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## Prognostic factors in patients with salivary gland malignancy: a retrospective cohort study

Moghira Iqbaluddin Siddiqui<sup>1</sup>, Haissan Iftikhar<sup>2</sup>, Umar Farooq Bhatti<sup>3</sup>, Mubasher Ikram<sup>4</sup>

### Abstract

Our objective was to determine the factors affecting the prognosis in patients with major salivary gland malignancy presenting to Aga Khan University Hospital in Karachi. Retrospective cohort study was carried out at our center on patients diagnosed and treated for salivary gland cancers. Presentation and treatment offered was reviewed from medical charts. Telephonic interviews were conducted to assess the survival of patients who were lost to follow-up. Log rank test was used to compare the mean survival times. A total of 36 patients were included in the study. The mean age was 45.1 +/- 14.6 years. Majority were male 21 (58.3%). The most common malignancy was mucoepidermoid carcinoma (36.1%) followed by adenoid cystic carcinoma (22.2%). Node positivity, grade of tumor, radiotherapy and chemotherapy were a significant indication of survival times on log rank test.

**Keywords:** Salivary gland malignancy, survival time, prognostic factors.

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### Introduction

Salivary gland malignancies are a heterogeneous group of tumours that have varying biological behaviours. These tumours comprise 3-10% of all head and neck malignancies.<sup>1</sup> The global annual incidence varies between 0.05 – 2/100,000.<sup>1</sup> The incidence of major salivary gland malignancies increases with age; the overall incidence is rare for below 40 years of age.<sup>1</sup> Males are more often affected than females.<sup>1</sup> Malignancy of salivary gland is uncommon and therefore there are few prospective studies on the subject.<sup>2</sup> Exact cause of Salivary gland neoplasms is unknown.<sup>3</sup> Low intake of cholesterol has shown to have a protective role.<sup>4</sup> Intake of dark yellow vegetables and liver also showed to reduce risk of salivary gland neoplasms.<sup>5</sup>

There is a knowledge gap regarding the behaviour and survival of patients suffering from salivary gland malignancy in our population. Studies have shown difference in survival with grade of tumour<sup>6</sup> and type of tumour.<sup>7,8</sup> Advanced radiation therapy techniques like IMRT have shown survival benefits.<sup>9,10</sup> We hypothesized

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that the prognostic factors differ in our cohort of patients than those reported in the West.

### Material Methods and Results

A retrospective cohort study was conducted at Aga Khan University Hospital Karachi Pakistan. Prior to the commencement of our survey, approval was obtained from the institutional ethical review committee. All the patients who were treated for a salivary gland malignancy from January 1, 2005 to December 31, 2015 were reviewed for the study. The data was obtained from a prospectively maintained database. The data were collected by a qualified and trained data collector. Patient demographics, tumour and treatment related variables were obtained from medical charts using a proforma. Information on the overall survival was obtained by telephonic interview of the patients who were lost to follow up. Patients that had a salivary gland malignancy on final histopathology and who were over the age of 18 years were included for the analysis. Those with benign lesions; those who received prior treatment before presentation at our institute, and those with distant metastasis at the time of arrival were excluded. Patients with incomplete records, and those who did not complete their treatment were also excluded from the study.

The data was analyzed using STATA version 12. Continuous variables are reported with mean ± standard deviation and categorical variables are reported with frequencies and percentages. Survival analysis was done using cox proportional hazard ratio and Kaplan Meier curves drawn to graphically illustrate the survival proportion. Schoenfeld's global test was used to assess if the data fulfilled the assumption of proportionality. A total of 36 patients matched the eligibility criteria. The mean age of the patients was 45.08 ± 14.57 years and the majority were male 21 (58.3%). The most common site of malignancy was the parotid gland 31 (58.3%). The fine needle aspiration cytology revealed malignancy in 12 cases (33.3%). Final histopathology reported mucoepidermoid carcinoma in 13 cases (36.1%) followed by adenoid cystic carcinoma in 8 cases (22.2%); 5 cases of Acinic cell carcinoma (13.9%), 3 of squamous cell carcinoma (8.3%) and a small proportion of other malignancies were also reported. Table-1.

Majority of the cases 19 (52.8%) were reported as high

Table-1: Patient demographics, tumour and treatment variables with respect to survival status.

