

Retrospective analysis of malignant salivary gland tumors in Hungarian population between 1987-2006

Analisi retrospettiva delle neoplasie maligne delle ghiandole salivari nella popolazione ungherese tra il 1987 ed il 2006

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Summary

Aim: In our study 64 cases of malignant salivary gland tumors diagnosed at the Otolaryngology, Head and Neck Surgery Clinic of Pécs University from 1987 to 2006 were analyzed. **Patients and Methods:** The analysis focused on: total number, relative frequency and incidence of the newly diagnosed cases according to gender, age distribution, location, and histopathology and time distribution in two 10-year-periods. **Results:** The mean age of patients was 59 years. The overall incidence of malignant salivary gland tumors was 0.73/100,000 inhabitants annually and the male: female incidence rate ratio was 0.93. 81.3% of the tumors arose in the parotid gland, 9.4% in the submandibular gland and 7.8% in the intraoral minor salivary glands. Adenoid cystic carcinoma was the most frequent histopathological diagnosis with 25% relative frequency followed by

Riassunto

Obiettivo: Nello studio, che presentiamo, sono stati analizzati 64 casi di tumori maligni delle ghiandole salivari, diagnosticati presso l'Istituto di Otorinolaringoiatria e Chirurgia Testa-Collo dell'Università di Pécs, nel periodo compreso tra il 1987 ed il 2006. **Pazienti e Metodi:** Lo studio è stato condotto analizzando: il numero totale, la relativa incidenza e frequenza dei nuovi casi diagnosticati, suddividendoli per sesso, per distribuzione di età, per localizzazione, per istopatologia e per distribuzione nei due intervalli di tempo di 10 anni. **Risultati:** L'età media dei pazienti era di 59 anni. L'incidenza complessiva annuale dei tumori maligni delle ghiandole salivari era di 0,73/100.000 abitanti ed il rapporto di incidenza maschio/femmina era di 0,93. L'81,3% dei tumori sorgevano dalla ghiandola parotide, 9,4 nella sottomandibolare ed il 7,85 nelle ghiandole salivari minori.

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mucoepidermoid carcinoma and anaplastic carcinoma with equal relative frequency of 14.1%. We compared two ten year time intervals of the 20 year study period by tumor occurrence, incidence and male: female incidence rate ratio. *Conclusions:* Our results provide the first epidemiological data on malignant salivary gland tumors in Hungarian population comparing different ethnicities and geographic areas to get deeper insight into the etiology of malignant salivary gland tumor development. *Eur. J. Oncol.*, 14 (4), 209-215, 2009

Key words: malignancy, salivary gland, tumor, retrospective analysis

Introduction

Salivary gland tumors represent a specific field in the oral and maxillofacial surgery and their epidemiology on Hungarian population has not been described. The reasons of this fact are due to the morphological heterogeneity and the low frequency of these neoplasms, although epidemiological data of these tumors could be helpful for a better understanding of their etiology and clinical characteristics. In order to establish a diagnostic standard for salivary gland tumors the World Health Organization's Histological Classification of Salivary Gland Tumors was established in 1971 and revised in 1991 and in 2005 (1-4).

Many epidemiological studies on different populations showing a wide range in the tumor incidence, (ranging from 0.4-13.5 annual cases per 100,000 inhabitants), possibly influenced by geographical and racial factors have been carried out (5-8). The incidence of malignant salivary gland neoplasms is in the range of 0.4 to 2.6 cases per 100,000/year (5, 7, 8). The anatomical distribution of salivary tumors has been shown as 64-80% in parotid, 7-11% in submandibular, 1% in sublingual and 9-23% in minor salivary glands (8). Out of the total number of salivary gland tumors 21.0-36.8% have been found to be malignant (9, 10), accounting for less than

Istopatologicamente il carcinoma adenoideo-cistico è stato il più frequente con un'incidenza relativa del 25%, seguito da quello mucoepidermoide e da quello anaplastico che hanno presentato una uguale incidenza relativa del 14,1%. In questa analisi abbiamo messo a confronto i dati dei due intervalli di tempo di 10 anni valutando l'incidenza del tumore, il rapporto di incidenza ed il rapporto di incidenza maschio/femmina. *Conclusioni:* Il nostro studio fornisce i primi dati epidemiologici sulle neoplasie maligne delle ghiandole salivari nella popolazione ungherese in rapporto con le diverse etnie, aree geografiche al fine di ottenere un'analisi più approfondita sull'eziologia dello sviluppo delle neoplasie delle ghiandole salivari maligne. *Eur. J. Oncol.*, 14 (4), 209-215, 2009

Parole chiave: malignità, ghiandole salivari, analisi retrospettiva

0.3% of all neoplasms and 6% of the head and neck tumors (11).

