

## Salivary gland cancer — epidemiology

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Salivary gland tumors represent 3–11% of all head and neck cancers and 0.2% of all neoplasms. Among Poles, malignancies involving the large salivary glands constituted 0.3% of all malignancies in Poland and 9.7% of head and neck neoplasms. In 2014, the morbidity rate was higher among women, but over the past 15 years there has been a slight prevalence among men. As for benign neoplasms in Poland, the most commonly seen are pleomorphic adenoma and Warthin's tumor. Cystic glandular cancer, mucoid epidermal carcinoma and adenocarcinoma are among the most frequent malignancies. Less common are lymphoma and squamous cell carcinoma. Salivary gland neoplasms are usually located in the parotid gland, then in the sub-mandibular gland. The best prognosis is for women whose cancers are located in the parotid gland and those with lobular carcinoma. Figures have been on the rise lately, however. Deaths have been on a stable level.

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**Key words:** cancer, epidemiology, etiology, histopathology, salivary gland

### Introduction

Salivary gland cancers are rare, constituting 3–11% of all head and neck neoplasms and 0.2% of all malignancies, depending on the author [1–3]. Most occur in the sixth decade of life [4]. The proportional morbidity for men and women is similar with men to women ratio being 1.3 : 1 [4]. This type of cancer develops both in large (parotid, sub-mandibular sublingual) as well as in small salivary glands located within the mucous membrane of the upper section of the gastrointestinal tract. Salivary gland cancers are a very non-homogenous group, in which 32 histological types and subtypes can be distinguished [5]. Therefore, the epidemiology of these neoplasms is not well recognized. Many studies include only data on parotid gland cancer, others contain data concerning only the large salivary glands. As a relatively large number of neoplasms are benign lesions, epidemiological data are incomplete and can in many ca-

ses be underestimated. Additionally, because of the rarity of incidence and great diversity of those neoplasms, data concerning the etiology of specific histopathological types are scant. In this paper, we present the latest epidemiological data concerning salivary gland neoplasms.

### Epidemiology of salivary gland neoplasms globally and in Europe

Data concerning the world population are incomplete. Malignant neoplasms of salivary glands are extremely rare, the figures range from 0.05–2/100,000 inhabitants. The highest number of new cases come from Croatia, where there are 1.8/100,000 new cases of this type of cancer found in men [6]. The highest number of salivary gland cancers are found in the European and North American population. Compared with Africa, the proportion is 40:6, whereas for Asia it is 40:1 [4]. Studies on the US population show a gro-

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wing tendency in the last few years. The number of new cases per 100,000 had grown in 1974–1999 from 0.1% to 1.1%. Of all head and neck cancers, this number was 6.3 in the years 1974–1976 while in the years 1998–1999 it was 8.3%. Analysis of the SEER (Surveillance, Epidemiology, and End Results) database points to a statistically significant fall in cases with locally contained disease (56.0% – 44.9%;  $p < 0.004$ ) and a statistically insignificant increase in cases with locally advanced and disseminated disease (27.0% – 31.2%;  $p = 0.060$  and from 10.4% to 15.6%;  $p = 0.859$ ) [2]. For many years, the percentage of 5-year survival has been stable at 68%, but the percentage of survival in locally advanced stages has improved slightly (83.7% – 88.5%;  $p = 0.012$ ) [2].

