

ORIGINAL RESEARCH

Preoperative evaluation and treatment consideration of parotid gland tumors

Katri Aro MD, PhD¹  | Jarkko Korpi MD, DDS, PhD¹  |
Jussi Tarkkanen MD, PhD²  | Antti Mäkitie MD, PhD^{1,3,4}  | Timo Atula MD, PhD¹ 

¹Department of Otorhinolaryngology—Head and Neck Surgery, University of Helsinki and Helsinki University Hospital, Helsinki, Finland

²Department of Pathology, HUSLAB, University of Helsinki and Helsinki University Hospital, Helsinki, Finland

³Research Program in Systems Oncology, Faculty of Medicine, University of Helsinki, Helsinki, Finland

⁴Division of Ear, Nose and Throat Diseases, Department of Clinical Sciences, Intervention and Technology, Karolinska Institutet and Karolinska Hospital, Stockholm, Sweden

Correspondence

Katri Aro, Department of Otorhinolaryngology—Head and Neck Surgery, Helsinki University Hospital, P.O. Box 263, FI-00029 HUS, Helsinki, Finland.
Email: katri.aro@hus.fi

Funding information

Helsingin ja Uudenmaan Sairaanhoidopiiri

Abstract

Background: The nature of parotid tumors often remains unknown preoperatively and final histopathology may reveal unexpected malignancy. Still, the use of fine-needle aspiration cytology (FNAC) and imaging varies in the management of these tumors.

Methods: We evaluated the preoperative examinations and management of all 195 parotid gland tumors diagnosed within our catchment area of 1.6 million people during 2015.

Results: Altogether 171 (88%) tumors were classified as true salivary gland neoplasms. FNAC showed no false malignant findings, but it was false benign in 5 (2.6%) cases. Preoperative MRI was utilized in 48 patients (25%). Twenty (10%) malignancies included 16 salivary gland carcinomas. Pleomorphic adenomas accounted for 52% of all adenomas. For 24 (40%) Warthin tumors, surgery was omitted.

Conclusion: The proportion of malignancies was lower than generally presented. Our proposed guidelines include ultrasound-guided FNAC with certain limitations. MRI is warranted in selected cases, but seems unnecessary routinely.

KEYWORDS

cytology, diagnosis, fine-needle aspiration, salivary gland, surgery

1 | INTRODUCTION

Parotid gland tumors constitute around 70% of all salivary gland tumors, and historic reports state that approximately 80% of them are benign.^{1,2} A recent study reported that the incidence of salivary gland cancer has been increasing through 1973 to 2009, most commonly in the parotid gland, although the causes still remain unknown.³ The latest World Health Organization (WHO) classification (2017) includes 11 different benign and 20 malignant salivary gland tumor types,⁴ which highlights the need to centralize their challenging management.

Differentiation between benign and malignant salivary gland tumors by clinical examination is often impossible. Successful outcome of parotid surgery warrants careful pre- and perioperative planning and decision making, since final histopathology may reveal unexpected malignancy. Further, inadequate surgery may lead to recurrences of even benign tumors, for example, pleomorphic adenomas (PAs) that can be very difficult to manage. The current imaging methods are not reliable enough for solid diagnosis and thus only guide management. Ultrasound (US) combined with fine-needle aspiration cytology (FNAC) should be adequate for the evaluation of parotid tumors that are considered benign by clinical means,⁵ and

This is an open access article under the terms of the Creative Commons Attribution-NonCommercial-NoDerivs License, which permits use and distribution in any medium, provided the original work is properly cited, the use is non-commercial and no modifications or adaptations are made.

© 2020 The Authors. *Laryngoscope Investigative Otolaryngology* published by Wiley Periodicals LLC on behalf of The Triological Society.

computed tomography (CT) or magnetic resonance imaging (MRI) are recommended for deep lobe tumors and whenever a malignancy is suspected.⁶ MRI is a preferred imaging method because of its higher contrast of soft tissues.^{7,8}

The difficulties in distinguishing the tumor type preoperatively makes proper surgical planning especially demanding. Obviously, malignant parotid tumors require more extensive surgery than benign neoplasms even though this anatomic location does not allow wide resection margins. Limited extent of surgery, for example, extracapsular dissection, is favored at many institutions when the tumor is expected to be benign,⁹ and some selected tumors may be managed by follow-up only. Preoperative knowledge of the most likely histologic subtype would guide treatment since in some low-grade carcinomas, extended parotidectomy can be avoided.¹⁰ The high rate of cervical lymph node metastases in high-grade and advanced-stage tumors warrants elective neck dissection (ND).

Proper primary management of parotid gland tumors demands guidelines and optimization of treatment. Consideration between follow-up only for selected patients, and the extent of surgical treatment require reliable methods for diagnostic evaluation. Therefore, we examined the incidence of different parotid gland tumor types and evaluated all parotid gland tumors at our institution diagnosed over a 1-year period and focused on their diagnostic challenges and preoperative evaluation. This work aims at offering some recommendations to better delineate their management.