In Hungary, head and neck cancers count up to 10% of all cancer cases as reported by the WHO/IARC statistics for Western and Central Europe with a mortality of 19/100,000 for males and 2.3/100,000 for females (<http://www.dep.iarc.fr/WHO>). The increasing trend in the morbidity and mortality of the head and neck tumors in the last two decades draws the attention for a more detailed analysis of the clinicopathologically different tumor types of this region. Scarce epidemiological data about salivary gland tumors concerning the Hungarian population are available.

In this study we analyzed 64 malignant salivary gland tumor cases that were observed in Otolaryngology, Head and Neck Surgery Clinic of Pécs University between 1987-2006. Our aim was to find out the occurrence, incidence and histological distribution of salivary gland tumors in our region and to correlate the results with location, gender and age of the population.

Patients and methods

This study reviewed all salivary gland tumor cases newly diagnosed between 1987 and 2006 in the

Otolaryngology, Head and Neck Surgery Clinic of Pécs University that represents a regional cancer center for head and neck tumors for the population of Baranya County. All the diagnoses were reevaluated on hematoxylin-eosin slides and tumors were reclassified according to the criteria suggested by the 2005 WHO histological classification. The major salivary glands included the parotid gland, the submandibular gland and the sublingual gland, while the minor salivary glands included the salivary glands of the lip and of the intraoral regions: the palate, the tongue, the bucca, the alveolar mucosal region and the floor of the mouth. The entire medical documentation of all cases was reviewed and data concerning date of birth, gender, histopathology, tumor location, treatment and the follow-up were obtained. Pathology report confirming the histological diagnosis was required for inclusion in the study focusing on malignant tumors; the metastatic tumors to the salivary glands were excluded. Analysis were focused on: total number, relative frequency and incidence of the newly diagnosed cases according to (1) gender and (2) age distribution, (3) location (4) histopathology and (5) time distribution in two 10-year-periods.

Statistical methods: Age adjusted incidence rates per 100,000 inhabitants were calculated for the

population of Baranya County, Hungary (based upon the census of 1986 and 1996).

Results

Site and Histology

During the revised 20-year period (1987-2006) 64 malignant salivary gland tumor cases were diagnosed. Out of the total number of salivary gland tumors, the parotid gland was the most common site ($n = 52$), representing 81.3% of the cases. It was followed by the submandibular gland ($n = 6$) with the relative frequency of 9.4% and the intraoral minor salivary glands ($n = 5$) with the relative frequency of 7.8%. The only sublingual gland tumor found in this period accounted for 1.6%. Regarding the gender differences in localization, we found the relative frequency of parotid gland tumors higher in females, whereas the frequency of submandibular gland tumors was much higher in male patients (Fig. 1).

According to the histological distribution, the most frequent malignant salivary gland tumor was adenoid cystic carcinoma comprising 25.0% of all tumors and 68.8% of the adenoid cystic carcinomas