Variable		Outcome status	
		Alive	Event (Dead)
		Mean ± SD (Continuous)	
		Frequencies n (%) (Categorical)	
Age		45.1 ± 14.6	
Gender	Male	16 (76.19)	5 (23.81)
	Female	12 (80)	3 (20)
Site	Parotid gland	25 (80.65)	6 (19.35)
	Submandibular gland	3 (60)	2 (40)
FNAC	Positive	9 (75)	3 (25)
	Negative	19 (71.17)	5 (20.83)
Final histopathology	Mucoepidermoid	10 (76.92)	3 (23.08)
	Adenoid cystic	6 (75)	2 (25)
	Acinic cell	5 (100)	0
	Squamous cell carcinoma	1 (33.33)	2 (66.67)
	Lymphoepithelial carcinoma	1 (100)	0
	Salivary duct carcinoma		
	Adenocarcinoma	0	1 (100)
	Carcinoma ex pleomorphic	1 (100)	0
	Poorly differentiated ca	2 (100)	0
	Tumor Grade	Low/Intermediate	17 (100)
	High	11 (57.89)	8 (42.11)
Neck dissection	Yes	13 (61.90)	8 (38.10)
	No	15 (100)	0
Node positivity	Yes	5 (41.67)	7 (58.33)
	No	23 (95.83)	1 (4.17)
Surgery	Parotidectomy	11 (100)	0
	Parotidectomy + Neck Dissection	13 (68.42)	6 (31.58)
	Submandibular gland excision	3 (100)	0
	Submandibular gland excision + Neck dissection	1 (33.33)	2 (66.67)
Radiotherapy	Yes	14 (66.67)	7 (33.33)
	No	14 (93.33)	1 (6.67)
Chemotherapy	Yes	1 (33.33)	2 (66.67)
	No	27 (81.82)	6 (18.18)

grade on final histopathology while 12 cases as low or intermediate grade (47.2%). Neck dissection was carried out on 21 cases (58.3%) due to clinical or radiological suspicion of malignancy, 12 cases (57.1%) had at least one positive lymph node on final histopathology. We had 31 cases of parotid gland and 5 cases of submandibular gland malignancy. Among those with parotid gland involvement, 19 cases (52.8%) underwent parotidectomy along with neck dissection and 11 cases (30.7%) only underwent parotidectomy. Majority of the patients 21 (58.3%) received adjuvant radiotherapy whereas only 3 cases received chemoradiotherapy.

The mean survival time of the patients are presented in

Table-2: Mean survival time (months) and log rank test.

Variable	Category	Mean survival time (Months)	Log rank test (p-value)
Gender	Male	209.59	0.36
	Female	122.79	
Site	Parotid gland	157.28	0.35
	Submandibular gland	55.4	
FNAC	Positive	105.56	0.21
	Negative	155.76	
Node positivity	Yes	54.52	0.001
	No	100.13*	
Radiotherapy	Yes	66.31*	0.06
	No	97.73*	
Chemotherapy	Yes	43.5	0.03
	No	83.76*	

\*Restricted Mean (last observation censored)

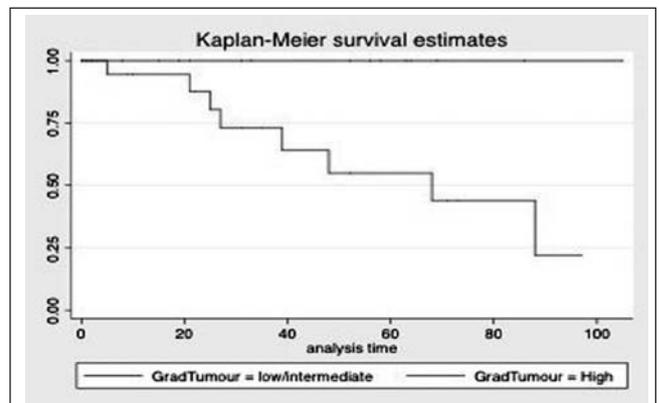


Figure-1: Kaplan Meier curves showing the mean survival time (months) of patients stratified on grade of tumor.

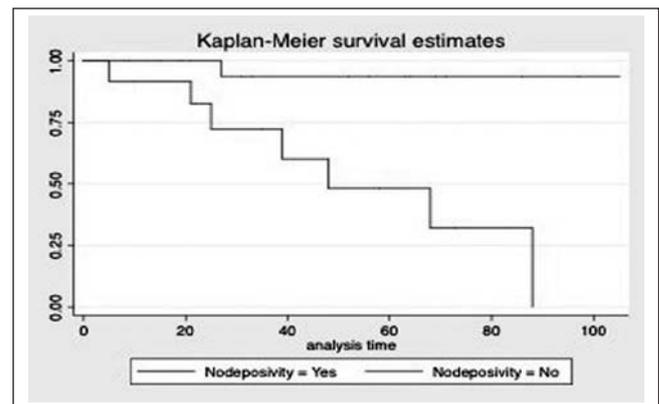


Figure-2: Kaplan Meier curves showing the mean survival time of patients in months stratified on node positivity.

Table 2. Log rank test was used to test the significance of survival time in stratifying the variables. The significant prognostic factors were Node positivity (p=0.001), radiotherapy (p=0.06) and chemotherapy (p=0.03).

Due to sparse data, further analysis (univariate and multivariable analysis) was not done.

Kaplan Meier curves graphically show the mean survival time of patients stratified by grade of tumour and node positivity. (Figure 1,2)

### Conclusion

Grade of the tumour, positive lymph node status and adjuvant therapy are the prognostic factors that significantly alter the survival time in our cohort of patients with salivary gland cancer. Patients with high grade tumour and positive neck nodes require aggressive adjuvant treatment and close follow-ups.

**Disclaimer:** None to declare.

**Conflict of Interest:** None to declare.

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