2 | PATIENTS AND METHODS

Our study included all patients with a suspicion or diagnosis of a parotid gland tumor during the year 2015 at the Department of Otorhinolaryngology—Head and Neck Surgery, Helsinki University Hospital. We did not include patients who had surgery of the parotid gland due to a known other neoplasm, such as malignancy of the skin. In 2015, the 2005 WHO classification of tumors was in use.¹¹ We reviewed the demographics, preoperative examinations, and surgical treatment. We also analyzed patients, who did not undergo surgery but who were diagnosed a neoplastic lesion of salivary gland origin by cytology. The original FNAC analysis was performed by several pathologists working in five different laboratories in Southern Finland. Re-evaluation of the cytological findings from carcinomas for this study was performed by an experienced pathologist in salivary gland tumors (JT). The outcome of all patients without surgical treatment and those with malignancy were reviewed after March 2019.

In addition, we analyzed the population-based incidence of all parotid gland neoplasms in Southern Finland, that is, in our university hospital catchment area, covering a population of 1.6 million people. In our series, we had two patients outside the catchment area who had a malignant tumor. Further, during the study period 2 benign tumors had been operated in the private sector and were not included in our series due to the lack of detailed data. However, these two benign cases were included in the population-based incidence rates.

We used SPSS 22.0 (SPSS, Chicago, Illinois) to perform the statistical analysis. Student *t* test was used to establish statistical significance of differences between the two independent groups. A *P* value <.05 was considered statistically significant.

This was a single institution retrospective study, and an institutional study permission was granted (HUS/§63/66/2018).

3 | RESULTS

Altogether 195 patients met the inclusion criteria. The mean age for the cohort was 60.0 years (range, 15-94). Patients with a malignancy were significantly older than those with a benign tumor (*P* = .001; mean difference 11.4 years; 95% confidence interval, 4.6 to 18.2; Table 1). Of the 195 patients, 171 (88%) underwent surgery, and 24 patients with a cytologically confirmed neoplastic lesion were followed up only.

3.1 | Tumor distribution

According to the current WHO classification,⁴ 171 were classified as tumors of salivary gland origin (153 adenomas, 16 carcinomas, 1 lipoma, and 1 MALT lymphoma; Table 2). The rest 24 were other type of lesions, including for example, 15 lymphoepithelial cysts. Of the 171 “true” salivary gland tumors (by histopathological WHO classification) 154 (90%) were benign and 17 (10%) malignant (16 carcinomas, 1 MALT lymphoma). Of the whole series of 195 patients, 20 (10%) had a malignant tumor. Pleomorphic adenoma (PA) was the most common epithelial neoplasm (80/169; 47%) followed by Warthin tumor (60/169; 36%). One patient with PA had a recurrent PA (RPA): the previous tumor had been operated elsewhere 13 years earlier.

Of the 16 malignant parotid carcinomas, salivary duct carcinoma (SDC) was the most common histological type (*n* = 5; 31%), followed by acinic cell carcinoma (ACiC; *n* = 3; 19%). One patient with a histopathologically confirmed squamous cell carcinoma (SCC) underwent thorough preoperative examinations to exclude any other primary tumor.

Four other malignant tumors in addition to carcinomas included one MALT lymphoma, and two other lymphomas in patients who had no other lesions than the parotid mass. Furthermore, one patient underwent parotid surgery, and the histopathology revealed that the intraglandular tumor was most likely an extension or a metastasis from adjacent skin although no cutaneous lesion was observed.

3.2 | Clinical presentation

The initial clinical finding was a visible or palpable mass at the parotid site in 189 patients, and two presented with parapharyngeal swelling. However, 30 of these patients had an incidental finding on MRI, CT, or US which were performed for other medical reasons. The most common incidental finding was a Warthin tumor (*n* = 12).

TABLE 1 Patient characteristics

	Benign salivary gland neoplasms (n = 153)	Malignant salivary gland neoplasms (n = 16)	All other lesions (n = 26)	Total (n = 195)
Age				
Mean (y)	58.8 (SD 14.6)	71.9 (SD 13.8)	59.2 (SD 13.2)	60.0 (SD 14.7)
Range (y)	15-94	45-92	33-86	15-94
Sex				
Male (%)	70 (46)	9 (56)	13 (50)	92 (47)
Female (%)	83 (54)	7 (44)	13 (50)	103 (53)

TABLE 2 Tumor characteristics (n = 195)

Benign salivary gland neoplasms (n = 153)	Number	Percentage of all tumors	Percentage of the benign salivary gland neoplasms
Pleomorphic adenoma	80	41.0	52.3
Warthin tumor ^a	60	30.8	39.2
Basal cell adenoma	8	4.1	5.2
Oncocytoma	3	1.5	2.0
Myoepithelioma	2	1.0	1.3
Malignant salivary gland neoplasms (n = 16)	Number	Percentage of all tumors	Percentage of the malignant salivary gland neoplasms
Salivary duct ca	5	2.6	31.3
Acinic cell ca	3	1.5	18.8
Mucoepidermoid ca	2	1.0	12.5
Ca ex pleomorphic adenoma	1	0.5	6.3
Squamous cell ca	1	0.5	6.3
Epithelial-myoepithelial ca	1	0.5	6.3
Large cell ca	1	0.5	6.3
Lymphoepithelial ca	1	0.5	6.3
Polymorphous low-grade adeno ca	1	0.5	6.3
Benign soft tissue lesions (n = 1)	Number	Percentage of all tumors	
Lipoma	1	0.5	
Haematolymphoid tumors (n = 3)	Number	Percentage of all tumors	
MALT lymphoma	1	0.5	
Other lymphomas	2	1.0	
Other lesions (n = 22)	Number	Percentage of all tumors	
Lymphoepithelial cyst	15	7.7	
Degenerative changes; no diagnostic changes	2	1.0	
Neurofibroma	1	0.5	
Solitary fibrous tumor	1	0.5	
Oncocytic hyperplasia	1	0.5	
Granulomatous lesion	1	0.5	
Metastasis (squamous cell ca; skin) ^b	1	0.5	

Abbreviation: ca, carcinoma.

