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Original research article

Patterns of treatment failure in salivary gland cancers



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ABSTRACT

Aim: The purpose of the study was to publish our experience of salivary gland cancer treatment with large number of patients treated at a single institution.

Background: Salivary gland cancers are rare tumors of the head and neck representing about 5% of cancers in that region and about 0.5% of all malignancies. Due to the rarity of the disease, most of the studies regarding treatment outcome consist of low number of patients, thus making it difficult to draw conclusions.

Material and methods: 115 patients with primary salivary gland cancer were included in a retrospective study. The subsites of tumor were the parotid gland (58% patients), submandibular gland (19%) and minor salivary glands (23%). All patients underwent primary surgical resection. The following were collected: age, stage of the disease, T status, N status, grade of tumor, perineurial invasion, lymphovascular invasion, extracapsular spread, final histological margin status and postoperative treatment. Details of local, regional or distant recurrence, disease free survival and overall survival were included.

Results: The majority (65%) of patients presented in early stage, T1 and T2 tumors. 81% of patients were N0. Free surgical margins were achieved in 18% of patients, close in 28% patients and positive surgical margins in 54% (62) patients. Factors that significantly increased the risk of recurrence: T stage ($p=0.0006$); N-positive status ($p<0.0001$); advanced stage of the disease ($p<0.0001$); high grade of tumor ($p=0.0007$); PNI ($p=0.0061$); LVI ($p=0.0022$); ECS ($p=0.0136$); positive surgical margins ($p=0.0022$). On multivariate analysis, high grade of tumor and positive surgical margins remained significant independent adverse factors for recurrence formation.

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Conclusions: This report shows a single institution results of oncological treatment in patients with malignant salivary gland tumors, where positive surgical margins strongly correlate with patients' worse outcome. Whether to extend the procedure, which very often requires sacrificing the nerve is still a question of debate.

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1. Background

Salivary gland cancers are rare tumors of the head and neck representing about 5% of cancers in that region and about 0.5% of all malignancies.¹ The WHO recognizes over 20 subtypes of the disease which can affect nearly any region of the head and neck, including major salivary gland, minor salivary glands within the oral cavity, oropharynx, sinonasal region and larynx.² Due to the histologic complexity, salivary gland tumors require a comprehensive treatment plan, nevertheless surgical treatment has become the treatment of choice for resectable disease.³ Adjuvant radiotherapy (RT) applies to patients with adverse treatment factors, including advanced stage of the disease, nodal disease, close resection margin, perineural invasion (PNI) or lymphovascular invasion (LVI). Chemoradiation can be considered when clear margins are not achieved and extracapsular spread (ECS) is detected in the lymph nodes.⁴ Due to the rarity of the disease, most of the studies regarding treatment outcome consist of low number of patients, thus making it difficult to draw conclusions. What is more, treatment recommendations for various histological grades and stages are controversial due to the discordance in literature.⁵

2. Aim

The purpose of the study was to compare our experience of salivary gland cancer treatment with large number of patients treated at a single institution with available published data and to highlight factors that significantly affected the outcome in our group of patients.

3. Material and methods

3.1. Patients

One hundred and fifteen patients with primary salivary gland cancer were included in a retrospective study, of which 71 (62%) were males and 54 (38%) were females. The mean age at time of presentation was 63.7 years (25–94 ± 15.8). The sub-sites of tumor were the parotid gland (67 patients – 58%), submandibular gland (22 patients – 19%) and minor salivary glands (26 patients – 23%). In terms of histology, the most common tumor subtype was adenoid cystic carcinoma (33 pts; 28.6%) followed by mucoepidermoid carcinoma (19 pts; 16.5%). All patients underwent primary surgical resection. The mean follow up was 25 months (range 3–110 ± 18.5 months).

For each patient, the following clinical parameters were collected: age at presentation, stage of the disease, T status,

Table 1 – Patient's demographics.

Variable		Number (%)
Sex	Male	71 (62)
	Female	54 (38)
Median age	63.7	
Site of primary tumor	Parotid	67 (59)
	Submandibular	22 (19)
	Oral cavity	12 (10)
	Oropharynx	5 (4)
	Sinonasal region	9 (8)
Histologic type	Adenoid cystic carcinoma	33 (28.6)
	Mucoepidermoid carcinoma	19 (16.5)
	Carcinoma ductale	14 (12.1)
	Acinic cell carcinoma	12 (10.4)
	Adenocarcinoma	12 (10.4)
	Carcinoma ex pleomorphic adenoma	10 (8.7)
	Carcinoma myoepithelial	7 (6.1)
	Other	8 (6.9)

N status, grade (G) of tumor, perineural invasion (PNI), lymphovascular invasion (LVI), extracapsular spread (ECS), final histological margin status and postoperative treatment. Details of local, regional or distant recurrence, as well as disease free survival (DFS) and overall survival (OS) were also included in analysis (Table 1).

3.2. Treatment

All patients were reviewed by the institutional multidisciplinary team (MDT), and were qualified for primary surgical treatment. When indicated, patients were qualified for adjuvant treatment. The standard radiotherapy protocol was 60–66 Gy (2.0 Gy/fraction) daily, Monday–Friday, over 6–7 weeks. Factors that qualified the patient for adjuvant radiotherapy were: pT3/4 tumor, close surgical margins (1–5 mm), positive nodes, and evidence of perineural/vascular invasion. The chemotherapy protocol comprised concurrent single-agent cisplatin at 100 mg/m² every 3 weeks or 40 mg/m² every week, alternatively; indications were positive surgical margins or extra capsular spread. Potential side effects and benefit were explained to each patient prior to adjuvant chemotherapy. Of 62 patients with indications for concomitant chemotherapy 54 refused such treatment and decided to proceed with adjuvant radiotherapy only. Written informed consent has been obtained from each patient.

Study approval was obtained from the Research Ethics Board at Poznan University of Medical Sciences.

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