Studies of the European database, RARECARE (Surveillance of Rare Cancers in Europe) from 1995–2002 indicate that the largest percentage of new cases is among the elderly > 65 years of age — 1.42/100,000, and among the middle aged from 25–64 years of age — 0.42/100,000. Salivary gland cancers slightly prevail among men (0.45/100,000) compared with women (0.32/100,000) [7]. The largest number of new cases is reported for West- (0.45/100,000) and Central Europeans (0.42/100,000). The fewest new cases are reported for Eastern European countries (0.32/100,000) [7]. Data from the EUROCARE-4 study [8], for the years 1995–1999 point to a 1.3 five-year survival rate at 83, 69, 65% respectively with male survival at 58% and female survival at 59%. The survival rate was falling with age and was 87% among patients aged 15–47 and 59 among patients over 74 years of age [8]. EUROCARE-5 data point to slightly worse survival. In 1999–2007, the percentage of 5-year survivals was 58% [9]. Similar results come from the RARECARE study [7]. The percentage rate of 1- and 5-year survival of patients treated in 2000–2005 in all Europe was 87% and 71% respectively. Among women it was higher and was 91 and 81% respectively. To compare, 1- and 5-year survival in men was 84 and 62% respectively. Younger patients had better prognoses. Among patients aged 25–64, 1- and 5-year survival was 91% and 74% respectively, and among older patients it was 82 and 64%. The highest survival rate was reported for Western Europe — 1- and 5-year survival there was 90 and 81% respectively. The lowest 1- and 5-year survival rate was reported for Eastern Europe and was 74 and 52% respectively [7].

### **Morbidity and death rate in Poland**

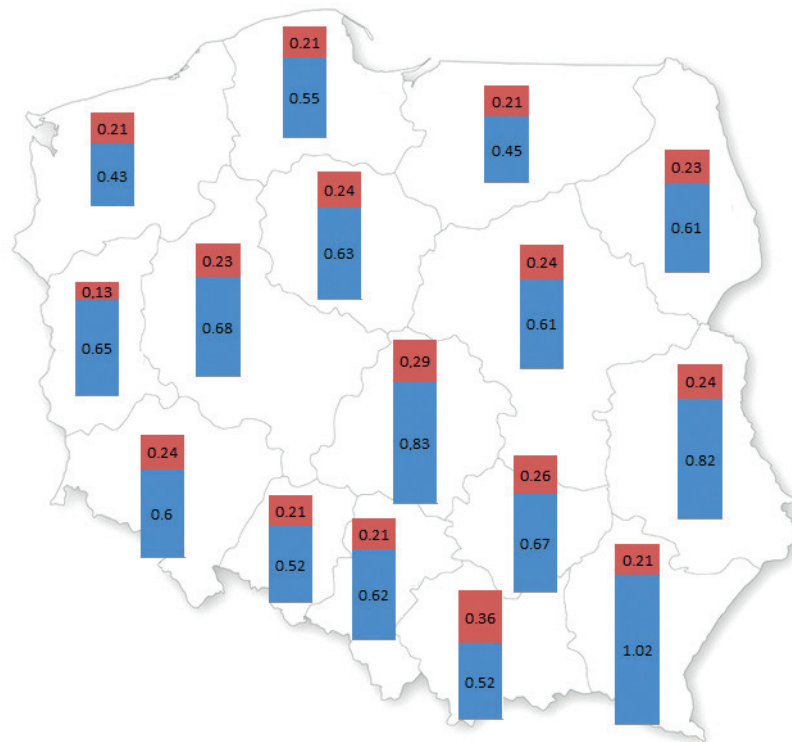
The Polish National Cancer Registry (KRN) allows analysis of morbidity and death incidence only in large gland malignancies. Data concerning small salivary gland neoplasms, due to common coding with other histopathological forms in specific anatomic locations, are incomplete. Similarly, data concerning non-malignant morbidity are unavailable. The analysis of KRN (10) data shows that in 2014 there were

478 new cases of large salivary gland cancer, of which 372 cases (78%) were located in the parotid gland. In Poland, large salivary gland neoplasms constituted 0.3% of all malignancies and 9.7% — of head and neck neoplasms [10]. The raw factor for parotid gland morbidity was 0.97 and for the sub-mandibular and sub-lingual salivary gland — 0.28. Factors standardized with respect to the European population, for the parotid and the other salivary glands, 0.78 and 0.23 respectively, and those standardized for the global population were 0.57 and 0.16 respectively [10].