^aTwenty-four were confirmed by cytology only.

^bCutaneous origin was not known preoperatively; contact to the skin verified on histopathology.

Facial dysfunction was observed in five patients: the final histopathology was malignant in three cases, and one had had previous surgery (RPA). In one patient, the dysfunction was mild and reversible, and the tumor turned out to be a cyst.

Other clinical signs among patients with carcinoma included growth through or into the skin (n = 1), palpable lymph nodes (n = 3; all pN+), and suspicious lymph nodes on palpation (n = 2; both pN0).

TABLE 3 Comparison of cytology and histopathology (n = 165)

Cytology (class)	Histology	
	Benign	Malignant
0 (inadequate)	7	2
I-II	133	5
III	6	6
IV	0	1
V	0	5

Altogether, 22 patients reported pain. Of them 16 had a benign tumor (PA, n = 4; Warthin tumor, n = 9; cyst, n = 3) and six had a malignancy. No statistical difference between the groups was observed.

3.3 | US-guided FNAC

US was performed on 190 patients (97%), and all but five of them (ie, 97% of patients with a benign tumor and 95% of patients with a malignant tumor) received FNAC under US guidance. In 15 patients FNAC was repeated a second time due to an inadequate sample (class 0). Of the total patient cohort of 195 patients, needle biopsy with or without US was not performed for six patients: one patient had SDC and an ulcerating tumor through the skin, one had had open biopsy taken elsewhere from the parapharyngeal mass, and other four patients who had also a parapharyngeal tumor, and whose histopathology revealed PA, had undergone MRI only. FNAC was performed with palpation only for four patients. Table 3 presents the results of all the 165 patients whose cytological finding was confirmed by histology.

All six tumors from which FNAC revealed a highly suspicious (class IV) or an obvious malignant (class V) lesion were also malignant on final histopathology, yielding a specificity of 100%. FNAC revealed a slight suspicion of malignancy (class III) in 12 tumors, of which 50% (n = 6) turned out to be malignant, and 50% (n = 6) benign on histology. Of the 138 FNACs (class I-II) showing a benign finding 5 (4%) were malignant on histology (Table 4 [patients 1-5]). Of these five cases, clinical examination, US and MRI revealed signs of malignancy in one patient (patient no. 4 in Table 4) necessitating more radical surgical treatment, but in four other patients, malignancy was not suspected before histopathological examination.

Altogether 74 FNAC samples showed signs of PA, and 70 (95%) of them proved to be correct. FNAC showed signs of a Warthin tumor in 54 cases, of which 24 were followed up and the rest 30 were histologically all confirmed as Warthin tumors. Additionally, in one other sample the possibility of Warthin tumor was speculated. This case was false malignant (Table 4, patient 4). Preoperatively, FNAC was reported as a cyst in 20 tumors, of which five turned out to be neoplasms (Warthin tumor, n = 2; oncocytoma, n = 1; PA, n = 1, and low-grade mucoepidermoid carcinoma), and 15 were non-neoplastic cysts.

The re-evaluation of the cytological findings from carcinomas is presented in Table 4. Re-evaluation showed that of the five false benign cytologic findings three showed signs raising suspicion of malignancy (class 3).

3.4 | US, MRI, and CT

In imaging, all lymph nodes appeared as normal in benign conditions. Of the six patients with pN+, three had palpable lymphadenopathy, and US raised signs or suspicion of abnormal lymph nodes in four. MRI did not reveal any further abnormal lymph nodes. MRI was utilized altogether in 48 patients (for 38 patients with a benign tumor and for 10 patients with a malignancy on histopathology). This imaging modality offers some advantages over US due to its serial imaging sections and possibility for later interpretation. In those five patients, who did not have US and FNAC, MRI was the only imaging modality: all had PAs extending to the parapharyngeal space. Seven patients underwent CT: two with a PA and five with a malignant tumor in histopathology. In these cases, the reason for choosing CT over MRI was probably due to patient-related factors, for example, contraindication for MRI or inability to stay still for a longer period.

When compared with the FNAC, MRI was used in 7 (78%) of the class 0 cases, in 24 (17%) of the class I and II cases, in 5 (42%) of the class III cases, and in 4 (67%) of the class IV and V cases.

3.5 | Adenomas

The mean size of the adenomas that were operated was 23 mm (range, 6-70). One of the patients with a histologically confirmed RPA underwent radical parotidectomy with mastoidectomy. Rest of the patients were operated either with partial or superficial parotidectomy (n = 131), including the patients with parapharyngeal tumors, or extracapsular dissection (n = 24).

