A retrospective study of parotid gland tumors at a single institution

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Abstract. The aim of the present study was to analyze the clinical characteristics, surgical treatments and clinical outcome of patients with parotid gland tumors and to compare the results with those cited in the literature. A retrospective study was conducted in 140 patients (male, n=77; female, n=63) with parotid gland tumors who underwent parotidectomy at Hokuto Hospital Department of Otolaryngology-Head and Neck Surgery (Obihiro, Japan) between April 2007 and December 2021. Of the 140 patients enrolled, 118 (84.3%) patients had benign tumors, including 63 (45%) patients with pleomorphic adenomas and 43 (30.7%) patients with Warthin tumors, and 22 patients (15.7%) had parotid carcinoma. Comparison of the three groups of patients with parotid gland tumors indicated that pack years as an indicator of smoking status were significantly higher in patients with Warthin tumors than in those with parotid carcinomas (P=0.011) or pleomorphic adenoma (P<0.001). Fine-needle aspiration cytology (FNAC) was non-diagnostic for only 6 (4.3%) of 140 patients. The sensitivity, specificity, positive predictive value, negative predictive value and accuracy of FNAC by both conventional smear and liquid-based cytology (LBC) for parotid carcinomas were 70, 99, 93.3, 94.4 and 82.9%, respectively. Among the 22 patients with parotid carcinoma, extended total/total and superficial parotidectomy were performed in 10 (45%) and 11 (50%) cases, respectively. Total and selective neck dissection of the area from level II to I, II and III were performed in 6 (24%) and 7 (32%) patients, respectively. Postoperative radiotherapy (50 Gy) was performed in 15 (68%) patients. The overall survival (OS) and disease-free survival (DFS) rates at 5 years were 51.5 and 76.4%, respectively. Univariate analysis revealed that age >65 years was significantly associated with poorer 5-year OS (P<0.001) and DFS (P<0.001). Multivariate analysis revealed that an age of more than 65 years combined with high-grade histologic malignancy was associated with worse DFS (P=0.02; hazard ratio, 3.628; 95% confidence interval, 1.283-9.514). In conclusion, the clinical characteristics and treatment outcomes of parotid gland tumors were consistent with the results of previous reports. Smoking may be closely related to the pathogenesis of Warthin tumors. LBC potentially provides improved accuracy in FNAC.

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Introduction

Parotid gland tumors consist of 70-80% of salivary gland tumors, 2-3% of head and neck tumors, and 0.6% of all tumors (1). Salivary gland tumors vary widely and are classified into 20 histologic types for malignant tumors and 11 for benign tumors, according to the 2017 classification of the World Health Organization (WHO) (1). Pleomorphic adenoma is the most common type and Warthin tumor is the second of benign parotid tumors. Mucoepidermoid carcinoma is the most common malignancy of the salivary glands. The etiology and pathogenesis of these tumors have not been understood. Due to the variety of parotid gland tumors, a successful outcome of parotid surgery requires careful pre- and perioperative planning and decision making, as inadequate surgery may lead to recurrence of not only parotid carcinomas but also benign parotid tumors such as pleomorphic adenomas. Ultrasound (US)-guided fine-needle aspiration cytology (FNAC) is the most reliable preoperative method for the evaluating parotid gland tumors (2). Recent reports indicate that liquid-based cytology (LBC) in addition to conventional smear (CS) in FNAC is useful for the diagnosis of salivary

gland tumors (3). With regard to the surgery for parotid carcinomas, several factors must be considered, including the extent of resection (i.e., extended total, total, or superficial parotidectomy), handling of facial nerves (i.e., preservation or resection), extent of neck dissection (i.e., total, selective or prophylactic). Intraoperative facial nerve monitoring (FNM) was recently reported as helpful in detecting and preserving the facial nerve (4). Whether postoperative radiotherapy to parotid carcinoma contributes to improvement of survival has not been fully evaluated. An independent prognostic factor of parotid carcinoma except for TNM stage has not been defined yet. We examined the incidence of different types of parotid gland tumors and evaluated all parotid gland tumors diagnosed at our institution, focusing on diagnostic challenges and preoperative evaluation. This work provides recommendations to better delineate the management of these tumors.