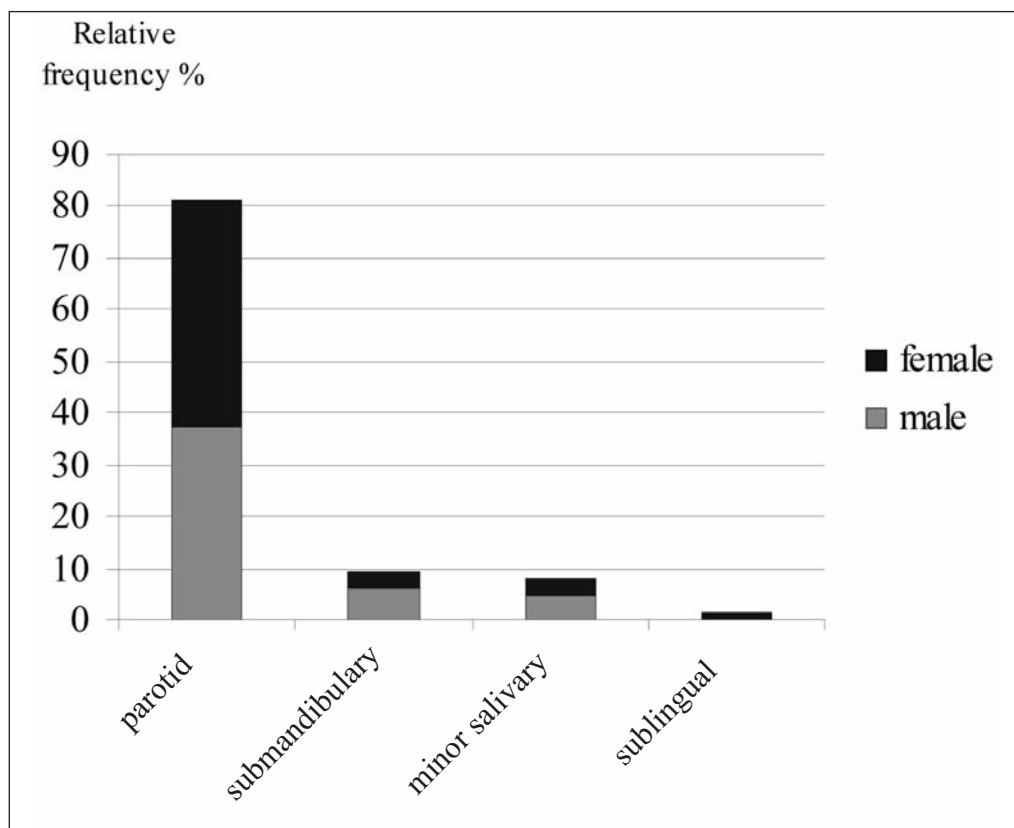


Fig. 1. Relative frequency of malignant salivary gland tumors in Baranya County, Hungary (1987-2006) by location and gender.

occurred in the parotid gland. Out of them, 75.0% were found in females. Considering only the tumors arising in the parotid, 21.2% of the tumors fell into this histopathological group and all the cases occurred in female patients.

The other more frequent histological entities were the mucoepidermoid carcinoma and the anaplastic carcinoma, both with the relative frequency of 14.1% of all tumor types; 88.9% of them arose from the parotid gland representing 15.4% of the parotid gland tumors; 67.0% of mucoepidermoid carcinomas occurred in male patients. Adenocarcinoma accounted for 12.5%, squamous cell carcinoma for 10.9%, pleomorphic carcinoma for 9.4% and acinic cell carcinoma for 7.8% (Fig. 2).

Age, gender and time intervals

The 64 malignant salivary gland tumor cases occurred in patients between the ages of 13 to 92 years (mean age = 59 years). Peak occurrence was observed in the 60-69 age group of both genders. Cumulative incidence rates adjusted over 12 strata of age by location are represented in Fig. 3. Two peaks at the 40-49 and 60-69 age groups in the parotid gland were present. The submandibulary gland tumor showed similar incidence rates in the middle and elderly age categories. No relevant difference

between genders in the incidence of salivary gland tumors was observed.

In summary, there was a slight overall female predominance with the male: female incidence rate ratio of 0.93. The calculation of the male: female incidence rate ratio (IRR) according to tumor location showed 0.91 IRR in the parotid gland, 2.14 in the submandibulary gland and 1.60 in the minor intraoral salivary glands. Therefore the female predominance in the incidence of salivary gland tumor is expressed by the female predominance of parotid gland tumors.

After the division of the 20-year period into two 10-year intervals we compared the tumor occurrence, the incidence and the relative frequency according to tumor location (Table 1). The absolute number of salivary gland tumors did not differ much between the two 10-year periods. In the first time interval (1987-1996) the relative frequency of parotid gland tumors was higher. On the contrary, the relative frequency of submandibulary gland tumors showed a nearly doubled increase in the second interval. The overall male: female IRR in the 20-year period was 0.93, showing a slight female dominance. Interestingly, while the male: female IRR in the first interval was 0.74, a strikingly higher female ratio, the male: female IRR in the second interval turned to 1.42, demonstrating a strong male predominance.