Altogether 24 patients who were diagnosed having a Warthin tumor by cytology did not undergo surgery but were followed up only. Twelve (50%) of these were incidental findings detected on imaging due to various other reasons. Because the patients had no symptoms and diagnosis was regarded reliable enough, surgery was omitted. Patients were advised to contact our department in case symptoms emerged in follow-up. Three years later one patient underwent surgery because the tumor had grown and caused pain. Additionally, two patients visited the outpatient clinic once, but surgery was not regarded necessary.

3.6 | Carcinomas of salivary gland origin

The mean diameter of the 16 salivary gland carcinomas was 26 mm (range, 10-60). Two patients underwent radical parotidectomy, six total parotidectomy, seven partial or superficial parotidectomy, and one extracapsular dissection. Eleven (11/16; 69%) of the patients

TABLE 4 Patients with malignant parotid gland tumors (n = 16) does the section "Clinical findings" show all content or is it just my settings??

Patient no.	Age/sex	Histology	PAPA (original), comment	PAPA (re-evaluated)	Milan classification (re-evaluated)	pTNM	Primary surgery, including neck levels	Postoperative RT (Gy)/CRT	Recurrence site and time (y) ^a	Status at last follow-up	Follow-up time (y) ^a	Clinical findings
1	69/Female	ACiC	2, Benign, adenoma?	3	Suspicious for malignancy	T2N0M0	Total parotidectomy, and ND I-IV later	66	Local, 1.4	DWD	2.7	Painless and mobile parotid gland mass
2	78/Male	MEC low grade	1, Cyst	1	AUS, mucoid cyst	T1N0M0	Extracapsular dissection			NED	1.1	Mildly painful and hard parotid gland mass
3	67/Female	MEC low grade	2, Benign	2	Neoplasm, SUMP, clear cells	T1N0M0	Partial parotidectomy			NED	1.8	Painless and mobile parotid gland mass
4	64/Female	PLGA	2, Benign	3	AUS, low cellularity suggestive of a neoplasm	T1N0M0	Total parotidectomy and radical ND II-III			NED	3.6	Painless, diffuse, and hard parotid gland mass
5	69/Female	Ca ex PA	2, Benign, adenoma?	3	Neoplasm, SUMP basoid cells	T1N0M0	Partial parotidectomy	60		DWND	2.8	Painless and mobile parotid gland mass
6	92/Female	ACiC	3, Suspicious for ca	3	Suspicious for malignancy	T1N0M0	Partial parotidectomy			NED	1.8	Painless and mobile parotid gland mass
7	64/Female	ACiC	0, Nondiagnostic scant	0	Nondiagnostic	T1N0M0	Partial parotidectomy and ND II		Local, 3.4	NED	3.4	Mildly painful and mobile parotid gland mass
8	89/Male	EMC	3, Suspicious for ca	3	Suspicious for malignancy	T2N0M0	Total parotidectomy and ND II			NED	1.3	Painless and mobile parotid gland mass
9	92/Male	SDC	5, Malignant	5	Malignant	T3N0M0	Total parotidectomy		Local, 0.4	DWD	0.5	Painless, fixed, and hard parotid gland mass
10	78/Female	SCC	3, Suspicious for ca	3	Suspicious for malignancy	T1N0M0	Partial parotidectomy and ND II			NED	4.0	Painless and mobile parotid gland mass
11	60/Male	SDC	3, Suspicious for ca	3	Suspicious for malignancy	T2N1M0	Total parotidectomy and II-III	66		NED	3.8	Painless and mobile parotid gland mass
12	50/Male	SDC	0, Nondiagnostic scant	0	Nondiagnostic	T4aN2aM1	Partial parotidectomy	50/Docetaxel		AWD	3.7	Painless and mobile parotid gland mass

TABLE 4 (Continued)

Patient no.	Age/sex	Histology	PAPA (original), comment	PAPA (re-evaluated)	Milan classification (re-evaluated)	pTNM	Primary surgery, including neck levels	Postoperative RT (Gy)/CRT	Recurrence site and time (y) ^a	Status at last follow-up time (y) ^a	Follow-up time (y) ^a	Clinical findings
13	45/Male	SDC	5, Malignant	5	Malignant	T3N2bM0	Total parotidectomy and radical ND I-V	66/Docetaxel	Lung, 0.6	NED	3.4	Painless, fixed, and hard parotid gland mass with abnormal lymph nodes
14	82/Male	SDC	3, Slightly suspicious	3	Suspicious for malignancy	T4aN2bM0	Radical parotidectomy and radical ND II-V	21		DWND	0.8	Painless, fixed, and hard parotid gland mass with abnormal lymph nodes and facial nerve dysfunction
15	79/Male	LCC	4, Suspicious for ca	4	Suspicious for malignancy	T1N2bM0	Partial parotidectomy and ND II-V	70		NED	3.0	Painless and mobile parotid gland mass
16	72/Male	LEC	5, Malignant	5	Malignant	T4aN2bM0	Radical parotidectomy, mastoidectomy and radical ND I-V		Spinal, 0.6	DWD	0.6	Painless, diffusely and hard parotid gland mass with abnormal lymph nodes and facial nerve dysfunction

