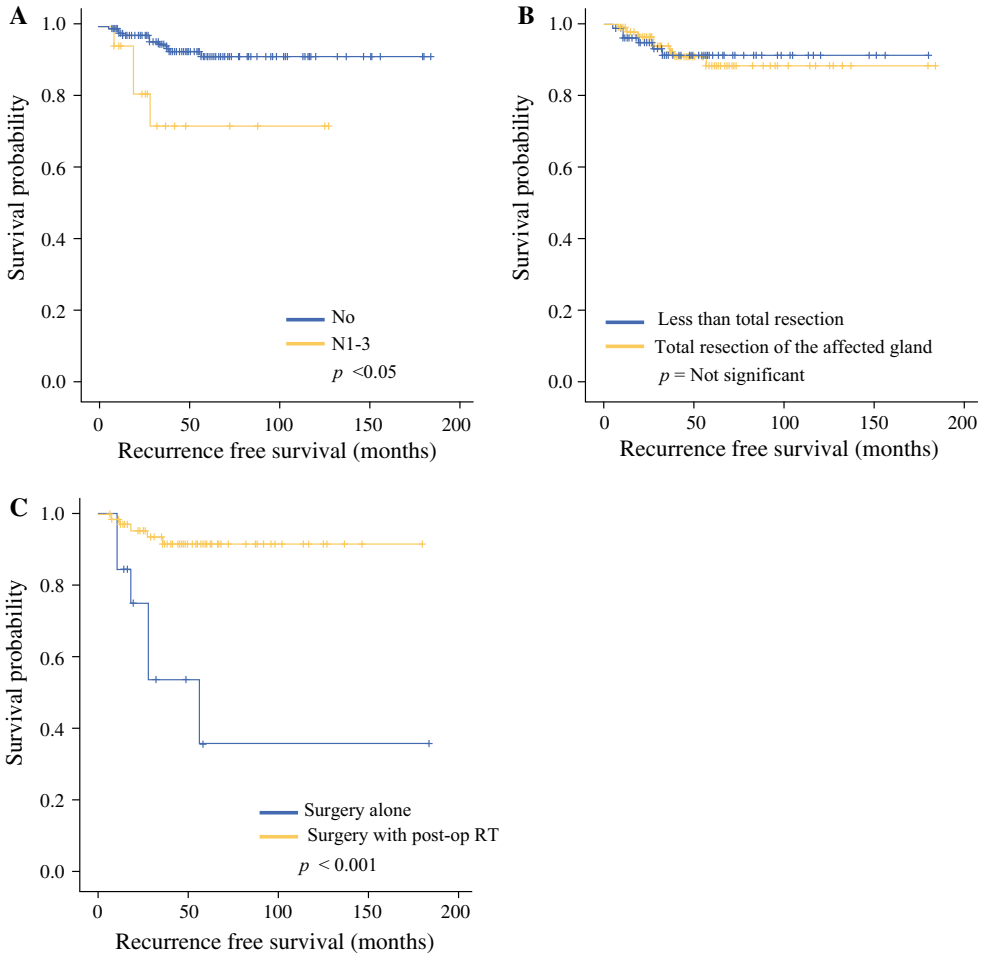

FIG. 1 Survival plots of low-grade salivary gland cancer patients. **a** Survival differences according to the nodal metastasis status; **b** comparison of survival plot between the differential extent of surgery for primary tumor sites; and **c** survival plots according to the treatment modalities (surgery alone vs. surgery with postoperative adjuvant radiation) in low-grade salivary gland cancer patients with pathology risk factor (+) or N(+) ($N = 87$). *post-op* postoperative, *RT* radiation therapy

analysis (cribriform or tubular subtypes).[18] The low-grade adenocarcinoma category included polymorphous low-grade adenocarcinomas and adenocarcinomas not otherwise specified (NOS) of low-grade features, where adenocarcinomas NOS were diagnosed by exclusion of other typical pathologies. The analyses only included tumors without high-grade histology features.[19] Similarly, among carcinoma ex pleomorphic adenomas, intracapsular/non-invasive tumors with low-grade histology were included.[19]

Other pathologies (acinic cell carcinomas, basal cell adenocarcinoma, epithelial–myoepithelial carcinomas, myoepithelial carcinomas, and oncocytic carcinomas) were diagnosed based on the histomorphologic pattern and cytologic features, and tumors showing high-grade histology were excluded. Equivocal cases were discussed in intradepartmental consultation, and some cases were diagnosed by external review.