Patients and methods

Patients. A retrospective study was conducted in 140 patients (male: 77; female: 63) with parotid gland tumors who underwent parotidectomy from April 2007 to December 2021 at Hokuto Hospital Department of Otolaryngology-Head and Neck Surgery. Patient median age was 60.5 years (range, 18 to 90 years). Data collected included cigarette smoking status (defined as pack years [packs/day x years]), symptoms, tumor location, maximum tumor size measured by US, preoperative FNAC diagnosis, operation time, histology, and postoperative complications. With regard to parotid carcinomas, staging, treatment, and prognosis were also analyzed. Patients with incomplete clinical and histologic data and malignant lymphoma were excluded in this study.

Fine-needle aspiration cytology. Both CS and LBC were utilized (5). Briefly, for US-guided FNAC, tumors were aspirated by 2 experienced otolaryngologists using a 21-gauge needle attached to a 20-ml disposable plastic syringe and aspirator developed by Chiba University. Aspirates were immediately processed on slides and then fixed in 95% ethanol for Papanicolaou staining and dried for Giemsa staining. The remaining aspirate in the syringe and needle were rinsed into a vial with 10 ml of CytoRich Red solution (Becton Dickinson, Franklin Lakes, NJ). Fluid cytology specimens were processed using the BD SurePath hand method (BD Biosciences, Franklin Lakes, NJ) and routinely stained with Papanicolaou solution. Tumors were cytologically classified by 2 experienced cytotechnologists into five categories: non-diagnostic, benign, indeterminate, suspicious for malignancy, or malignant. FNAC diagnosis of suspicious for malignancy and malignant and postoperative histologic diagnosis of parotid carcinoma were categorized as positive. Other benign results were categorized as negative. The sensitivity, specificity, and positive and negative predictive values for detecting malignant lesions by FNAC were estimated based on the histology results, excluding non-diagnostic and indeterminate results. Accuracy was estimated based on true positives and negatives/total number of cases, including non-diagnostic and indeterminate cases.

Surgical treatments. Surgery for benign parotid tumors was performed by partial superficial parotidectomy (6). Briefly, after a preauricular to postauricular (modified Blair incision) S-shaped incision, the trunk of the facial nerve was identified by intraoperative FNM with 1.0 mA of stimulation (NIM-Response 3.0 system, Medtronic Inc., Jacksonville, FL). The tumor was resected with a 1-cm margin with following the branches of the facial nerve (7,8). For patients who were diagnosed with malignant tumors by preoperative FNAC, total parotidectomy was performed. Otherwise, extended total parotidectomy, defined as resection of adjunct structures such as either skin, the sternocleidomastoid muscle, the masseter muscle or the external meatus in addition to total parotidectomy, was performed (9). For patients with clinical or imaging evidence of nodal disease (cN+), total neck dissection (Level I to V) was performed. For patients without lymph node metastasis (cN0), selective neck dissection of the area from Level II to I, II and III was performed; otherwise, no neck dissection was not performed, at the consideration of imaging and FNAC results. For patients with tumor invasion of the facial nerve determined intraoperatively, the facial nerve was resected and transplanted. Skin defects were reconstructed with a free flap. Histologic diagnosis was assessed by two experienced pathologists and classified based on the WHO Classification of Head and Neck Tumours-2017 (1).

Statistical analysis. Associations between groups were determined using Fisher's exact test for categorical variables, and using the Kruskal-Wallis test and Steel-Dwass test for continuous variables. Temporary facial nerve palsy was defined as the complete recovery of facial palsy within 6 months after surgery. Persistent facial palsy was defined as any facial palsy lasting more than 6 months. Time was defined as the period starting from the date of diagnosis to the date of disease relapse or that of last follow-up visit for Disease-free survival (DFS) or to the date of death by any cause for overall survival (OS). DFS and OS rates were calculated using the Kaplan-Meier method and compared using the log-rank test. For determination of factors related to DFS and OS, a Cox proportional hazards model was used. The final results of these analyses are hazard ratios (HR), their 95% confidence intervals (CI) and P-value. A p-value less than 0.05 was considered indicative of statistical significance. BellCurve for Excel (Social Survey Research Information, Tokyo, Japan) statistical software was used for all analyses.