Abbreviations: ACiC, acinic cell carcinoma; AUS, atypia of undetermined significance; AWD, alive with disease; Ca ex PA, carcinoma ex pleomorphic adenoma; CRT, chemoradiotherapy; DOD, dead of disease; DWD, dead with disease; DWND, dead with no evidence of disease; Gy, Gray; EMC, epithelial-myoepithelial carcinoma; LCC, large cell carcinoma; MEC, mucoepidermoid carcinoma; ND, neck dissection; NED, no evidence of disease; PAPA, Papanicolaou class; PLGA, polymorphous low-grade adeno carcinoma; pTNM, pathologic TNM; RT, radiotherapy; SCC, squamous cell carcinoma; SDC, salivary duct carcinoma; SUMP, salivary gland neoplasm of uncertain malignant potential.

^aTime from the end of primary treatment.

underwent some degree of ND: level II (n = 3), levels II to III (n = 2), levels II to V (n = 2), levels I to IV (n = 1), and levels I to V (n = 3).

The pathological T classifications were as follows: T1, n = 8 (50%); T2, n = 3 (19%); T3, n = 2 (13%); and T4, n = 3 (19%). Histological examination revealed metastatic lymph nodes (pN+) in six patients. Ten (63% of salivary gland carcinomas) patients had no metastatic lymph nodes, either in their ND specimen (n = 5) or clinically (n = 5; no ND, including follow-up).

After the final histopathological diagnosis, the multidisciplinary tumor board concluded that one patient required additional surgery on the neck without delay due to the type of histology (high-grade ACiC). However, the ND specimen from the second surgery did not reveal any metastatic lymph nodes. Distant metastasis was detected immediately after diagnosis in one patient with SDC.

Postoperative radiotherapy (RT) was given to five patients and chemoradiotherapy (CRT) to two patients with a malignant tumor. The follow-up of the 16 patients with carcinomas is presented in Table 4. During follow-up two patients developed distant metastases.

3.7 | Other lesions

Twenty-two other lesions included 15 non-neoplastic cysts with a mean diameter of 21 mm (range, 7-40). Preoperative imaging (US, n = 15; MRI, n = 4) had raised suspicion of a neoplasm in two of the cysts.

3.8 | Population-based incidences

The population-based analysis showed that within the catchment area there were 171 tumors classified as salivary gland origin (by WHO classification), including 156 benign and 14 malignant neoplasms, yielding an annual incidence of 9.8/100000 inhabitants for benign neoplasms and 0.88/100000 inhabitants for malignant neoplasms.

4 | DISCUSSION

This study covers all parotid gland tumors diagnosed within a population area of 1.6 million people in Southern Finland during a 1-year period. Malignant parotid gland tumors represented 10% of all neoplasms, which is in line with the study published by Bradley et al in 2013¹² but significantly less than in some other recent studies reporting 14% to 32%.¹³⁻¹⁷ Due to the national health care system with centralized treatment we were able to gather a patient series that represents the true distribution of benign and malignant tumors within our geographic area. We report an annual incidence of 0.88/100 000 inhabitants for malignant parotid neoplasms, which follows the estimation presented previously from the UK.¹² PAs typically cover two thirds of the benign tumors of the salivary glands,¹¹ but only 47% of the benign epithelial tumors in the present study. In addition, 36% were Warthin tumors, which is significantly more than in other series (8%-15%),^{15,17} but reflects figures presented by Perkins

et al.¹⁸ Most malignant tumors in our study were SDCs (31%), a significantly differing finding from other studies where other tumor types predominate.^{13,14,16,19} We encountered no adenoid cystic carcinomas (ACC), but noteworthy, the overall number of malignancies remained low. In our previous study of submandibular gland neoplasms, ACC was the most common type of malignancy.²⁰

US was performed on most patients (97%), and only for five without a simultaneous FNAC. In the present study, the rate of false benign and malignant finding reported from FNAC are well in line with the current literature,^{15,17,21,22} and we had no false malignant findings (class IV and V). Although a repeated FNAC sample was obtained in 15 (8%) patients, the FNAC remained inadequate (class 0) in 5% of the patients, which compares well with other series with figures ranging between 6% and 7%.^{13,15,17} The proportion of inconclusive or inadequate cytological samples and lack of accuracy of grading for malignant tumors remains a challenge in management planning.

Recently, a new cytological classification for salivary gland tumors has been launched.²³ The Milan classification includes six different diagnostic categories, which incorporate cytopathology, risk of malignancy, and treatment recommendations. For this study, we re-analyzed cytological samples from the 16 malignant neoplasms although their malignant nature was evident at that time. Nevertheless, the key issue still remains: is the lesion non-neoplastic, a benign adenoma or malignant.

Certain cytological findings, such as those showing PA, are considered highly reliable with a correct diagnosis in 91% to 94% of cases.^{14,20,24} Somewhat less reliable figures have also been presented: We found previously that 10% of submandibular gland tumors with a benign cytology turned out malignant,²⁰ and Suzuki et al¹⁴ showed this risk to be even 14% in parotid tumors. Thus, a risk for malignancy remains: in our series, one such tumor turned out to be carcinoma ex PA.