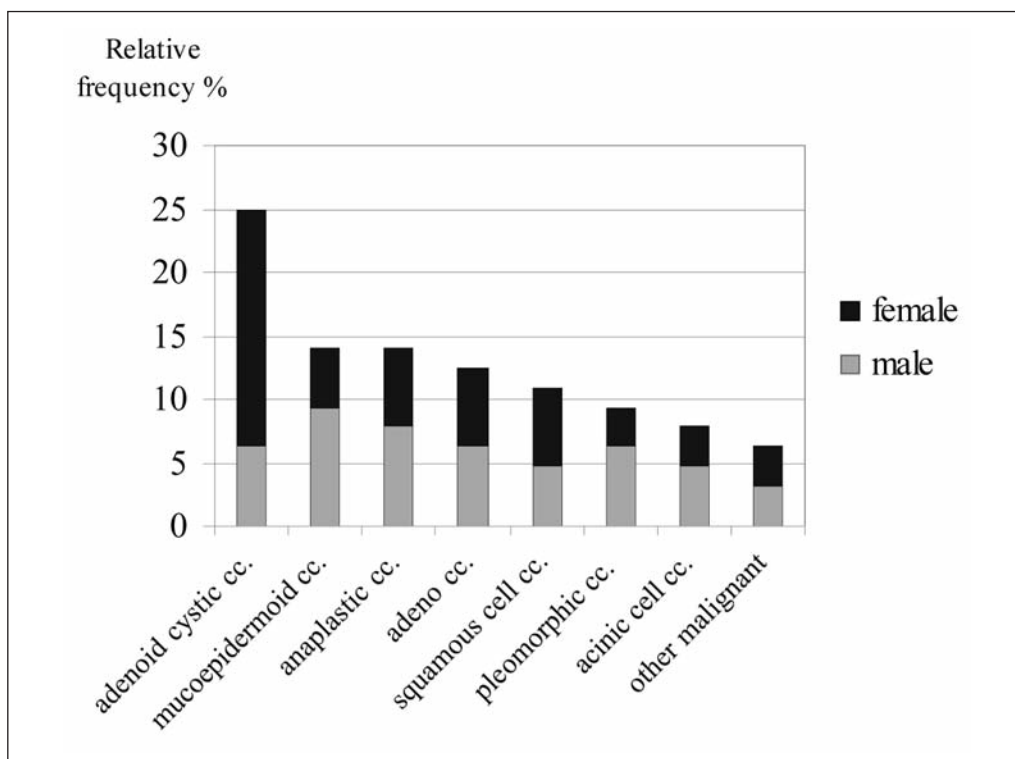


Fig. 2. Relative frequency of malignant salivary gland tumors in Baranya County, Hungary (1987-2006) by histotype and gender.