Results

Histologic classification. Histologic classification of the 140 patients with parotid gland tumors included 118 cases (84.3%) of benign tumors, with 63 (45%) of pleomorphic adenomas, 43 (30.7%) of Warthin tumors, 6 (4.3%) of myoepitheliomas, and 2 (1.4%) of basal cell adenomas (Table I). A total of 22 of the 140 patients (15.7%) had parotid carcinoma, of which 10 (7.1%) were of high-grade, 2 (1.4%) of intermediate-grade, and 10 (7.1%) of low-grade in terms of histologic malignancy.

Clinicopathologic features. Patients with parotid gland tumors were categorized into three groups based on clinical features: parotid carcinomas including all histology, pleomorphic adenoma, and Warthin tumor (Table II). In terms of age

Table I. Histologic classification of 140 patients with parotid gland tumors.

Tumor type	No. (%)
Benign tumors	118 (84.3)
Pleomorphic adenoma	63 (45)
Warthin tumor	43 (30.7)
Myoepithelioma	6 (4.3)
Basal cell adenoma	2 (1.4)
Others	4 (2.9)
Parotid carcinomas	22 (15.7)
Low grade	10 (7.1)
Mucoepidermoid ca.	3 (2.1)
Ca. ex pleomorphic adenoma	3 (2.1)
Epithelial myoepithelial ca.	2 (1.4)
Mammary analogue secretory ca.	1 (0.7)
Intraductal ca.	1 (0.7)
Intermediate grade	2 (1.4)
Adenoid cystic ca.	1 (0.7)
Lymphoepithelial ca.	1 (0.7)
High grade	10 (7.1)
Squamous cell ca.	3 (2.1)
Adenocarcinoma NOS	3 (2.1)
Mucoepidermoid ca.	2 (1.4)
Salivary duct ca.	2 (1.4)

distribution, patients with pleomorphic adenoma were significantly younger than those with Warthin tumor (P<0.001). Pleomorphic adenoma was more frequent among females than parotid carcinoma (P=0.003) or Warthin tumor (P<0.001). Pack years was significantly higher in patients with Warthin tumor than patients with parotid carcinomas (P=0.011) or pleomorphic adenoma (P<0.001). Pain was significantly more frequent in patients with parotid carcinoma than in those with pleomorphic adenoma (P=0.001) or Warthin tumor (P=0.006). Facial nerve palsy was present in 2 patients with parotid carcinomas. There were no significant differences among the three groups in terms of the location of the tumor (right or left side; superficial or deep lobe), and maximum tumor size. Operation time was significantly longer in patients with parotid carcinoma than in those with pleomorphic adenoma (P<0.001) or Warthin tumor (P=0.002). Transient facial nerve palsy occurred in 10 (16%) patients with pleomorphic adenoma and 9 (21%) patients with Warthin tumor. Persistent postoperative facial nerve palsy was significantly more frequent in patients with parotid carcinoma than in those with pleomorphic adenoma (P<0.001) or Warthin tumor (P=0.003).

Results of fine-needle aspiration cytology. FNAC was non-diagnostic for only 6 (4.3%) of 140 patients. The sensitivity, specificity, positive predictive value, and negative predictive value of FNAC for malignant tumors were 70, 99, 93.3, and 94.4%, respectively (Table III). The accuracy of FNAC for all parotid gland tumors was 82.9%. Histologic presumption by FNAC corresponded with the results of histologic analysis of surgical specimens in 53 (84.1%) of 63 patients with pleomorphic adenoma and 37 (86%) of 43 patients with Warthin tumor.