In the present series, 5 (4%) patients who had a false benign FNAC from their malignant tumor warrant special attention. In four of them, malignancy was diagnosed unexpectedly. Re-evaluation of the cytology of these five cases showed no signs of malignancy in two and error in interpretation in three. Class III will require special caution as in 50% (n = 6/12) of these cases the tumors turned out to be malignant. It is common for the radiologists who take the FNAC under US guidance to use a 22-gauge needle. Recent data have shown the superiority of US-guided core-needle biopsy (CNB) compared with FNAC especially in increasing the sensitivity to 95% in detecting a malignancy.²⁵ This practice might enable more specific histological tumor typing preoperatively,²⁶ and even molecular testing.^{27,28} These reports indicate that using a larger needle would minimize the number of inadequate samples and increase the quality of the method. Further, as salivary gland malignancies are rare and include various histological types, we recommend centralization of sample evaluation or very low threshold level for consultations among pathologists. Especially when omitting surgery, for example, in elderly patients or in patients who are in high risk for surgery, this practice to avoid false FNAC findings would be of utmost importance. Frozen section analysis was not employed in our series, and based on the previous results, CNB might replace this practice in selected cases.

The incidence of Warthin tumors has increased steadily over the years.^{29,30} The imaging modalities have improved, and more patients are susceptible to have imaging for various reasons, leading to incidental findings also in the parotid gland. In our cohort, 40% of patients (n = 24) diagnosed with a Warthin tumor were omitted surgery because they experienced no symptoms and diagnosis was regarded reliable enough for this policy. In one patient, the cytological diagnosis had remained speculative and was eventually malignant in histopathology. This raises a question of appropriate indications to choose follow-up only. In practice, patients are well counseled to acknowledge the risks related to parotid gland surgery,³¹ and when all cytological criteria for Warthin tumor are fulfilled, the diagnosis is nearly 100%.^{14,32,33}

We had 15 patients with a final histopathology showing a cyst. This raises a question whether surgery was even beneficial for them. A cytological finding of a cyst is a risk for false diagnosis and thus surgery is indicated if a neoplasm is suspected. A study by Suzuki et al¹⁴ reported that 16% of nondiagnostic FNACs turned out as cysts and Eytan et al¹⁷ showed that 21% of all false positive FNACs were cysts in histopathology. In our series, two lesions with a FNAC indicative of a cyst turned out as malignant.

In our cohort, MRI was utilized in 25% of cases, and either MRI or CT was used in 75% of tumors that turned out malignant. MRI is superior to CT, especially in defining perineural spread,^{34,35} and we prefer MRI at our institution for parotid tumors. MRI has a positive predictive value of 96% for PA,³⁶ and we had five patients with a suspicion of PA in MRI who underwent surgery without any additional preoperative information. The benefit of offering MRI for all patients remains uncertain, although apparently some centers prefer this. We recommend preoperative MRI for all patients having class III, IV or V on FNAC, as it could also help to guide treatment more effectively and also lymph node status can be assessed and documented with higher certainty. Efforts to minimize the occurrence of inadequate/inconclusive FNAC are required but additional imaging might also prove of value in these cases. Perkins et al stated that combining preoperative imaging significantly improves the results of FNAC.¹⁸ We feel that when a lesion is regarded as benign and if omission of surgery is planned, further imaging (MRI) and/or follow-up seem advisable and informing the patient to contact the department in case of new symptoms.

In benign parotid tumors, the extent of surgery should follow recommendations based on the size and location of the tumor.³⁷ Treatment protocol for the neck in malignant cases remains unclear especially in cases with a clinically negative neck (cN0), and the variety of histological tumor types will cause further confusion. Due to the uncertainty of the exact histology and grade of the tumor preoperatively or perioperatively, some suggest elective ND for all salivary gland cancer patients.³⁸ We suggest ND for all those who have a cytology class of IV or V, or clinical signs of malignancy, although in some cases, for example, with ACC,³⁹ the need still remains contradictory. The positive predictive value of malignant cytology is high, as shown also in the present series. The extent of ND should be tailored based on the findings on imaging and the likelihood of tumor grade on cytology. Due to the variety of salivary tumors and various postoperative treatment options, a detailed guideline for managing these neoplasms will be beyond the scope of this study.

Each metastatic lymph node on the neck up to four confers a 34% increased risk of salivary gland cancer mortality.⁴⁰ Still, the current tumor staging systems do not account for the absolute number of metastatic lymph nodes in salivary gland cancer, which might influence adjuvant treatment recommendations. Adjuvant RT is commonly recommended in high-grade malignancies, and postoperative RT/CRT was given in this series for 7 (44%) patients who had metastatic disease and/or a high-grade tumor. Although the addition of chemotherapy shows no clear survival benefit, adjuvant RT improves survival if negative prognostic factors exist.⁴¹

We find that US and FNAC should serve in the primary examination of parotid gland masses. If FNAC shows class III finding or malignancy, or remains repeatedly inadequate, we recommend MRI. Additional imaging is also advisable if the patient presents symptoms or signs suggestive of a malignancy (eg, tumor with irregular borders, enlarged lymph nodes, nerve deficits, or pain). In selective cases with cytologically confirmed Warthin tumor, omitting surgery is a reasonable option. These guidelines necessitate co-operation with the radiologist and pathologist, all of whom are expected to pose experience in diagnosing salivary gland tumors. The rarity of all salivary gland tumors warrants centralized management. We find that one of the key issues to improve preoperative diagnostics is to refine cytology by using large needles, pay attention to proper sampling technique, preferably to obtain fragments for histological evaluation. Centralized evaluation of the samples is also mandatory.