Statistical Analyses

From our cohort, we evaluated the recurrence and death event according to the disease pathological characteristics (histologic subtypes, surgical margin status, presence of perineural invasion, lymphovascular invasion, and extra-parenchymal extension, as well as pT/pN classification of tumors). Baseline variables at diagnosis of LGSGC (age, sex, and primary site) were also considered as variables for outcome. In addition, treatment modalities and surgical extent were included as clinical variables.

The primary endpoint was recurrence-free survival (RFS) because there were only two disease-specific deaths in our series. RFS and overall survival (OS) were calculated as the time elapsed from the end of definitive treatments until the time of recurrence and any deaths, respectively. Cases without events (recurrence or death) at the last clinical follow-up were censored. Survival curves were estimated using Kaplan–Meier methods, and group differences were tested using the log-rank test. Prognostic significance of variables was assessed by univariate and multivariate analyses using the Cox proportional hazard model. For statistical analyses, all variables were stratified into two or three groups. Associations between risk group and clinical/pathological characteristics were tested using the Wilcoxon test or Fisher's exact test. Statistical analyses were executed using SPSS version 20.0 (IBM Corporation,

TABLE 3 Extent of surgery for primary sites

Variables	Extent of surgery		
	Less-than-total resection of the affected gland ($N = 83$)	Total resection of the gland ($N = 96$)	p value
Age, mean ± SD[a]	44.9 ± 14.7	47.9 ± 15.2	0.969
Sex, male/female	31/52 (37.3/62.7)	56/40 (58.3/41.7)	0.007
Primary site			
Parotid gland	80 (96.4)	51 (53.1)	<0.001
Submandibular gland	1 (1.2)	36 (37.5)	
Others	2 (2.4)	9 (9.4)	
Disease extent			
T3–4/T1–2	21/62 (25.3/74.7)	37/59 (38.5/61.5)	0.078
N1–3/N0	3/80 (3.6/96.4)	15/81 (15.6/84.4)	0.011
Stage III–IV/I–II	22/61 (26.5/73.5)	45/51 (46.9/53.1)	0.006
Pathology			
Mucoepidermoid carcinoma, low grade	36 (43.4)	38 (39.6)	0.180
Adenoid cystic carcinoma, non-solid type	13 (15.7)	29 (30.2)	
Others	34 (41.0)	29 (30.2)	
Pathology risk factors			
Perineural invasion (Y/N)	9/74 (10.8/89.2)	21/75 (21.9/78.1)	0.070
Lymphovascular invasion (Y/N)	3/80 (3.6/96.4)	9/87 (9.4/90.6)	0.145
Extraparenchymal extension (Y/N)	16/67 (19.3/80.7)	29/67 (30.2/69.8)	0.120
Resection margin (positive/close + negative)	16/67 (19.3/80.7)	29/67 (30.2/69.8)	0.120
Neck dissection	7/76 (8.4/91.6)	38/58 (39.6/60.4)	<0.001
Postoperative radiation (Y/N)	51/32 (61.4/38.6)	74/22 (77.1/22.9)	0.033
Outcomes (recurrence)	6 (7.2)	8 (8.3)	0.999

Y yes, *N* no

[a] Two sample *t* test. Other statistical comparisons used Fisher's exact test with Bonferroni's correction for multiple testing

Armonk, NY, USA). All tests were two-sided and $p < 0.05$ indicated statistical significance.