Treatments and clinical outcomes of parotid carcinoma. Staging and treatment methods for the 22 patients with parotid carcinoma are summarized in Table IV. Extended total/total and superficial parotidectomy were performed in 10 (45%) and 11 (50%) patients, respectively. Total and selective neck dissection were performed in 6 (24%) and 7 (32%) patients, respectively. In 10 patients with malignant diagnosis on FNAC, extended total parotidectomy with total neck dissection was performed in 3 patients, total parotidectomy with total neck dissection in 2 patients, and total parotidectomy with selective neck dissection in 5 patients. The trunk and part of the facial nerve were resected in 1 (4%) and 4 (18%) patients, respectively, due to tumor invasion of the facial nerve intraoperatively. All resected facial nerves were transplanted with the greater auricular nerve. Two (9%) patients were reconstructed with an ALT flap to repair the defect resulting from tumor invasion of the skin. Postoperative radiotherapy (50 Gy) was performed in 15 (68%) of the 22 patients with parotid carcinoma. A total of 3 of 22 patients (14%) died of parotid carcinoma, and 4 (18%) patients died of diseases other than parotid carcinoma. The median of the observation period was 32 months (range, 1-132 months). The 5-year OS and DFS rates among the 22 patients with parotid carcinoma were 51.5 and 76.4%, respectively (Fig. 1). Univariate analysis revealed that age >65 years was significantly associated with poorer 5-year OS (P<0.001) and DFS (P<0.001) (Table V). Male and high-grade histologic malignancy tended to exhibit worse 5-year OS (P=0.083) and 5-year DFS (P=0.061), respectively. Multivariate analysis revealed age >65 years with high-grade histologic malignancy was associated with worse DFS in this group (P=0.02, hazard ratio: 3.628; 95% confidence interval: 1.283-9.514).

Discussion

This study examined parotid gland tumors treated with surgery at a single institution. The ratios of parotid carcinomas and benign parotid tumors were 15.7 and 84.3%, respectively. The ratio of parotid carcinoma was similar to rates reported in several other studies of 13.9-31.8% (2,10,11). With regard to symptoms, mass in the parotid region is the most common symptom of both benign parotid tumor and parotid carcinoma. The possibility of malignancy should be considered in the presence of sudden growing masses, pain, facial nerve palsy, and swelling of lymph nodes (12). In the present study, pain in the parotid area was present in 9 (41%) of 22 patients with parotid carcinoma, and the incidence of pain was significantly higher than among patients with benign parotid tumors. The frequency of pain in the parotid area is reportedly 31-52% in patients with malignant parotid tumors (13-15). As the frequency of pain was approximately 10 times higher in patients with parotid carcinoma than in those with benign tumors, the presence of pain was considered the first indicator of possible malignancy (15). In the present study, facial nerve palsy was present in 2 (9%) of 22 patients with parotid carcinoma, including a patient with squamous cell carcinoma and a patient with adenocarcinoma NOS, but facial nerve palsy was absent in the 118 patients

Table II. Clinicopathologic features of parotid gland tumor patients categorized according to parotid carcinoma, pleomorphic adenoma, or Warthin tumor.

Clinicopathologic factor	Parotid carcinoma (n=22)	Pleomorphic adenoma (n=63)	Warthin tumor (n=43)	P-value
Age, years[a]	61 (44-77)	54 (42-68)	64 (59-70)	PA vs. WT <0.001
Gender, male:female[b]	16 (73%):6 (27%)	23 (37%):40 (63%)	33 (77%):10 (23%)	PC vs. PA 0.003; PA vs. WT <0.001
Smoking, pack years[a,c]	6 (0-25)	0 (0-20)	38 (18-50)	PC vs. WT 0.011; PA vs. WT <0.001
Symptoms[b]				
Pain	9 (41%)	5 (8%)	4 (9.3%)	PC vs. PA 0.001; PC vs. WT 0.006
Facial nerve palsy	2 (9%)	0	0	
Location[b]				
Side, right:left	11 (50%):11 (50%)	33 (52):30 (48%)	19 (44%):24 (56%)	
Lobe, superficial:deep:uncertain	18 (82%):1 (4%):3 (14%)	48 (76%):15 (24%)	37 (86%):6 (14%)	
Maximum tumor size, mm[a]	25 (19-32)	23(18-30)	32 (23-40)	
Operation time, min[a]	119 (74-160)	70 (58-85)	71 (57-97)	PC vs. PA <0.001; PC vs. WT 0.002
Postoperative complications[b]				
Postoperative bleeding	0	2 (3%)	0	
Transient facial nerve palsy	3 (14%)	10 (16%)	9 (21%)	
Persistent facial nerve palsy	5 (23%)	0	0	PC vs. PA <0.001; PC vs. WT <0.003
Frey syndrome	1 (2%)	0	0	
Recurrence	4 (18%)	1 (2%)	0	