In 2014, 221 new cases of salivary gland neoplasms were found in men, of which 168 cases concerned the parotid gland (76%). Salivary gland neoplasms constituted 0.27% of all malignancies and 8.5% — of head and neck neoplasms. In 2014, there were 257 new cases of salivary gland neoplasms, of which 203 cases concerned the parotid gland (76%) [10]. Salivary gland neoplasms constituted 0.32% of all neoplasms and 20.8% of head and neck cancers. In 2010–2014, among the male population, men who contracted the disease were those aged 85+ (the raw factor 7.75 was for the parotid gland and 1.2 — for the rest of the salivary glands). Similarly, among women the majority of new cases of salivary gland cancer in the recent years of 2010–2014 concerned patients over after 85 years of age (the raw factor 2.5 was for the parotid gland and 1.23 for the remaining salivary glands) [10]. Population studies in laryngological care units point to the highest morbidity in the 50–65 age bracket, which probably results from the highest percentage of patients qualifying for surgery in this age group and not from the real number of patients [1, 14, 20].

With the parotid gland, the highest morbidity was in 2014, reported in the Carpathian Province (raw factor 5.54, 118 new cases of salivary gland cancer). The lowest morbidity was noted in Lesser Poland Province (raw factor 0.36, 12 new cases) [10]. The highest number of new cases concerning other salivary gland neoplasms was reported in Podlasie Province (raw factor 0.48, 12 cases) and the lowest — in Lesser Poland Province (raw factor 0.15, 5 cases) [10]. Over the last 10 years, the most malignancies of the parotid gland were noted in the Carpathian Province and of other salivary glands neoplasms in Lodz Province. The fewest new cases of parotid gland neoplasms were in Warmia-Masuria Province and of other salivary gland neoplasms in Podlasie Province (Fig. 1) [10].

In 2014, 230 patients died of salivary gland cancer (169 of parotid gland cancer, 51 of other salivary gland neoplasms). The raw factor for deaths was 0.44 for parotid gland and 0.16 for other salivary gland malignancies [10]. Deaths due to salivary gland neoplasms were 0.24% of all deaths caused by malignancy and 8.5 of deaths caused by head and neck malignancy. Among men in 2014, there were 134 deaths, of which 98 concerned the parotid gland (73%), 0.53 — the parotid gland and 0.19 some other malignancy.



**Figure 1.** The raw factors for new cases of the parotid gland neoplasms in individual provinces (blue color) and the rest of the large salivary glands (red color) in the years of 2004–2014. Own study based on the KRN database

Salivary gland malignancies constituted 0.25% of deaths due to all malignancies and 6.7% of deaths caused by head and neck malignancy. Among women there were 96 deaths in 2014, of which in 71 cases the cause was the parotid gland cancer (74%). The raw factor was 0.36 for the parotid gland and 0.13 for the salivary gland neoplasms. Salivary gland neoplasms constituted 0.22% of deaths among all malignancies and 14% of deaths among head and neck neoplasms [10].

### Histopathological types and anatomical location

As we mentioned before, the WHO classification distinguishes 32 histopathological types, of which 23 types 85–90% of all salivary gland neoplasms [12–13]. In the Polish population, benign neoplasms constitute 79–85% of all neoplasm [5]. Benign neoplasms constitute 79–85% of salivary gland neoplasms [1, 12]. Major differences in the incidence of the particular histopathological types are in some measure caused by heterogenic reports in different countries. For example, in the population of Great Britain the majority of cancers are squamous cell carcinoma (17%) while muco-epidermoid carcinoma constitutes only 2.1% of salivary gland neoplasms [5, 15]. In the 1950s in the US population the most dominant was lymphoepithelial cancer, which accounted for as much as 25% of cases [5]. In most regions, there are two dominant histopathological types: among malignancies it is mucoepidermoid cancer

and *epithelioma adenoides cysticum* while pleomorphic adenoma and Warthin's tumor account for most cases of benign cancers [16–19].