5 | CONCLUSION

The proportion of malignant parotid gland tumors was lower in our material than in many other series. Our study supports the conception that US combined with FNAC is a sufficient diagnostic method for most parotid gland tumors. Whenever there is even the slightest suspicion of malignancy in US or FNAC, further imaging (MRI) with the assessment of adjacent lymph nodes is mandatory. All efforts to eliminate inadequate and inconclusive FNACs are imperative to better target treatment in the primary setting or when omitting surgery as the therapeutic approach.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

ORCID

Katri Aro  <https://orcid.org/0000-0001-8103-5237>

Jarkko Korpi  <https://orcid.org/0000-0002-5057-2379>

Jussi Tarkkanen  <https://orcid.org/0000-0002-5807-1085>

Antti Mäkitie  <https://orcid.org/0000-0002-0451-2404>

Timo Atula  <https://orcid.org/0000-0002-6560-1128>

BIBLIOGRAPHY

1. Eveson JW, Cawson RA. Salivary gland tumours. A review of 2410 cases with particular reference to histological types, site, age and sex distribution. *J Pathol.* 1985;146:51-58.

2. Spiro RH. Salivary neoplasms: overview of a 35-year experience with 2,807 patients. *Head Neck Surg.* 1986;8:177-184.
3. Del Signore AG, Megwalu UC. The rising incidence of major salivary gland cancer in the United States. *Ear Nose Throat J.* 2017;96:E13-E16.
4. El-Naggar AK, Chan JKC, Gramdis JR, Takata T, Slootweg PJ, eds. World Health Organization classification of tumours. *Tumours of the Salivary Glands.* Lyon: IARC Press; 2017.
5. Cheng PC, Chang CM, Huang CC, et al. The diagnostic performance of ultrasonography and computerized tomography in differentiating superficial from deep lobe parotid tumours. *Clin Otolaryngol.* 2019;44:286-292.
6. Kato H, Kanematsu M, Watanabe H, Mizuta K, Aoki M. Salivary gland tumors of the parotid gland: CT and MR imaging findings with emphasis on intratumoral cystic components. *Neuroradiology.* 2014;56:789-795.
7. Mocnik D, Ibragimov B, Xing L, et al. Segmentation of parotid glands from registered CT and MR images. *Phys Med.* 2018;52:33-41.
8. Mantravadi AV, Moore MG, Rassekh CH. AHNS series: do you know your guidelines? Diagnosis and management of salivary gland tumors. *Head Neck.* 2019;41:269-280.
9. Foresta E, Torroni A, Di Nardo F, et al. Pleomorphic adenoma and benign parotid tumors: extracapsular dissection vs superficial parotidectomy—review of literature and meta-analysis. *Oral Surg Oral Med Oral Pathol Oral Radiol.* 2014;117:663-676.
10. Olsen KD, Quer M, de Bree R, Vander Poorten V, Rinaldo A, Ferlito A. Deep lobe parotidectomy—why, when, and how? *Eur Arch Otorhinolaryngol.* 2017;274:4073-4078.
11. Barnes L, Eveson JW, Reichart P, Sidransky D, eds. World Health Organization classification of tumours. *Tumours of the Salivary Glands.* Lyon: IARC Press; 2005.
12. Bradley PJ, McGurk M. Incidence of salivary gland neoplasms in a defined UK population. *Br J Oral Maxillofac Surg.* 2013;51:399-403.
13. Grasl S, Kadletz L, Janik S, et al. Fine-needle aspiration cytology and intraoperative frozen section in parotid gland tumour surgery: a retrospective multicenter analysis of 417 cases. *Clin Otolaryngol.* 2019;44:461-465.
14. Suzuki M, Kawata R, Higashino M, et al. Values of fine-needle aspiration cytology of parotid gland tumors: a review of 996 cases at a single institution. *Head Neck.* 2019;41:358-365.
15. Feinstein AJ, Alonso J, Yang SE, St John M. Diagnostic accuracy of fine-needle aspiration for parotid and submandibular gland lesions. *Otolaryngol Head Neck Surg.* 2016;155:431-436.
16. da Silva LP, Serpa MS, Viveiros SK, et al. Salivary gland tumors in a Brazilian population: a 20-year retrospective and multicentric study of 2292 cases. *J Craniomaxillofac Surg.* 2018;46:2227-2233.
17. Eytan DF, Yin LX, Maleki Z, et al. Utility of preoperative fine needle aspiration in parotid lesions. *Laryngoscope.* 2018;128:398-402.
18. Perkins C, Toll E, Reece P. Fine-needle aspiration cytology and radiological imaging in parotid gland tumours: our experience in 103 patients. *Clin Otolaryngol.* 2019;44:1124-1127.
19. Luukka H, Klemi P, Leivo I, et al. Salivary gland cancer in Finland 1991-96: an evaluation of 237 cases. *Acta Otolaryngol.* 2005;125:207-214.