Data are presented as the median (interquartile range) or a N (%). Statistical analysis was performed using a [a]Kruskal-Wallis test for continuous variable or a [b]Fisher's exact test for categorical variables. P-value <0.05 was considered statistically significant. [c]Pack-years=number of packs/day x years. PC, parotid carcinoma; PA, pleomorphic adenoma; WT, Warthin tumor.

with benign parotid tumors. The incidence of preoperative partial and complete facial nerve palsy in patients with parotid carcinoma was reported as 18-35% (16,17), whereas none of 965 patients with benign tumors presented with preoperative facial nerve dysfunction (17).

Warthin tumor is the second most common type of benign parotid tumor, comprising 15-36% of all benign parotid tumors (18). Studies have revealed that these tumors predominantly occur in males and those in the fourth to seventh decades of life. In the present study, 77% of patients with Warthin tumor were male with a median age at the surgery of 64 years and ratio of superficial lobe origin of 86%. Warthin tumor can present bilaterally in 7-10% of cases, either metachronously (90%) or synchronously (10%) (19,20). The risk for bilateral Warthin tumors was significantly correlated with nicotine intake (19). In the present study, patients with Warthin tumor had higher pack years as indicator of cigarette smoking status than those with pleomorphic adenoma and those with parotid carcinoma. Smoking has been identified as a risk factor for Warthin tumor in several series (21,22). Evidence for the etiology and pathogenesis of Warthin tumor remains unclear. To our knowledge, only a few mechanisms have been proposed to date to explain the association between Warthin tumor and smoking: 1) direct contact between inhaled irritants in smoke and the parotid duct lining that initiate a metaplastic response, which induces the proliferation of glandular, cystic, and lymphoid elements (21); 2) immune reaction with delayed hypersensitivity (23); 3) high level of oxidative damage associated with cigarette smoking that increases mitochondrial DNA damage in oncocytes (24); and 4) metaplasia of the glandular tissues entrapped in the parotid lymph nodes triggered by antigens or chemical irritants in cigarette smoke (25,26). This may favor the hypothesis of heterotropia (assuming that Warthin tumor originates in the salivary gland nests entrapped in intraparotid lymph nodes during encapsulation of the parotid gland) (27) along with an immunologic interaction between the epithelial tumor cells and the lymphocytic infiltration.

Preoperative diagnosis by FNAC (whether benign or malignant, grade of malignancy, and whether a tumor is a pleomorphic adenoma or Warthin tumor) is essential for adequate surgical management (15). In the present study, the non-diagnostic rate was 4.6%, lower than rates reported in previous studies of 4.2-12.3% (28). We employed LBC in addition CS to reduce the non-diagnostic rate and to improve the accuracy of FNAC results. The methodology of LBC for specimens obtained from thyroid tumor and lymph node has many

Table III. Correlation between FNAC and histologic diagnosis among 140 patients with parotid gland tumors.

	Histologic diagnosis						
	Parotid carcinoma (n=22)			Benign tumors (n=118)			
FNAC	High grade (n=10)	Intermediate grade (n=2)	Low grade (n=10)	Pleomorphic adenoma (n=63)	Warthin tumor (n=43)	Myo-epithelioma (n=6)	Others (n=6)
Non-diagnostic (n=6)					5		1
Malignant (n=10)	7	1	2				
Suspicious for malignancy (n=5)	2		2	1			
Indeterminate (n=11)		1	1	3	1	4	1
Benign (n=108)	1		5	59	37	2	4
Pleomorphic adenoma (n=57)			3	53		1	
Warthin tumor (n=40)	1		2		37		
Others (n=11)				6		1	4