Studies on the Polish population show that among benign neoplasms, dominant are pleomorphic adenoma and Warthin's tumor. The incidence of the former was, according to different authors, 63–75% and of the latter — 23.5–29% [1, 14, 20]. In the case of malignant neoplasms, the most common is *epithelioma adenoides cysticum* (23–25%), mucoepidermoid carcinoma (14–27%) and adenocarcinoma (14–22%). Less common is lymphoma (about 10%) and squamous cell carcinoma (6–14%). As we mentioned before, the percentage of female and male patients with salivary gland neoplasms is similar, whereby among patients with non-malignant neoplasms there is a slight prevalence of women [1, 20]. Studies based on data coming from care units operating salivary gland neoplasms show that the average age for benign neoplasms is about 10 years lower than for malignant neoplasms (50 and 60 years of age respectively). Survival data concerning the British population show that lobular carcinoma has the best prognosis (5-OS 97%), followed by mucoepidermoid carcinoma (5-OS 81%) and *epithelioma adenoides cysticum* (5-OS 80%). The worst prognoses are reported for adenocarcinoma (5-OS 50%) [11].

Boukheris et al. (29) compared the incidence of large salivary gland neoplasms in the American population according to the sex and age of 6391 patients. Among men

with the most common neoplasms, a more frequently occurring cancer was squamous cell carcinoma (20% with men and 8% with women). The median age of patients with squamous cell carcinoma was also significantly higher than the age of those with other types of neoplasm (72 vs 63 years) [21]. Survival data for the British population show the best prognosis for lobular cancer (5-OS 97%). The worst prognosis was for adenocarcinoma (5-OS 50%) [11]. Similarly, in the Dutch population the best prognosis was for lobular cancer (5-year relative survival was 97% and the worst was for adenocarcinoma (54%) and squamous cell carcinoma (46%)) [29].

Studies of the Polish population show that salivary gland neoplasms are most often located in the parotid (77–82%) and sub-mandibular gland (11–12%). Less frequently the neoplasms are situated in small salivary glands (6–11%) [1, 10, 14, 20]. These data are in accordance with analyses from other countries. In a Brazilian study, the percentage of the parotid gland neoplasms was 69.5%; for the sub-mandibular location it was 16% and in small glands it was 15% [22]. In an Iranian study in turn, 63% developed in the parotid gland, 23% were in the sub-mandibular region and 14% were located in small salivary glands [23]. Data coming from an African study, however, reveal a much higher occurrence of small salivary gland neoplasms (41.8–57.6%) [24–26]. Studies of the Polish population showed that in the parotid and sub-mandibular gland the dominant neoplasms were benign compared to malignant (82% and 71% respectively), and in the case of small salivary glands benign neoplasms occur only slightly more frequently (54 vs 46%) [14].

Studies of the Polish population show that the majority of patients are diagnosed as stage III (80%) (14). 11 (10%) of the cases were stage T4. 8 (7%) cases were qualified as T2 and 3 cases (3%) as T1 [14]. Data from the Dutch popu-

lation show that among men there is a similar percentage of patients at early stages of advancement (stage I, II and III, IV were 46 and 47.5% respectively). Female patients were most often those presenting early stages of advancement (stage I, II — 2.1%, stage III, IV — 31.6%) [29].