RESULTS

Subject Characteristics

The most common site was the parotid gland (73.2 %); tumors were classified as pT1–2 in 67.6 % of cases and pT3–4 in 32.4 % of cases (Table 1). Most patients (89.9 %) were diagnosed as having N0 disease. Low-grade mucoepidermoid carcinoma (41.3 %) was the most common histologic subtype, followed by the non-solid type of adenoid cystic carcinoma (23.5 %). Perineural invasion was identified in 30 patients (16.8 %), lymphovascular invasion in 12 patients (6.7 %), and extraparenchymal extension in 45 patients (25.1 %). Complete resection with sufficient safety margin ≥5 mm was performed in 70 patients (39.1 %). Sixty-four patients (35.8 %) were diagnosed as close surgical margin (<5 mm) and malignant cells at resection margin were detected in 45 patients (25.1 %).

Fifty-four patients (30.2 %) were treated with surgery alone, and 125 patients underwent surgical resection with adjuvant RT. During the study period, radiation techniques were mainly three-dimensional conformal radiation ($N = 98$) and intensity-modulated RT ($N = 27$), with a median dose of 59.4 Gy (range 49.5–66.6) by 1.8 or 2.0 Gy per fraction over 5.5–6 weeks.

Ninety-six patients (53.6 %) received total resection of the affected gland and 83 patients (46.4 %) underwent less-than-total resection. Selective or modified neck dissections were conducted in 45 patients (25.1 %) with suspicious clinical node metastases. Recurrence events occurred in 14 patients (four adenoid cystic carcinomas, four low-grade mucoepidermoid carcinomas, three acinic cell carcinomas, two epithelial-myoepithelial carcinoma, and one non-invasive type carcinoma ex pleomorphic adenoma). There were six local recurrences, four regional recurrences, and six systemic metastases (with overlapping numbers); 10 of 12 were salvaged successfully, and the remaining two cases

TABLE 4 Role of postoperative adjuvant radiation treatments for LGSGC with pathology risk factors, or node-positive (N +)

Variables	Pathology risk factor (−) and N0			Pathology risk factor (+) or N(+)		
	RT(+) ($N = 51$)	RT(−) ($N = 41$)	p value	RT(+) ($N = 74$)	RT(−) ($N = 13$)	p value
Age, mean ± SD[a]	45.0 ± 14.2	46.8 ± 16.9	0.308	48.1 ± 14.1	42.1 ± 16.7	0.383
Sex, male/female	22/29	15/26	0.669	41/33	9.4	0.544
Primary site						
Parotid gland	39	33	0.896	49	10	0.571
Submandibular gland	11	7		16	3	
Others	1	1		9	0	
Disease extent						
T3–4/T1–2	9/42	1/40	0.039	43/31	5/8	0.234
N1–3/N0	0	0		16/58	2/11	0.729
Stage III–IV/I–II	9/42	1/40	0.039	51/23	6/7	0.126
Pathology						
Mucoepidermoid carcinoma, low grade	22 (43.1)	18 (43.9)	0.201	26 (35.1)	8 (61.5)	0.018
Adenoid cystic carcinoma, non-solid type	12 (13.0)	2 (4.9)		30 (40.5)	0 (0.0)	
Others	19 (37.3)	21 (51.2)		18 (24.3)	5 (38.5)	
Outcomes (recurrence)	2 (3.9)	1 (2.4)	NS	5 (6.8)	6 (46.2)	0.001

Pathology risk factors: Perineural invasion, lymphovascular invasion, extraparenchymal extension or cancer cells detected at the resection margin

RT postoperative radiation treatment, *NS* not significant, *N0* node-negative, *N(+)* node-positive

[a] Two sample t test. Other statistical comparisons used Fisher's exact test with Bonferroni's correction for multiple testing

were followed-up regularly with asymptomatic distant metastases (electronic supplementary Table 1).

Significant Prognostic Factors for Recurrence in Low-Grade Salivary Gland Cancers

Univariate analyses revealed that the significant risk factors for recurrence were the presence of lymph node metastases, lymphovascular invasion, and positive cancer cells at resection margin (Table 2). Patients with N0 status had better 5-year RFS than patients with metastatic lymph node (91.4 vs. 72.0 %; $p = 0.005$) (Fig. 1a); however, we could not find significant differences in recurrence among variables of close surgical margin and extent of surgery.