FNAC, fine-needle aspiration cytology.

advantages, including: 1) decreased screening area; 2) lack of air-drying artifacts; 3) a more monolayer cellular surface that is easier to screen; 4) consistently well-preserved cells, 5) collection of tumor cells from cystic fluid, 6) possibility of application to immunohistology and genetic analyses (3,5,29). However, some disadvantages of LBC for parotid gland tumors include new artifacts that alter the cellular, architectural and extracellular matrix appearance, and decreased lymphocytes and mucinous material in the background (3). The reported sensitivity and specificity for diagnosing malignant tumors by FNAC with CS ranges from 56 to 100% and from 57 to 98%, respectively (30-33). In the present study in which FNAC was combined with CS and LBC, our data indicated 70% sensitivity and 99% specificity, which was consistent with these previous results. In general, the relatively low sensitivity for parotid carcinoma is caused by the high rate of false-negative results, (i.e., FNAC diagnosis of benign but histologic diagnosis of malignant). In the present study, 2 patients diagnosed with pleomorphic adenoma by FNAC were histologically diagnosed with carcinoma ex pleomorphic adenoma. These results were thought to have been caused by aspiration of part of the pleomorphic adenoma but not part of the carcinoma. Other 2 patients diagnosed with Warthin tumor by FNAC were histologically diagnosed with low-grade mucoepidermoid carcinoma. To reduce these false-negative results, especially in cystic lesions, aspiration from several points of the same solid tumor in the same tumor under US guidance is recommended (34).

The goal of surgical management of benign parotid tumors is to completely remove the tumor and preserve the facial nerve (6). Partial superficial parotidectomy was characterized by the preservation of part of the unaffected parotid tissue and the dissection of a smaller area of facial nerve branches (6). Partial superficial parotidectomy was associated with fewer complications and lower recurrence rates than superficial parotidectomy (35,36). In the present study, recurrence after partial superficial parotidectomy was observed in only 1 patient (2%) with pleomorphic adenoma. Even if the facial nerve is completely preserved, a certain rate of postoperative facial nerve palsy is inevitable (6). The incidence of transient facial nerve palsy after parotidectomy for benign parotid tumors ranges from 10-65%, with persistent palsy seen in <5% of cases (37-39). A report from a single-center study indicated postoperative facial palsy rate of 20% in pleomorphic adenoma and 17.9% in Warthin tumor (6). In the present study, the rate of postoperative transient facial nerve palsy in pleomorphic adenoma was 16 and 21% in Warthin tumor, and no persistent facial palsy was observed. These frequencies were consistent with previous reports. The risk factors for facial nerve palsy reportedly include older age, tumor size (6,40), tumor in the deep lobe, long operation time, extensive bleeding, and lack of FNM (41,42). However, controversy exists, in that some researchers contend that there is no significant difference in complication rates relative to tumor size and tumor in the deep lobe (43), the length of the dissected facial nerve (44), and the extent of parotidectomy (45). We usually identify the trunk of the facial nerve using FNM and follow the branch to confirm nerve integrity. Some studies have reported that intraoperative FNM decreases the incidence of facial nerve palsy (4) and the operation time in parotidectomy (41,46).

Mucoepidermoid carcinoma is the most common malignancy of the salivary glands, accounting for 10-15% of all salivary gland neoplasms and 30% of all salivary malignancies (47,48). In the present study, mucoepidermoid carcinoma was the most common parotid carcinoma in 5 patients (23%) including 3 with low-grade and in 2 with high-grade in terms of histologic malignancy. To date, several histologic grading systems for mucoepidermoid carcinomas have been used (47,48). Low-grade tumors tend to be better circumscribed, more cystic, contain more mucous cells, show minimal cytologic atypia or mitoses and lack perineural invasion. On the other hand, high-grade lesions are more infiltrative, more solid, have less mucous cells and more epidermoid cells, show more cytologic atypia, necrosis and perineural invasion.

Table IV. Staging and treatment of 22 patients with parotid carcinoma.