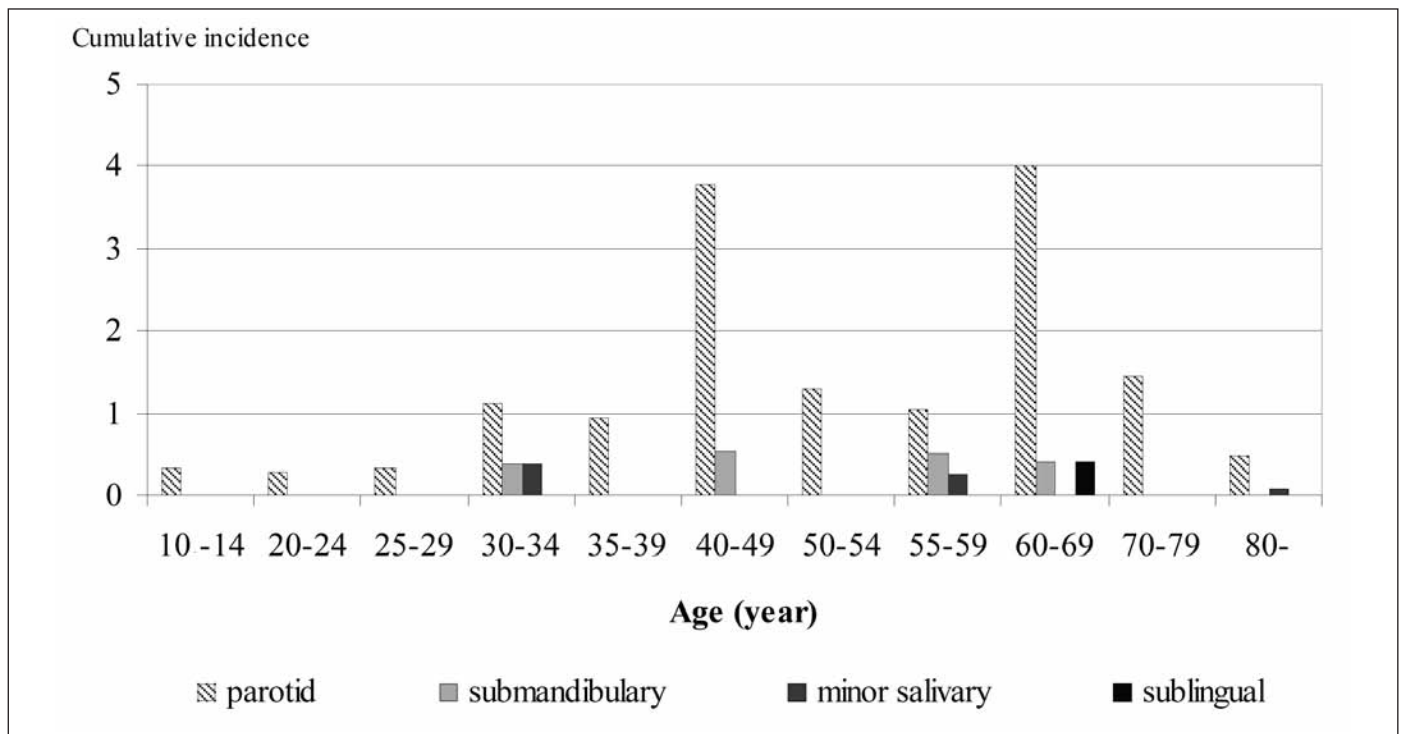


Fig. 3. Cumulative incidence per 100,000 population for malignant salivary gland tumors in the 20-year period (1987-2006) by groups and location.

Table 1 - Malignant salivary gland tumors in Baranya County, Hungary, during two 10-year time intervals 1987-1996 and 1997-2006: total number of cases, relative frequency, incidence rate per 100,000/year and male: female incidence rate ratio by location and gender

	Number of tumors Total	Relative frequency(%) M	Incidence		Incidence rate ratio					
			F	Total	M	F	Total	M	F	
I. interval: 1987-1996										
Parotid	29	12	17	85.2	85.7	85	0.33	0.29	0.38	0.75
Submandibulary	2	1	1	5.8	7.14	5	0.02	0.02	0.02	1
Minor salivary	2	1	1	5.8	7.14	5	0.02	0.02	0.02	1
Sublingual	1		1	2.9		5	0.03		0.02	-
All	34	14	20	53.1	41.1	58.9	0.39	0.33	0.45	0.74
II. interval: 1997-2006										
Parotid	23	12	11	76.6	70.6	84.6	0.28	0.31	0.26	1.18
Submandibulary	4	3	1	13.3	17.6	7.6	0.05	0.08	0.02	3.25
Minor salivary	3	2	1	10	11.7	7.6	0.04	0.05	0.02	2.17
Sublingual										-
All	30	17	13	46.9	56.6	43.3	0.37	0.44	0.31	1.42

Follow up

Up to 2008, we obtained a five-year follow up for 55 cases. We enrolled 30 female patients with an average age of 62.5, whose 5-year survival rate was

43%, and 25 male patients whose average age was 53.2 and their 5-year survival rate was 32%.

Survival was analyzed according to histopathology. Patients with squamous cell carcinoma and anaplastic carcinoma were found to have the

worst survival rates (0-1 years and 2 years) and patients with adenoid cystic carcinoma had the best (over 10 years) survival rates.

Discussion

Malignant salivary gland tumors form a specific group of neoplasms among head and neck tumors, since they are uncommon and different in their histopathology. This is observed in the relative absence of reports regarding the Hungarian population, in spite of the fact that head and neck tumors are in the focus of interest especially for their public health importance.

