

# A 20-Year Retrospective Study of Salivary Gland Adenoid Cystic Carcinoma in a Sample of Iranian Patients

M. Khalili<sup>1,2</sup>✉, F. Salamat<sup>2</sup>

<sup>1</sup>Assistant Professor, Dental Research Center, School of Dentistry, Tehran University of Medical Sciences, Tehran, Iran

<sup>2</sup>Assistant Professor, Department of Oral and Maxillofacial Pathology, School of Dentistry, Tehran University of Medical Sciences, Tehran, Iran

<sup>3</sup>Dentist, Private Practice

## Abstract:

**Objective:** The aim of the present study was to investigate the demographic and pathological aspects of adenoid cystic carcinomas (ACC) in an Iranian sample based on a 20-year archive review.

**Materials and Methods:** In this descriptive study, tumors of the head and neck registered between 1980 and 2000 were evaluated and cases of ACC were selected. Patients' medical records and pathology reports were reviewed. Variables such as age, sex, duration of disease, symptoms, site of tumor involvement and tumor diameter as well as pathologic features were recorded. Analysis was performed using chi-square and t-tests;  $P < 0.05$  was considered as the level of significance.

**Results:** ACC was the most common malignant tumor followed by mucoepidermoid carcinoma and adenocarcinoma NOS. A total of 120 ACCs were found, of which 50.8% occurred in females and 49.2% in males. Patients' ages ranged from 5 to 90 with a mean of 49.2 (SD=15.9) years. In 60.9% of cases, minor salivary glands were involved and the palate was the most common site. The greatest tumor diameter was between 2-15cm with a mean of 4.6 cm (SD=2.9). The most prevalent histologic appearance was cribriform, followed by tubular pattern. No significant relation was observed between lymph node metastasis and patients' age, sex, disease duration, greatest tumor diameter and site of involvement.

**Conclusion:** Our findings were relatively similar to other reports from different parts of the world. Further analytic and case-control studies are recommended to gain a better understanding of different aspects of ACC.

**Key Words:** Carcinoma, Adenoid Cystic; Salivary Glands; Iran

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✉ Corresponding author:  
M. Khalili, Department of Oral and Maxillofacial Pathology, School of Dentistry, Tehran University of Medical Sciences, Tehran, Iran.  
mkhalili@tums.ac.ir

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## INTRODUCTION

Adenoid cystic carcinomas (ACC) are relatively common, well-known salivary malignancies that display a protracted clinical course. These tumors can originate from any type of salivary gland tissue; however almost half of them occur in minor salivary glands, while the other 50% involve the parotid and submandibular glands. They usually demonstrate a gradual

increase in size and affect both sexes equally. ACC is frequently associated with pain, which is considered as an early finding in the course of the disease. Histopathologically, it consists of myoepithelial and ductal cells arranged in different patterns, with cribriform, tubular, and solid being the three most prevalent types. Most ACCs are composed of a combination of these patterns and the final classification of

this neoplasm depends on the predominant type [1].

In order to have a better perception of the clinical and biologic behaviors of neoplasms, epidemiologic reports from various countries can provide valuable information for further studies. Numerous investigations have been conducted on different aspects of ACC and reported variations in its clinical and molecular characteristics [2-6].

The aim of this study was to evaluate the demographic and pathological features of ACC in a sample of Iranian patients referred to the Cancer Institute, Tehran University of Medical Sciences, during a 20-year period. This service is considered a major center for tumor diagnosis and it receives a remarkable number of referred cases from throughout the country. To our knowledge, this is the first report from Iran discussing the general characteristics of ACC in a large number of patients.

## MATERIALS AND METHODS

In this descriptive study, the archive of the department of statistics and epidemiological research of Cancer Institute, Imam Hospital, Tehran University of Medical Sciences was the source of data collection. Tumors of the head and neck registered between 1980 and 2000 were reviewed and salivary gland cases selected. Because the study was limited to salivary gland ACC, tumors from other sites such as lacrimal glands were excluded. Pa-

tients' medical records along with their pathology reports were reviewed. Information on age, sex, duration of disease, symptoms, site of tumor involvement and tumor size (greatest diameter) were retrieved from medical files.

