

Survival from major salivary gland cancer in a Spanish population: follow-up of patients diagnosed between 1978 and 2002

Sopravvivenza al cancro delle ghiandole salivari maggiori in una popolazione spagnola: follow-up di pazienti diagnosticati dal 1978 al 2002

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Summary

Aim. This article aims at studying major salivary gland cancer survival from the Population-Based Cancer Registry of Zaragoza, Spain, for the period 1978-2002. **Materials and Methods.** The survival rates were calculated by the Kaplan-Meier method. The automated calculation of the Catalan Institute of Oncology was utilized to obtain the relative survival. **Results.** The observed survival rate was of 70.2% in the first year and 41.8% in the fifth year. The one-year relative survival for both genders was 71.8% (CI 95%: 64.5-80.0) and five-year relative survival was 46.8% (CI 95%: 38.5-56.9). Comparison of survival rates by sex revealed statistically-significant differences (p value = 0.036) with higher survival rates in women. No differences were observed when comparing the two age groups and the three studied time periods (1978-1986, 1987-1994, and 1995-2002). **Conclusions.** The data indicate no significant changes in major sali-

Riassunto

Finalità. L'obiettivo di questo articolo è lo studio della sopravvivenza al cancro delle ghiandole salivari maggiori sulla base dei dati contenuti nel Registro Tumori degli abitanti di Saragozza, Spagna, nel periodo dal 1978 al 2002. **Materiali e Metodi.** Il tasso di sopravvivenza è stato calcolato secondo il metodo Kaplan-Meier. Per ottenere la sopravvivenza relativa è stato utilizzato il calcolo automatico dell'Istituto Catalano di Oncologia. **Risultati.** Il tasso di sopravvivenza osservato è stato del 70,2% nel primo anno e del 41,8% nel quinto anno. La sopravvivenza relativa nell'arco di un anno, per entrambi i sessi, è stata del 71,8% (IC 95%: 64,5-80,0), mentre nel caso dei cinque anni è stata del 46,8% (IC 95%: 38,5-56,9). Il paragone del tasso di sopravvivenza a seconda del sesso ha evidenziato differenze statisticamente significative (p = 0,036) con tassi di sopravvivenza più elevati nelle donne. Nessuna differenza è stata invece osservata nel paragone tra le due fasce d'età

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Introduction

Major salivary gland cancers are a heterogeneous group of rare cancers, comprising less than 3% of all head and neck malign tumors and, compared to other cancers, present low global variability in incidence rates (1, 2). Incidence rates are higher in men, although gender difference is small and incidence increases after the fifth decade of life. The highest adjusted rates in the world do not exceed 2 per 100,000 persons/year (3).

The epidemiology of salivary gland tumors is not well documented. Major salivary gland cancers have not been fully studied at a population level. Several studies that have included these cancers in analyses grouped data of other types of tumors, mainly oral cavity and oropharynx. Nevertheless, salivary gland cancers present a different epidemiologic profile from oral cavity and different locations of pharynx (oropharynx, hypopharynx, and nasopharynx). Grouped analysis with other locations prevents the generation of hypothesis on carcinogenesis and contributes to lack of knowledge on risk factors (4).

In Spain, population aging and the improvements in cancer survival are factors that have increased the demand for treatment of different types of cancer (5). Nevertheless, little is known on the epidemiology of salivary gland tumors and survival rates (6). Obtaining epidemiological indicators on cancer, principally for rare tumors and defined populations, are essential information to deepen knowledge on the disease and direct the search for more effective therapeutic alternatives (7-9).

This study aims at defining the major salivary gland survival rates, from data of the Population-Based Cancer Registries (PBCR) of Zaragoza, Spain. Analysis of cancer survival from population-

e i tre periodi di tempo presi in esame (1978-1986, 1987-1994 e 1995-2002). *Conclusioni.* I dati non evidenziano nessun cambiamento sostanziale nella sopravvivenza al cancro delle ghiandole salivari maggiori nella provincia di Saragozza. *Eur. J. Oncol.*, 17 (4), 175-180, 2012

Parole chiave: tumori delle ghiandole salivari, sopravvivenza, Spagna

based data is a powerful tool to evaluate the health services offered and guide the diagnose and treatment strategies (10, 11).

Materials and Methods

The population studied was diagnosed with major salivary gland cancer in the province of Zaragoza, Spain, between January 1, 1978 and December 31, 2002, with data collected, analyzed and monitored actively by the PBCR of Zaragoza until December 31, 2007. The difficult in establishing survival at a population level lies firstly in obtaining reliable data on cancer incidence for the population, and secondly, in carrying out the monitoring with accuracy and integrity. Monitoring of cases was carried out by the Cancer Registry itself through the mortality registry of the Aragon Government, which is administered by the Statistical Institute of Aragon. Database crossing and processing was initially carried out manually and gradually become computerized. All new cases registered as major salivary gland cancer were included in the analysis, except for the cases diagnosed through death certificates. Data were directly obtained from the Cancer Registries. The PBCR data of Zaragoza were the first Spanish data to be published in CI5, appearing in this publication since volume III. A set of quality indicators evaluates the data prior to publication in CI5; the registry data of Zaragoza fulfills the established quality standards and presents excellent quality (12, 13).

