Risk factors for salivary gland cancers in France: Results from a case-control study, the ICARE study

Loredana Radoï,a,b,⁎, Christine Barulc, Gilles Menvielle,c, Matthieu Carton,c, Mireille Matraf,g,h,i,
Marie Sanchez,a, Corinne Pilorget,h,i, Michel Velten,j, Isabelle Stücker,a, Danièle Luce,c, ICARE Study Group1

a University Paris Sud, Paris Saclay University, UVSQ, CESP, INSERM, Environmental Epidemiology of Cancer Team, Villejuif, France
b University Paris Descartes, Faculty of dental surgery, Oral surgery department, Paris, France
c University Paris 13, Sorbonne Paris Cité, IPSL, PSL Research University, IRCCS, Biostatistic, Saint-CLOUD, France
d University Paris Est Créteil, Faculté de médecine, Créteil, France
e Institut Curie, PSL Research University, DRCI, Biométrie, Saint-Cloud, France
f Université Paris Est Créteil, Service des Pathologies Professionnelles et de l’Environnement, Créteil, France

1 Members of ICARE Study Group: Anne-Valérie Guizard (Registre des cancers du Calvados, France); Arlette Danzon, Anne-Sophie Worono (Institut National de la Santé et de la Recherche Médicale, UMR 8027, Paris, France); Claude Barulc, Gwenn Menvielle (Sorbonne Universités, Université Paris 06, INSERM, Hôpital Paul Brousse, Bat 15 /16 16 av PV Couturier, 94807 Villejuif Cedex, France).

⁎ Corresponding author at: Centre de Recherche en Épidémiologie et Santé des Populations, U1018, INSERM, Hôpital Paul Brousse, Bat 15 /16 16 av PV Couturier, 94807 Villejuif Cedex, France.
E-mail address: loredana.radoi@inserm.fr (L. Radoï).

1 University Lyon, Claude Bernard Lyon1 University, Ifsttar, UMRESTTE, UMR T 9405, Lyon, France
2 The French Public Health Agency, Department of Occupational Health, Saint Maurice, France
3 Centre Hospitalier Intercommunal, Service des Pathologies Professionnelles et de l’Environnement, Créteil, France
4 The French Public Health Agency, Department of Occupational Health, Saint Maurice, France
5 University Lyon, Claude Bernard Lyon1 University, Ifsttar, UMRESTTE, UMR T 9405, Lyon, France
6 Bas-Rhin Cancer Registry, Strasbourg, France

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ABSTRACT

Objectives: Epidemiological studies on the risk factors for salivary gland cancers (SGC) are rare, concern a small sample size, and show inconsistent results. The aim of the present work was to analyze several risk factors for SGC, using the data from the ICARE study, a multicenter, population-based case-control study.

Materials and methods: Data from 73 SGC cases and 3555 controls were collected using a standardized questionnaire on lifestyle habits, personal and family medical history, and lifetime occupational history. Odds ratios (OR) and 95% confidence intervals (CI) were estimated using unconditional logistic regressions.

Results: Tobacco use and alcohol consumption were not associated with the risk of SGC. A history of head and neck cancer or that of cervicofacial radiotherapy was associated with a higher risk of SGC (OR = 17.06, 95% CI: 4.34–67.05, and OR = 31.74, 2.48–405.25, respectively). Significantly increased risks were observed for some occupations: waiter (OR = 2.94, 1.11–7.78), charwoman (OR = 3.02, 1.38–6.60), electrical and electronic equipment assembler (OR = 7.16, 2.02–25.38), plumber (OR = 3.95, 1.33–11.67), electric arc welder (OR = 6.15, 1.76–21.48), sheet-metal worker (OR = 2.89, 1.01–8.32), building painter (OR = 3.42, 1.01–11.49), and material handling equipment operator (OR = 5.05, 1.71–14.84). Results for industries were consistent with those observed for occupations.

Conclusion: Our results showed that a history of head and neck cancer, cervicofacial radiotherapy, and several occupations and industries, were associated with an increased risk of SGC. Further studies with larger sample sizes are indicated to confirm our results.
Introduction

The major salivary glands occur in three pairs (the parotid, submandibular, and the sublingual glands), while the minor salivary glands occur as several hundred structures scattered within the mucous membranes of the mouth, oropharynx, larynx, nose, and the paranasal sinuses. In France, the cancers of the major salivary glands are rare, with an estimated incidence of 0.7/100,000 person-years in men and 0.5/100,000 person-years in women [1], and account for 1.9% and 8.6% of head and neck cancers (HNC) in men and in women, respectively [2]. The incidence rates of the cancers of the minor salivary glands have not been estimated.

The etiology of salivary gland cancers (SGC) is not well known. Unlike most HNC, the SGC are not generally considered to be related to tobacco smoking and alcohol drinking, although some studies showed an increased risk in smokers [3–5] and drinkers [4,6]. The only established risk factor is the exposure to ionizing radiation, particularly during radiotherapy [4,6–10] and during dental or cervicofacial radiological examinations [4,9,11]. The role of several occupational exposures has been suggested [4,6,10–23], a high body mass index (BMI) [13,23], the use of mobile telephones [24–29], a family history of cancer [13], and certain viral infections [30–35].