Pathologic features like tumor invasion, growth pattern and necrosis, margin involvement as well as lymph node metastasis were extracted from the pathology reports.

Cases with recurrence, unknown origin, or uncertain diagnosis were excluded. Data were analyzed using t-test and chi-square test with  $P < 0.05$  as the limit of significance.

## RESULTS

From a total of 811 cases of salivary gland tumors, 482 (59.4%) were malignant. ACC was the most common malignant tumor comprising 24.9% ( $n=120$ ) of cases followed by mucoepidermoid carcinoma and adenocarcinoma NOS. The female to male ratio of the 120 salivary gland ACCs was 1.03 with 50.8% occurring in females and 49.2% in males. Patients' age ranged from five to ninety with an average of 49.2 (SD=15.9) years. The mean age in men and women was 46.9 (SD=17.8) and 51.4 (SD=13.7) years, respectively, with no significant difference ( $P=0.119$ ). The distribution of patients according to age and sex is shown in Table 1.

Disease duration was recorded in 93 patients and was less than 12 months in 56 cases (60.2%). The mean disease duration was not

**Table 1.** Age distribution of cases according to patient sex.

Age	Male		Female		Total	
	N	%	N	%	N	%
<20	3	100	-	-	3	2.5
21-30	9	69.2	4	30.8	13	10.8
31-40	13	54.2	11	45.8	24	20.0
41-50	9	36.0	16	64.0	25	20.8
51-60	9	40.9	13	59.1	22	18.3
61-70	13	46.4	15	53.6	28	23.3
>70	3	60.0	2	40.0	5	4.2
<b>Total</b>	<b>59</b>	<b>49.2</b>	<b>61</b>	<b>50.8</b>	<b>120</b>	<b>100</b>

N=number

significantly different between males and females ( $P=0.618$ ).

Table 2 presents the site of involvement in 120 cases of ACC. The minor salivary glands were affected with ACC in 60.9% of cases whereas the major glands were involved in 39.1% of the patients. Swelling was the main symptom in 61.7%, ulceration or bleeding was observed in 20.9%, and pain, limited mouth opening and difficulty to swallow were found in 13.9%, 2.6%, and 0.9% of the individuals, respectively.

The greatest tumor diameter was recorded in 53 cases ranging from two to fifteen centimeters with a mean of 4.6 cm ( $SD=2.9$  cm). Based on TNM classification, 18.9% of cases were classified as T1, 30.2% as T2 and 50.9% as T3 neoplasms. This variable was not significantly different between men and women ( $P=0.12$ ).

According to microscopic information provided in the patients' records, 10.8% of the cases had neural invasion, while 23.3% showed infiltration into adjacent bone and muscles. Skin invasion and necrosis was recorded in 3.3% and 4.2% of subjects, respectively. The most common histologic pattern was cribriform (54.4%), followed by tubular which was reported in 7.9% of the cases. A combination of cribriform and tubular patterns was found in 17.9%, cribriform and solid in 9.9% and a mixture of all three in 9.9% of the specimens. Surgical margin involvement was recorded in 75.7% of the samples.

Information regarding lymph node metastasis was available for 56 cases of which 67.9% were positive and the rest were negative. Radical neck dissection was performed on 16 (13.3%) patients with 50% positive and 50% negative results. No significant relation was observed between lymph node metastasis and patients' age, sex, disease duration, greatest tumor diameter and site of involvement (Chi-square test,  $P>0.05$ ). Data on distant metastasis was accessible for nine patients, with five

(55.6%) positive cases demonstrating lung involvement.