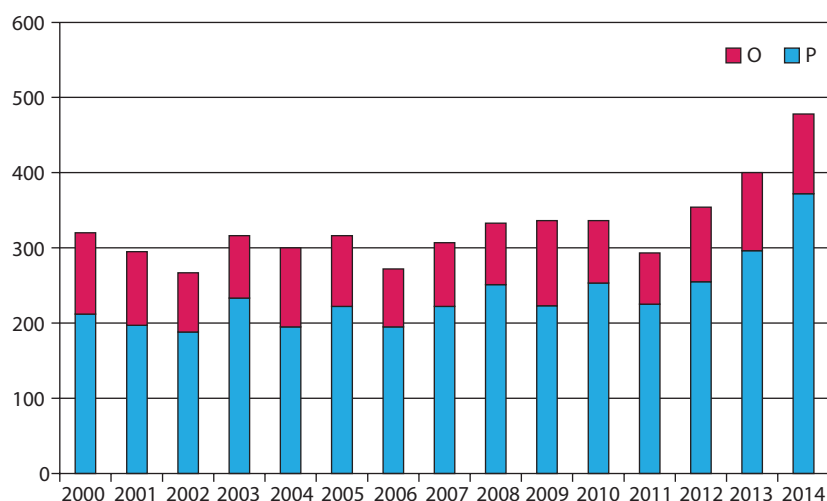
### Trends of incidence and deaths

KRN data analysis from the last 15 years reveals a similar incidence rate for salivary gland neoplasms with a slight increase of incidence in the past two years, which may, however, be connected with increased reporting of that incidence [10]. Men account for a slim majority (51–62%). 2014 was an exception, though, where the rate was higher for women (54). The highest incidence concerned the parotid gland, although there has been a slight growth in the last years (66% in 2000, 78% in 2014) [10] (Fig. 2, 3).

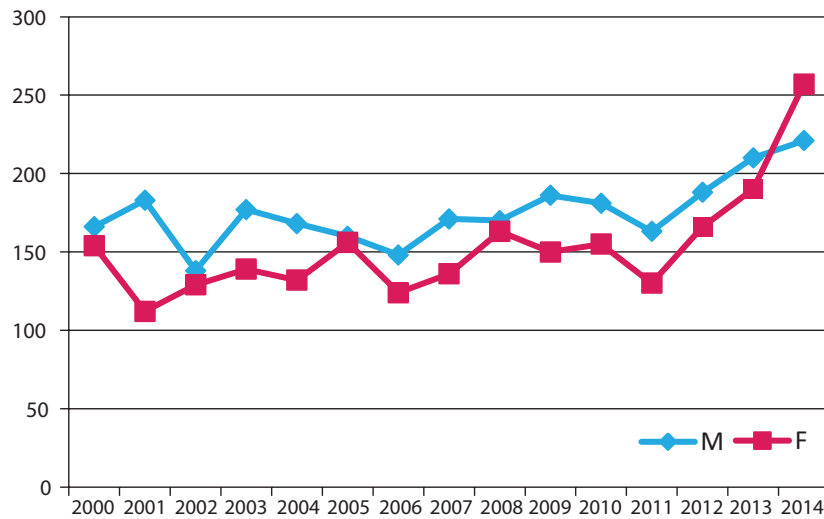
In the last few years there has been a minor increase in deaths from 158 in 2000 to 230 in 2014. The majority of deaths concerned men (52–66%). Deaths occurred mostly in the case of neoplasms located in the parotid gland (57–73%) and, like with the morbidity rate, there has been an insignificant rising tendency from 57% in 2000 to 73% in 2014 (Fig. 4, 5).

Studies of world literature show a slight increase of the number of cases in the last few years (1990–2005). In a large study by DAHANCA, the raw factor for morbidity was 1.1/100 000 and has been exhibiting a rising tendency in the last few years (1990–2005).

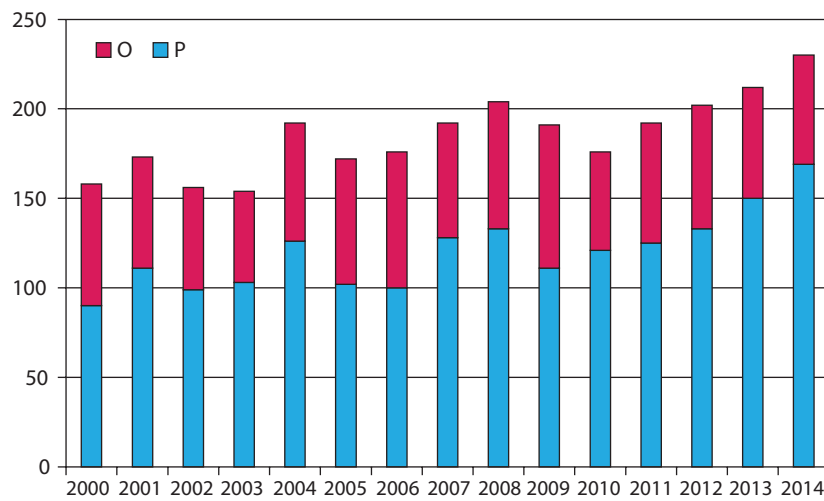
Similarly, there has been a small growth in the Chinese and British population [11, 28]. On the other hand, in the Dutch and Swedish population the incidence has been stable [21, 29, 30]. As was mentioned before, over the previous 25 years, the percentage of US patients with salivary gland neoplasms has grown significantly (from 0.1% to 1%) [2].