Epidemiological studies on the risk factors for SGC are rare, concern a low number of cases, and show inconsistent results. Moreover, most studies have focused on the major SGC (occasionally restricted to parotid gland neoplasms), and have sometimes included both benign and malignant tumors, despite the fact that certain types of benign tumors (e.g., Warthin’s tumor) are strongly related to tobacco smoking [5,12,36]. Only two studies have included both major and minor SGC [3,37].

In this context, the objective of the present work was to study the role of several non-occupational and occupational risk factors in the occurrence of SGC, based on the data from the ICARE (Investigation of occupational and environmental CAUSES Of REspiratory cancers) study.

Material and methods

Study population

The details of the study design have been reported previously [38]. Briefly, the ICARE study is a multicenter, population-based case-control study, which was conducted between 2001 and 2007 in 10 French départements (geographic and administrative areas), covered by general cancer registries. The study included 2926 lung cancer cases, 2415 HNC cases, and 3555 control subjects. Incident cases were identified in collaboration with the French cancer registries. All cases were histologically confirmed primary tumors occurring in patients aged 18 to 75 years at diagnosis. Controls were selected by list-assisted random digit dialing sampling and an incidence density sampling method, from the general population of the départements included in the study. In each département, controls were frequency-matched to all cases (lung cancer and HNC) by sex and age. Additional stratification was used to achieve a socioeconomic status distribution among the controls comparable to that of the general population of each département.

Study sample

The present analysis was restricted to SGCs and the controls of the ICARE study. Patients with primitive cancers of the major salivary glands (parotid, submandibular, and sublingual glands) (topographical codes C07-C08 and all morphological codes of the International Classification of Diseases for Oncology, ICD-O-3) or with primitive cancers of the minor salivary glands (topographical codes C00-C14, C30.0, C31, and C32 and morphological codes 8147, 8200, 8290, 8310, 8430, 8440, 8450, 8480, 8500, 8525, 8550, 8562, 8941, 8980, and 8982 of the ICD-O-3) [39] were identified. Among the 116 eligible patients, 22 could not be reached, 7 were deceased, and 3 were too sick to be interviewed. Of the 84 patients who were contacted, 11 refused to participate. Among the 4673 eligible control subjects, 230 could not be reached, 5 were deceased, and 27 were too sick to participate. Of the 4411 subjects who were contacted, 856 refused to participate. Finally, 73 patients and 3555 controls were included in the analysis (participation rates: 86.9% and 80.6%, respectively). Eligible subjects who were contacted but who refused to participate had a sex and age distribution similar to that of the included subjects.

Each subject gave written informed consent. The study was approved by the Institutional Review Board of the French National Institute of Health and Medical Research (IRB-Inserm, No. 01-036), and by the French Data Protection Authority (CNIL No. 901220).

Data collection

Using a standardized questionnaire, subjects were interviewed face-to-face by trained interviewers to collect information on socio-demographic characteristics, anthropometric characteristics, personal and family history of cancer, lifetime tobacco and alcohol consumption, and lifetime occupational history, with a detailed description of each job held for at least one month during the working life.

Several parameters were available for both tobacco smoking and alcohol drinking: status (never, current, former), quantity, duration, and lifetime cumulative quantity (pack-years/glass-years). Ever smokers were defined as subjects who had smoked at least 100 cigarettes in their lifetime or those who had smoked at least one pipe, cigar, or cigarrillo per week for at least one year. Ever drinkers were defined as subjects who had consumed at least one drink per month for at least one year. Former smokers and former drinkers were defined as subjects who had not smoked or consumed alcohol for at least two years before the interview for the controls and before the diagnosis for the cases. The quantity of tobacco smoked (g/day) and alcohol consumed (standard glasses/day) were calculated by using the average lifetime daily consumption of all types of products consumed.

BMI was computed as weight (kg) divided by height squared (m²) and categorized into four classes: < 18.5 (underweight), 18.5–24.9 (normal weight), 25.0–29.9 (overweight), and > 30 (obesity).

Using data from the occupational history questionnaire, trained coders blinded to case or control status coded industries according to the French Nomenclature of Activities (NAF, 1999) [40] and coded occupations according to the International Standard Classification of Occupations (ISCO, 1968) [41].

The assessment of occupational exposures (to chlorinated, oxygenated and petroleum solvents, asbestos, silica, cement, refractory ceramic fibers, and mineral wool) was made by using job-exposure matrices (JEMs), developed by the French Public Health Agency [42].

For each combination of ISCO and NAF codes, the JEMs assigned three exposure indices: probability of exposure (percentage of exposed workers), intensity of exposure, and frequency of exposure (percentage of the working time during which the subject was exposed) [42]. For each subject, we derived from his or her entire occupational history the exposure status, the cumulative duration of exposure, and the cumulative exposure index (CEI). Regarding the exposure status, a subject was considered ‘ever exposed’ if he had at least one job with a non-zero probability of exposure. The cumulative duration of exposure was defined as the sum of all exposure durations. The CEI was calculated as the sum of the values obtained by multiplying the weighted duration, probability, intensity, and frequency of exposure for each exposure period in the entire professional life.

Statistical analysis

Unconditional multivariable logistic regression was used to estimate odds ratios (ORs) and 95% confidence intervals (95% CI) for tobacco
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