In the present study we reviewed 64 malignant salivary gland tumors with reference to their epidemiological characteristics. We found that the majority of the tumors occurred in the parotid gland followed by the submandibular gland, the minor salivary glands and only one sublingual salivary gland tumor in the revised period was observed. In literature, the relative frequency of parotid gland tumors is reported to range between 57.5%-86% (12, 13). Large population based studies (14, 15) found the minor intraoral salivary glands as the second most frequent location of tumor occurrence, ahead of the submandibular region. Malignant sublingual tumors are extremely rare comprising 0.3% of total cases according to a large study (10). We also observed a gender difference in tumor frequency with reference to the localization: parotid gland tumors had higher frequency in females, while the submandibular and the minor salivary gland tumors were more frequent in males.

Considering the histological classification, adenoid cystic carcinoma was the most frequent histological type ahead of the mucoepidermoid and anaplastic carcinoma, which had equal distribution. This result correlates with the findings of a Swedish large population based study (15) in which also the frequency of adenoid cystic carcinoma was the highest, but in studies from the United States (13), and results from Nigerian (16), Brazilian (17), Mexican (18), Iranian (19) and Chinese (14) populations mucoepidermoid carcinoma was reported as the most common salivary gland malignancy. This difference suggests ethnic and geographic diversity but may be also related to sex difference. Thus, when histological groups were broken down according to gender, we found adenoid cystic carcinoma more

frequently in females and the mucoepidermoid carcinoma in males, while we had a female predominance. This finding supports the role of behavioral and hormonal influences on the tumor development.

In our present study the overall incidence of salivary gland tumors in Baranya County was 0.73/100,000/year. Corresponding data reported from other studies (13, 15, 20, 21, 24) ranges between 0.4 to 1.08/100,000/ year.

Dividing the reviewed 20-year period in two 10-year intervals, no change in tumor incidence or tumor relative frequency was observed. However a gender shift to a male predominance (IRR: 0.74-1.42) and in parallel a double tumor frequency in the submandibular gland was found (but in relatively low case numbers). Sex predilection for salivary gland tumors has been reported to be related to ethnic variations (17, 22, 23), but such shift from female to male predominance in tumor incidence has not been described in the literature and needs further investigation. Regarding similar studies on Western population (13, 24) they indicate a male: female IRR of 1.3-1.1 and the Hungarian population seems to follow their trends, which might be explained by the influence of changing environmental risk factors (smoking, environmental exposure, lifestyle).

Prognosis of malignant salivary gland tumors strongly depends on disease stage, tumor histology and biological behavior. In the present study the 5-year survival rates were under 50% in both sexes, which is considered to be relatively poor, but similar to other reports (19, 25). The higher rate of adenoid cystic carcinoma with the best prognosis (over 10-year survival) in females seems to play a crucial rôle in the 11-year difference between the survival of men and women in favor of women.

Conclusions

Our results provide the first epidemiological data on malignant salivary gland tumors in Hungarian population although refer to a specific geographical region and a very specific group of relatively rare tumor types; thereby we wish to use our data principally for the enhancement of oral cavity screening in a wider population in this region. Although primary preventive actions to repress smoking and alcohol consumption in Hungary are essential and the most effective in reducing the overall head and neck cancer mortality, the quickest tool for reducing the

mortality would be an effective oral cavity screening. The effectiveness of stomato-oncologic screening programs is under debate in several countries in Europe and also in the United States. The reason is that an isolated screening program, in spite of the low specific expenditures, is less cost effective on the mortality outcome than the primary prevention strategies to suppress risk factors. However an oral cavity screening program could reach a higher effectiveness if it is linked to the routine physical examinations in the general medical practice and in the occupational medical practice and included in the screening of the population in homeless shelters and in the organized periodical screening of the disadvantaged settlements. Based upon our data we suggest screening actions to be introduced in Baranya County in both women and men over 35 years of age. Our results have implications for further, large population based study in Hungary that could open the possibility for a more detailed epidemiological analysis and comparison with different ethnicities and geographic areas to get deeper insight into the etiology of malignant salivary gland tumor development.

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