## DISCUSSION

ACC was the most common malignant tumor (24.9%) in the present investigation. Figures from other studies show slight differences with 50% reported in Japan [5], 41% in Brazil [2] and South Korea [3], and 10% in England and the USA [4,6]. Although race and ethnic factors may influence the relative frequency of tumors, the observed variations are most probably due to different methods of sampling as well as the source of data collection. It is noteworthy that ACC can arise in salivary glands and also other mucous glands from different anatomic like the upper aerodigestive tract, eye and skin. In some reports, ACC from other head and neck sites such as the nose, sinuses, nasopharynx and larynx are included and this may be responsible for the differences between the results. Seaver and Kuehn [4] believe that if ACC arises in areas other than major salivary glands it often simultaneously involves intraoral glands as well; although it may be found in other sites such as the larynx or trachea. In our study, minor salivary glands were limited to intraoral sites because we presume that a gland cannot be considered as salivary, unless it participates in saliva production.

According to the results obtained in the current investigation, ACC occurred in both sexes with a slight female tendency, which was in accordance with the sex distribution described in several other studies [3,6-9]. The mean age of patients in our archive was 49.2 years, similar to the 55 years reported from England [4], 54 years from Canada [10], 60 years from Louisiana (USA) [11], 51.3 years from Brazil [3], 43 years from South Korea [2] and 50 years from Iowa (USA) [12].

The most common tumor location in our study was the minor salivary glands, which was also reported by Spiro et al [6] and Garden et al [13]. This finding was in contrast to that pub-

lished by Seaver and Kuehn [4], in which only 14% of tumors originated from the minor salivary glands. Boko et al [14], in their study on accessory salivary glands, concluded that ACC was the most prevalent malignant tumor.

Regional lymph node metastasis is not a common finding in ACC; therefore, elective radical neck dissection (RND) is not routinely performed for patients with this tumor. In suspicious cases and in the presence of palpable lymphadenopathy, RND is recommended; however, some investigators suggest that this procedure should be performed for all tumors of submandibular glands [4,6]. Khafif et al [15] in a review and long-term follow-up of ACC recommended meticulous evaluation of cervical lymph nodes for patients with minor salivary gland involvement. They also suggested that "radical surgery with complete resection" should be considered as a general approach for treating all individuals with ACC of the salivary glands.

According to our findings, RND was performed for 16 (13.3%) cases with 8 (50%) showing lymph node metastasis (6.6% of all cases). These figures show primary involvement of lymph nodes at the time of diagnosis, which according to Ampil and Misra [11] is not a common finding. However, they stated

that the relative frequency of lymph node involvement in the course of treatment is 3-20%. Spiro et al [6] reported lymph node metastasis in 15% of their cases with 8% at the time of diagnosis and 7% in the follow-up period. In our country, information regarding patients' outcome and follow-up is not available and prospective and case-control studies are needed to compare the results.

This study was a descriptive, archive-based evaluation and the findings are not completely representative of the whole population, but since Cancer Institute is considered as a major referral center, relative frequencies and demographic results are authentic and may be useful for comparison with other studies. The main limitation of such investigations in our country is a lack of follow up information and incomplete patient records. Therefore evaluation of prognosis and survival could not be easily performed.

## CONCLUSION

To our knowledge, this study is the first analysis of ACC to be published based on data of Iranian patients. Despite a number of unavoidable limitations, some of our results can be reliable and may be used for comparison with other studies. In addition, these findings could

**Table 2.** Distribution of ACC according to sex and site of involvement.

Age	Male		Female		Total	
	N	%	N	%	N	%
Parotid	15	51.7	14	48.3	29	24.2
Submandibular	10	58.8	7	41.2	17	14.2
Sublingual	-	-	1	100.0	1	0.8
Palate	19	61.3	12	38.7	31	25.8
Tongue	1	11.1	8	88.9	9	7.5
Mandible	-	-	5	100.0	5	4.2
Maxilla	5	45.5	6	54.5	11	9.2
Floor of Mouth	4	44.4	5	55.6	9	7.5
Buccal Mucosa	1	33.3	2	66.7	3	2.5
Lower Lip	1	100.0	-	-	1	0.8
Miscellaneous	3	75.0	1	25.0	4	3.3
<b>Total</b>	<b>59</b>	<b>49.2</b>	<b>61</b>	<b>50.8</b>	<b>120</b>	<b>100</b>

N=number

provide a preliminary guideline for further analytical and case-control investigations.

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