20. Atula T, Panigrahi J, Tarkkanen J, Mäkitie A, Aro K. Preoperative evaluation and surgical planning of submandibular gland tumors. *Head Neck.* 2017;39:1071-1077.
21. Schmidt RL, Hall BJ, Wilson AR, Layfield LJ. A systematic review and meta-analysis of the diagnostic accuracy of fine-needle aspiration cytology for parotid gland lesions. *Am J Clin Pathol.* 2011;136:45-59.
22. Liu CC, Jethwa AR, Khariwala SS, Johnson J, Shin JJ. Sensitivity, specificity, and posttest probability of parotid fine-needle aspiration: a systematic review and meta-analysis. *Otolaryngol Head Neck Surg.* 2016;154:9-23.
23. Faquin W, Rossi E, Baloch Z, et al., eds. *The Milan System for Reporting Salivary Gland Cytopathology.* New York, NY: Springer; 2018:1-182.
24. Aro K, Tarkkanen J, Saat R, Saarihahti K, Mäkitie A, Atula T. Submandibular gland cancer: specific features and treatment considerations. *Head Neck.* 2018;40:154-162.
25. Zbaren P, Triantafyllou A, Devaney KO, et al. Preoperative diagnostic of parotid gland neoplasms: fine-needle aspiration cytology or core needle biopsy? *Eur Arch Otorhinolaryngol.* 2018;275:2609-2613.
26. Novoa E, Gurtler N, Arnoux A, Kraft M. Role of ultrasound-guided core-needle biopsy in the assessment of head and neck lesions: a meta-analysis and systematic review of the literature. *Head Neck.* 2012;34:1497-1503.
27. Skalova A, Stenman G, Simpson RHW, et al. The role of molecular testing in the differential diagnosis of salivary gland carcinomas. *Am J Surg Pathol.* 2018;42:e11-e27.
28. Evrard SM, Meilleroux J, Daniel G, et al. Use of fluorescent in-situ hybridisation in salivary gland cytology: a powerful diagnostic tool. *Cytopathology.* 2017;28:312-320.
29. Franzen AM, Kaup Franzen C, Guenzel T, Lieder A. Increased incidence of Warthin tumours of the parotid gland: a 42-year evaluation. *Eur Arch Otorhinolaryngol.* 2018;275:2593-2598.
30. Kadletz L, Grasl S, Perisanidis C, Grasl MC, Erovic BM. Rising incidences of Warthin's tumors may be linked to obesity: a single-institutional experience. *Eur Arch Otorhinolaryngol.* 2019;276:1191-1196.
31. Ruohoalho J, Mäkitie AA, Aro K, et al. Complications after surgery for benign parotid gland neoplasms: a prospective cohort study. *Head Neck.* 2017;39:170-176.
32. Shkedy Y, Alkan U, Mizrahi A, et al. Fine-needle aspiration cytology for parotid lesions, can we avoid surgery? *Clin Otolaryngol.* 2018;43:632-637.
33. Sood N, Borah P. Warthin's tumor: Cyto histological spectrum with emphasis on diagnostic difficulties. *Diagn Cytopathol.* 2018;46:613-619.
34. Christe A, Waldherr C, Hallett R, Zbaeren P, Thoeny H. MR imaging of parotid tumors: typical lesion characteristics in MR imaging improve discrimination between benign and malignant disease. *AJNR Am J Neuroradiol.* 2011;32:1202-1207.
35. Antoniou AJ, Marcus C, Subramaniam RM. Value of imaging in head and neck tumors. *Surg Oncol Clin N Am.* 2014;23:685-707.
36. Heaton CM, Chazen JL, van Zante A, Glastonbury CM, Kezirian EJ, Eisele DW. Pleomorphic adenoma of the major salivary glands: diagnostic utility of FNAB and MRI. *Laryngoscope.* 2013;123:3056-3060.
37. Quer M, Vander Poorten V, Takes RP, et al. Surgical options in benign parotid tumors: a proposal for classification. *Eur Arch Otorhinolaryngol.* 2017;274:3825-3836.
38. Nobis CP, Rohleder NH, Wolff KD, Wagenpfeil S, Scherer EQ, Kesting MR. Head and neck salivary gland carcinomas—elective neck dissection, yes or no? *J Oral Maxillofac Surg.* 2014;72:205-210.
39. Luksic I, Suton P. Elective neck dissection in adenoid cystic carcinoma of head and neck: yes or no? A systematic review. *Eur Arch Otorhinolaryngol.* 2019;276:2957-2962.
40. Aro K, Ho AS, Luu M, et al. Development of a novel salivary gland cancer lymph node staging system. *Cancer.* 2018;124:3171-3180.
41. Aro K, Ho AS, Luu M, et al. Survival impact of adjuvant therapy in salivary gland cancers following resection and neck dissection. *Otolaryngol Head Neck Surg.* 2019;160:1048-1057.

How to cite this article: Aro K, Korpi J, Tarkkanen J, Mäkitie A, Atula T. Preoperative evaluation and treatment consideration of parotid gland tumors. *Laryngoscope Investigative Otolaryngology.* 2020;5:694-702. <https://doi.org/10.1002/lio2.433>