Variable	No. (%)
Clinical classification	
cT T1:T2:T3:T4	6 (27%):6 (27%):6 (27%):4 (18%)
cN N0:N1:N2b	16 (68%):3 (18%):3 (14%)
cStage I:II:III:IVA	5 (23%):6 (27%):5 (23%):6 (27%)
Parotidectomy	
Extended total and total	10 (45%)
Superficial	11 (50%)
Deep lobe	1 (5%)
Resection of facial nerve	
Trunk	1 (4%)
Partial	4 (18%)
Not performed	17 (82%)
Neck dissection	
Total	6 (27%)
Selective	7 (32%)
Not performed	9 (41%)
Reconstruction with ALT flap	
+	2 (9%)
-	20 (91%)
Radiotherapy	
+	15 (68%)
-	7 (32%)

ALT, anterolateral thigh; -, not present; +, present.

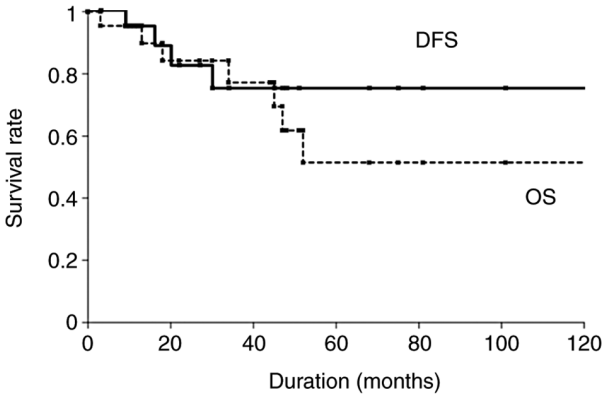

Figure 1. Kaplan-Meier curves of DFS and OS of 22 patients with parotid carcinoma. DFS, disease-free survival; OS, overall survival.

High-grade is known to be poor prognostic factor of mucoepidermoid carcinoma (47,48). A unique translocation t(11; 19) (q21; p13), the most common genetic alteration in mucoepidermoid carcinomas, can produce a fusion oncogene known as *CRTC1-MAML2* (49). Accumulating evidence revealed that the CRTC1-MAML2 expression correlates with a significantly better prognosis in patients with mucoepidermoid carcinoma (50). CRTC1-MAML2 expression is present in 75-93% of low to intermediate-grade mucoepidermoid carcinoma and 50-89% high-grade mucoepidermoid carcinoma, aiding in histologic diagnosis (51,52).

Surgical resection is the first choice of the treatment for parotid carcinoma. For T1-size tumors that are located in the superficial lobe, have low-grade histology, and are N0 parotid carcinoma, superficial parotidectomy with safety margins may suffice (53). Otherwise, total parotidectomy or extended total parotidectomy with safety margins is advised according to the extension area. Total neck dissection (Level I to V) should be carried out in cN+ patients. However, neck dissection for cN0 patients is still controversial. In cN0 patients with parotid carcinoma, histologic lymph node metastasis reportedly ranged from 4.2-30.3% (53-56). A prophylactic selective neck dissection (Level I to III) should be performed in cases involving T3 and T4 tumors with high-grade histology (57), facial nerve palsy, age >54 years, and tumor invasion of adjacent organs (58). In the present study, 9 (41%) of 22 patients who did not undergo neck dissection had a preoperative diagnosis of either cN0, cT1, or benign or indeterminate result on FNAC. In the present study, the trunk and part of the facial nerve were resected in 1 (4%) and 4 (18%) patients, respectively, due to tumor invasion of the facial nerve. A functioning facial nerve should be preserved unless found to be infiltrated with the tumor itself at the time of resection (15). If the nerve is sacrificed because of invasion, then primary nerve grafting should be performed. The greater auricular nerve as a donor is an option, but if that nerve is involved, the sural nerve from the leg may be preferable. We used ALT flap in 2 patients with skin defects caused by invasion of the subauricular skin. The ALT flap has been shown to be effective for covering large defects resulting from the radical removal of parotid malignancies (59). Postoperative radiotherapy was associated with improved survival among patients with salivary gland carcinomas for whom neck dissection was deemed necessary in an analysis of 4,145 cases (60). Criteria proposed by the National Comprehensive Cancer Network for postoperative radiotherapy after the complete resection include intermediate or high-grade, close or positive margins, neural/perineural invasion, lymph node metastasis, lymphatic/vascular invasion, T3 and T4a tumors, and adenoid cystic carcinoma. Following these guidelines, 15 patients (68%) received postoperative radiotherapy in the present study. We recommended postoperative radiotherapy for all patients with parotid carcinoma. The other 7 patients refused radiotherapy for reasons of advanced age or difficulty traveling to the hospital due to distant from home.