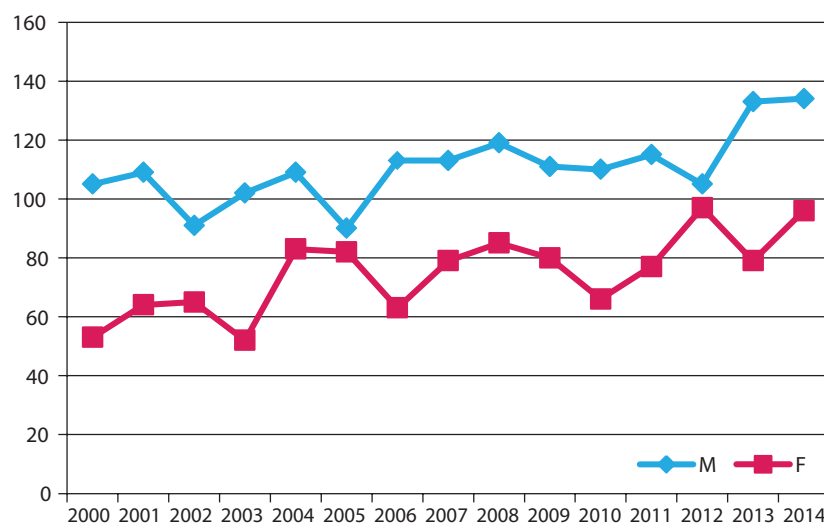
**Figure 2.** The incidence rate of salivary gland neoplasms in the years 2000–2014 including the site. P – parotid gland, O – other. Own study based on KRN data



**Figure 3.** The incidence rate of salivary gland neoplasms in the years 2000–2014 according to sex. M – men, F – women. Own study based on KRN data



**Figure 4.** Deaths due to salivary gland cancer in the years 2000–2014 according to site. P – parotid gland, O – other. Own study based on KRN data



**Figure 5.** Deaths due to salivary gland cancer in the years 2000–2014 according to sex. M – men, F – women. Own study based on KRN data

The US data show a constant level of survival at 68% [11]. On the other hand, the British data show a small improvement of survival [11]. In the periods 1994–2003 and 2004–2013, 5-OS improved by 5% and 10-OS — by almost 6% [11]. Dutch data, on the other hand, reveal slightly poorer survival [29]. Assuming that the relative co-efficient of survival in the years 1989–1993 was 1, in the years 1994–1998 it was 0.97 and in the years 2007–2010 it was 0.84. In the years 1999–2002 and 2003 there was a minor improvement of survival. RER (Relative Excessive Risk of Dying) was 1.1 and 1.03 respectively during that period [29]. The analysis of the RARECARE database shows that survival data are close to those from the previous years [7]. The percentage of 1- and 5-year survival of patients treated in the years 1995–1999 was 87 and 69% respectively. For men, the values were 84 and 60% and for women they were 91 and 80%. As in the years 2000–2002, younger patients and the Western European population had a better outlook [7].

## Conclusion

Epidemiological data show that salivary gland cancer both in the global population as well as in the Polish population is a rare head and neck cancer, and it occurs slightly more often in women. The most frequently occurring salivary gland neoplasm is parotid gland cancer. Salivary gland neoplasms are histologically a highly heterogeneous group differing in the frequency of occurrence, course and prognosis. In the last few years, the number of new cases has been roughly similar with a slightly rising tendency. The percentage of deaths has stayed on the same level in the said period. Women as well as patients with lobular and parotid gland cancer have a better outlook.

**Conflict of interest:** none declared

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