Multivariate Cox regression analyses were conducted, including variables with $p < 0.2$ in univariate analyses. Patients with metastatic lymph nodes showed significantly poorer outcome than patients with N0 disease [hazard ratio (HR) 6.492; $p = 0.013$]. In addition, the presence of cancer cells at the resection margin (HR 14.639; $p = 0.003$) was another significant adverse prognostic factor for RFS, but not close surgical margin. Postoperative RT reduced recurrences significantly (HR 0.129; $p = 0.001$).

Extent of Surgery for the Primary Tumor

Ninety-six patients underwent total resection of the affected gland, and 83 patients underwent less-than-total resection. No significant difference was evident in RFS between these two groups. Less-than-total resection of the affected gland was performed more in the parotid gland than in the submandibular gland, which might have reflected technical issues (partial or superficial parotidectomy) (Table 3). In comparison, total resections were more common in males (58.3 vs. 37.3 %; $p = 0.007$), lymph node metastasis (15.6 vs. 3.6 %; $p = 0.011$), and advanced stage (46.9 vs. 26.5 %; $p = 0.006$). Moreover, patients with total resection were more likely to undergo neck dissection (39.6 vs. 8.4 %; $p < 0.001$) and postoperative RT (77.1 vs. 61.4 %; $p = 0.033$).

No significant differences were observed between the two groups with regard to resection margin status. The number of recurrence outcomes was similar, with a total of eight in the resection group (7.2 %) and six in the less-than-total resection group (8.3 %) during follow-up ($p = 0.999$). No significant impact in RFS was found between the differential surgical extents for primary tumor sites (Fig. 1b).

Indications for Postoperative Adjuvant Radiation Therapy

The main indications of postoperative RT in these patients were advanced T stage (T3–4), node metastasis, and tumors with pathology risk factors (electronic supplementary Table 2). However, some patients having pT1–

2N0 tumors without any pathology risk factors ($N = 42$) received postoperative RT, mainly because of surgical dissection in close proximity to tumors for facial nerve preservation (not enough safety surgical margin). Meanwhile, patients with pathology risk factors or node metastasis ($N = 13$) did not undergo postoperative RT with unknown reasons (Table 4). Interestingly, patients who underwent surgery with postoperative RT showed significantly better outcome than with surgery alone, even though the group of postoperative RT patients had more advanced tumors with frequent pathology risk factors (Table 2 and electronic supplementary Table 2).

In order to define the cohorts who benefited more from postoperative RT, we stratified the total subjects into two groups—pathology risk factor (−) and N0 group, and pathology risk factor (+) or N(+) group—because the previous analyses revealed that one of the pathology risk factors and N(+) were significant risk factors for recurrence, but not T classification (Table 2). Ninety-two patients had no adverse pathologic risk factors or lymph node metastasis, and 87 patients had more than one pathologic risk factor or lymph node metastasis (Table 4). In the negative risk factor and N0 group, primary tumor status was the only distinction between the RT(+) and RT(−) subgroups, and there was no significant impact on treatment outcome regardless of adjuvant RT. The majority of patients (85.1 %) with adverse risk factors or N(+) underwent postoperative RT; of these, only five patients had recurrent disease (6.8 %). However, among 13 patients without postoperative RT, six experienced recurrence (46.2 %; $p = 0.001$), which suggested that postoperative RT significantly reduced recurrences in patients with risk factors. Kaplan–Meier analyses also showed less recurrence in patients with surgery and postoperative RT (Fig. 1c).