Calculation of the observed survival rate was carried out by the Kaplan-Meier method, and the relative survival was calculated through the webpage of the Catalan Institute of Oncology (CIO). The relative survival rate is defined as the relationship

between the observed survival and the expected survival in a group of healthy people of similar age and gender. In practice, the survival of people without cancer is difficult to predict, and for this reason the general mortality rate of the population is used. The webpage of CIO uses the Hakulinen method to calculate the relative survival of the database sent by the user, and is based on the mortality tables of the Mortality Registries of the autonomous communities and provinces of Spain (14, 15).

When the number of risk patients was lower than 10, these results were not considered in the analysis, as the final estimations are unstable (9). Survival was studied by gender and age groups (40-64 and over 65 years of age). In order to study the dynamics of survival, the data was stratified in three study periods (1978-1986, 1987-1994 and 1995-2002) and the survival indicators were compared. The effect of each prognostic factor (sex, age group, and time period) on the survival was evaluated by the log-rank test. The Log-rank test is a statistical hypothesis contrast test, used to compare two or more survival curves, and the null hypothesis is that the survival of the groups under comparison is the same.

Results

After exclusion of the cases registered through death certificates, the number of incidence cases

Table 1 - Distribution of cases, the number of deaths according sex, age and period

	number of persons at risk	%	number of deaths
Sex			
Male	92	65.2	67
Female	49	34.8	26
Total	141	100	93
Age			
0-39	9	6.4	4
40-64	54	38.3	35
65+	78	55.3	54
Period			
1978-1986	38	26.9	25
1987-1994	48	34	31
1995-2002	55	39	37

included in the study was 141. Table 1 presents the distribution of cases, the number of deaths, and the percentage of censored cases according to sex, age, and period. It was observed that 65.2% of cases occurred in men. The censored percentage was 34% (27.2% men and 46.9% women).

The observed survival (Table 2) after one year of diagnosis of major salivary gland cancer was 70.2% (CI 95%: 62.9-77.4) and after five years, survival was 41.8% (CI 95%: 33.5-50.0). One-year relative survival was 71.8% (CI 95%: 64.5-80.0)

Table 2 - Observed and relative survival after 1, 3 and 5 years of diagnosis of major salivary glands

Survival	Observed						Relative					
	1 year		3 years		5 years		1 year		3 years		5 years	
	%	CI 95%	%	CI 95%	%	CI 95%	%	CI 95%	%	CI 95%	%	CI 95%
Sex												
Men	66.3	57.0-75.5	45.7	35.5-55.8	37	27.2-46.8	68.5	59.2-79.2	50.1	40.1-62.6	43.6	33.4-57.0
Women	77.6	65.8-89.3	59.2	45.4-72.9	51	37.0-64.9	78	67.1-90.7	60.2	47.7-75.9	52.9	40.2-69.6
Total	70.2	62.9-77.4	50.4	42.1-58.6	41.8	33.5-50.0	71.8	64.5-80.0	53.6	45.5-63.1	46.8	38.5-56.9
Age												
0-39	-	-	-	-	-	-	-	-	-	-	-	-
40-64	81.1	70.5-91.6	56.6	43.2-69.9	47.2	33.6-60.7	77.9	67.4-90.1	57.8	45.6-73.1	49.1	36.9-65.2
65+	66.7	56.3-77.0	43.6	33.6-54.5	34.6	24.0-45.1	67.7	57.3-79.9	50.5	39.2-65.0	45.8	33.7-62.1
Period												
1978-1986	65.8	50.7-80.8	47.4	31.5-63.2	44.7	28.8-60.5	67.4	53.6-84.8	50	35.7-69.8	52.2	36.7-74.3
1987-1994	68.8	56.8-80.7	54.2	40.0-68.3	41.7	27.7-55.6	70.3	58.1-85.1	57.9	44.6-75.1	46.8	33.5-65.5
1995-2002	74.5	62.9-86.0	49.1	35.9-62.2	40	27.0-52.9	76.2	65.3-88.9	51.6	39.4-67.5	43.4	31.4-59.9

and five-year relative survival was 46.8 (CI 95%: 38.5-56.9).

Comparison of survival rates by sex revealed statistically-significant differences (p value = 0.036) with better survival in women. No differences were observed when comparing the two age groups and the three studied time periods.

Discussion

Cancer survival is directly related to the quality of the health services offered, and for this reason the survival rates are different depending on the population studied. Research indicates that more developed countries with better health service structure present higher survival rates (16, 17).