In terms of parotid carcinoma prognosis, the 5-year DFS is 60.2-78% (15,61,62). The 5-year DFS rate in the present study was 76.4%, which is not inferior to the rate described in previous reports. Prognostic factors for parotid carcinoma described in previous studies include age >60 years (63), pain (64), facial paralysis (64), skin invasion (64), TNM classification (62,65), lymph node metastasis (63,66), high-risk histologic grade (15,62,63,66,67), perineural invasion (64), lymphovascular invasion (62,63), and involved surgical margins (64). We found that age >65 years with high-grade

Table V. Univariate analysis of factors associated with treatment outcome in 22 patients with parotid carcinoma.

		5-year OS		5-year DFS	
Characteristic	No. (%)	Rate, %	P-value	Rate, %	P-value
Age, years			0.001		0.001
≤65	13 (59)	88		100	
>65	9 (41)	0		0	
Gender			0.083		0.178
Female	6 (27)	100		100	
Male	16 (73)	37		0	
Pain			0.204		0.549
-	13 (59)	69		80	
+	9 (41)	25		43	
Facial nerve palsy			0.797		0.719
-	20 (91)	56		79	
+	2 (9)	50		50	
Facial nerve invasion			0.858		0.472
-	17 (77)	55		83	
+	5 (23)	53		53	
Histologic grade			0.249		0.061
Low and intermediate	12 (55)	44		100	
High	10 (45)	67		49	
Pt			0.88		0.285
pT1-2	12 (55)	51		89	
pT3-4	10 (45)	53		49	
pN			0.647		0.566
pN0	15 (68)	58		82	
pN+	7 (32)	48		56	

OS and DFS were evaluated using Kaplan-Meier analysis and log-rank tests were used to compare the two groups. OS, overall survival; DFS, disease-free survival.

histologic malignancy was an independent prognostic factor in determining DFS. Overall, the advantage of this study was that only 2 otolaryngologists were able to perform FNAC and surgery using the same surgical methods and techniques. The major limitations of this study were the small number of the parotid carcinoma cases and the retrospective study design; thus, the results should be validated through further prospective comparative studies.

In conclusion, clinical characteristics and treatment outcomes of parotid gland tumors at our institution were consistent with the results of previous reports. Smoking may be closely related to the pathogenesis of Warthin tumors. LBC potentially provides better accuracy in FNAC. Considering the variety of histologic types of parotid gland tumors, it is critical to obtain the most-accurate preoperative diagnosis and employ the most-appropriate surgical procedure, including parotidectomy and neck dissection.

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Availability of data and materials

All data generated or analyzed during this study are included in this published article.

Authors' contributions

SSu, NB and YH conceived and designed the analysis. TG, AK, AU, MK, RS, RT, SSa, TYI, HN and HT contributed to the treatments, and collection, analysis and interpretation of

the data. MK, RS, RT and SSa confirm the authenticity of all the raw data. SSu and NB drafted the manuscript, tables and figures. All authors read and approved the final manuscript.

Ethics approval and consent to participate

The present study was approved by the Ethics Committee of Hokuto Hospital (approval no. 1110; Obihiro, Japan). The requirement for informed consent was waived due to the retrospective nature of the study using medical records only. The research content was available publicly on the website of the Ethics Committee of Hokuto Hospital, which ensured opportunities for participants to opt out of the research without any disadvantage.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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