DISCUSSION

Because of disease rarity, it is hard to conduct prospective clinical comparisons of the efficacy of each treatment modality in LGSGC. Surgery with postoperative RT is the treatment of choice for LGSGC.[7,11,12,17,20] Moreover, the definite diagnosis of LGSGC is usually reached after detailed pathological examination of surgical specimens; thus, accurate information about pathology is usually lacking at the time of initial treatment decision. Few reports have been published about optimal treatment and its outcomes, particularly in LGSGC. We conducted analyses of outcomes in pathologically confirmed LGSGC patients to evaluate treatment outcomes and the adequacy of treatment modalities. We strove to identify which surgical extent is optimal for salivary gland tumors suspected of being LGSGC, and which patients benefit more from postoperative RT (or could avoid it safely).

The analysis revealed a very high overall (96.6 %) and RFS rate (89.6 %) at 10 years; only two disease-specific deaths occurred due to recurrence in the skull base. Of note, all recurrences ($N = 14$) were detected within 5 years, indicating that this length of follow-up can be optimal in patients with LGSGC. Interestingly, lymph node metastasis from LGSGC occurred in 10 % of cases, even though the cellular features of the primary tumors fit into the low-grade pathology. All N2–3 diseases were detected by pretreatment imaging (computed tomography, magnetic resonance imaging, or ultrasonography), and 9 of 12 N1 diseases (75 %) were also suspected, preoperatively. Thus, considering the relatively low incidence of occult lymph node metastasis (1.8 %), we do not recommend the routine use of elective neck dissection in clinically node-negative LGSGC patients.

Treatment decisions largely depend on the grade of tumor: low- versus high-grade (+intermediate) in salivary gland malignancies,[21] which we previously confirmed.[22,23] For example, wide sialadenectomy with neck dissection is a common surgical procedure for tumors suspected of being high-grade salivary gland cancers, but not for LGSGC. Clinically, it is hard to preoperatively differentiate between benign salivary gland tumor and low-grade salivary gland malignancies.[22] Thus, in most cases, the extent of surgery depends on the size and location of tumors in the affected gland. Usually, the surgical safety margin is not sufficient because of facial nerve preservation, particularly in the parotid gland, which results in the frequent use of postoperative adjuvant RT.[20] The present data demonstrate that the close surgical margin itself is not a risk factor for recurrence in LGSGC if surgery can achieve the cancer cell negative resection margin (R0). Thus, partial removal of the affected gland can be justified with a complete removal of tumor in the gland.

Our results also demonstrate that postoperative RT is very effective in reducing recurrence in LGSGC, more specifically in tumors having one of the pathology risk factors (perineural invasion, lymphovascular invasion, extraparenchymal extension, or cancer cell positive resection margin), or node metastasis. Even in T3–4 tumors, radiation could reduce the incidence of recurrence to that of T1–2 tumors without pathology risk factors (Table 4). Thus, postoperative RT should be applied for patients with LGSGC showing pathology risk factors, advanced T tumors, and node metastasis in order to achieve better outcomes. Reciprocally, the oncological outcome was very good, even without postoperative RT, in cases of pT1–2N0 tumors without pathology risk factors. In this regard, our results are consistent with the paper by Seethala.[19]

One of the limitations of this study was a potential selection bias in the application of postoperative adjuvant

RT due to the retrospective nature of the analyses. Indeed, we could not find clear reasons why patients with pathology risk factors or node metastasis ($N = 13$) were left unirradiated postoperatively (Table 4). Thus, our results need to be validated by the following clinical studies, before clinical applications.

CONCLUSIONS

The presence of nodal metastasis and cancer cells at the resection margin were significant unfavorable prognostic factors for recurrences in LGSGC, but not the close surgical margin. Less-than-total resection of the affected gland appeared to be oncologically safe, so far as achieving cancer cell-free resection margin. Postoperative RT clearly benefits patients with LGSGC having pathology risk factors, advanced T tumors, and node metastasis. Oncological outcomes are very good with surgery alone in cases of pT1–2N0 LGSGC without pathology risk factors.

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CONFLICT OF INTEREST Jae-Keun Cho, Byung-Woo Lim, Eun-Hye Kim, Young-Hyeh Ko, Dongryul Oh, Jae-Myoung Noh, Yong Chan Ahn, Kwan-Hyuck Baek, and Han-Sin Jeong have no conflicts of interest to declare.

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