The most important survival data for the comparison of results originate from EUROCARE studies. EUROCARE is a multicentre project that started with data from 11 countries, being currently in its fourth edition and combining 23 countries. The results of the fourth edition of EUROCARE, for adults diagnosed between 1995 and 1999, demonstrates that five-year relative survival for Europe was 59% (CI 95%: 56.7-61.4) (16). For the period 2000-2002, according to the survival estimations based on EUROCARE study data, it is expected that the relative survival in Europe for major salivary gland cancer is 85.3% (CI 95%: 83.5-87.1) after a year of diagnosis, 63.6% (CI 95%: 60.6-66.6) after five years and 58% (CI 95%: 54.2-61.8) after 10 years (18).

The best relative five-year survival rates were registered in Sweden (70.3%, CI 95%: 64.1-77.1), United Kingdom – Wales (66.8%, CI 95%: 56.9-78.5) and Netherlands (66.5%, CI 95%: 57.4-77.1), while Northern Ireland (49.2%, CI 95%: 35.8-67.5), Poland (42.0%, CI 95%: 31.7-55.5), and Malta (36.3%, CI 95%: 22.3-59.1), presented the lowest survival rates. Spain is situated amongst the countries with higher rates (68.5%, CI 95%: 59.8-78.5), at the average European level (59.0%, CI 95%: 56.7-61.4) (16). In Zaragoza, the five-year relative survival rate is lower than the Spanish average: 46.8 (CI 95%: 38.5-56.9).

In the United States, a study on salivary gland cancer based on population-based cancer registries

(1973 to 2006) has also encountered a survival rate of 58% in adults and 95% in patients under 20 years of age (19).

There is no doubt that the economic situation of a country, along with the amount of resources destined to medical attention, are the reasons behind the variability in survival rates, and are the main explanation for lower survival rates in Western countries. Nevertheless, lower survival rates in countries such as Ireland or other regions of the United Kingdom reveal that survival rates could also be related to other factors, such as the structure of the health service system, risk factor pattern, and comorbidity (18, 20).

It is worthwhile mentioning that data coverage in EUROCARE studies not always represents the entire population of the country. For example, in EUROCARE 3, Denmark, Norway, Sweden, Slovakia and other countries presented coverage of 100% of the population, while Germany presented data for only 2% and Spain, of 12% of the population. The differences encountered must be therefore analyzed with caution (21).

The analysis of survival rates by incidence years is important to study the evolution of treatments. It is assumed that the patients recently diagnosed benefited from surgical and pharmaceutical technological advances and presented better survival rates than those patients previously treated. However, when evaluating data from different periods, information quality must be considered, as some anterior data may be less accurate, mainly in studies with a long follow-up period. In Zaragoza, no improvement in survival rates was verified when comparing the dynamics of the survival rates in the periods 1978 to 1986, 1987 to 1994, and 1995 to 2002.

A study carried out with population-based European data has analyzed the evolution of salivary gland-adenoid cystic carcinoma survival, comparing data from 1983 to 1994, divided into four periods and, as in Zaragoza, no improvement was observed in the survival rates. For the period 1983-1985 the five-year relative survival rate was 79.9% (CI 95%: 75.5-84.0), and for the period 1992-1994 the survival rate was 76.4% (CI 95%: 72.1-80.7). The results also showed that the cases diagnosed in the last period (1992-1994) presented a 50% higher risk than in the first period (1983-1985). It must be high-

lighted that the study includes salivary gland-adenoid cystic carcinoma in all locations of head and neck, and not only major salivary glands. Results suggest that despite recent possible improvements in the diagnosis of salivary gland tumors, it seems that high quality treatment did not perform as expected or the access to such treatment is still limited (22).

Regarding gender, the analysis of survival rates for Zaragoza has revealed better rates in women. In Europe, for the period 1990-1994, the five-year relative survival rate was 51% (CI 95%: 45.9-56.7) for men and 68.7% (CI 95%: 63.6-74.3) for women. Survival rates were also better in women in Italy, Scotland, Spain and UK-Wales. In the majority of European countries the gender differences were not statistically significant, such as in Austria, Czech Republic, Denmark, Estonia, Finland, France, Norway, Poland and Sweden (17). The possible explanations for the higher survival rates in women could be a higher level of conscience towards the body, and consequently an early diagnosis and/or a biological superiority of women in response to the disease or treatment (20, 23).

In conclusion, our data suggest lower survival rates in Zaragoza when compared to Spanish data published in other studies. Additionally, no significant changes were observed in the survival rates when comparing three study periods. The results must be interpreted with caution because of the added difficulty in monitoring these cases due to a long follow-up period. The authors consider that the survival studies based on PBCR, despite their limitations, must be carried out and published, allowing for a global evaluation of the disease for the studied population. These studies are also the basis for future investigations, prevention and control of cancer, and improvements on the follow-up process of patients.

Advances in cancer treatment and the increase in the number of survivors require a broader monitoring of the population. Currently in Spain, more than 50% of patients are alive after five years of being diagnosed with cancer, and the trend indicates increasing survival rates (24). Nevertheless, there is still lack of data on these patients. Cancer survival studies must extend the follow-up time and widen perspectives, with the objective of establishing knowledge on physical, psychological, and social consequences of this disease (5, 25).

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