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Original article

Epidemiological features of cancers of the oral cavity, oropharynx, hypopharynx and larynx cancer in Réunion Island

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ABSTRACT

Introduction: This study had two objectives: firstly, to identify and compare characteristics of cancer of the oral cavity, oropharynx, hypopharynx and larynx in Réunion Island, a tropical French overseas territory in the southern hemisphere; and secondly, to discuss how incidence of these cancers is presented in the international literature.
Material and method: A retrospective study included 599 patients diagnosed with cancer of the oral cavity, oropharynx, hypopharynx or larynx between 2009 and 2013 in Réunion Island. Demographic characteristics and data on alcohol consumption, smoking habits and HPV infection were analyzed. Standardized incidences were calculated for the worldwide population for both genders.
Results: Sex ratio was 7.7 and mean age was 60 years. Cancer consisted of squamous cell carcinoma in 99.1% of patients. Three hundred and forty over 375 patients (81.25%) showed alcohol abuse; 309/359 (86.1%) were smokers; 31/184 (16%) had HPV infection. On the International Agency for Research on Cancer (IARC) anatomic classification, the incidence of "other pharynx" locations was 9.3/100,000 for men and 0.7/100,000 for women, and incidence of "larynx" locations was 6.4/100,000 for men and 0.4/100,000 for women.
Conclusion: Réunion Island features some particularities in terms of incidence: women are less than half as likely as in Metropolitan France to develop any type of cancer, whereas incidence in males is among highest in France. The presentation of results in cancer registries could be improved in line with everyday practice in head and neck surgery.

1. Introduction

In 2013, the French national health-watch institute (Institut National de Veille Sanitaire: INVS) reported that the 4 most frequent cancer locations in France, taking male and female patients together, were the breast, colon/rectum, lung and bladder [1]. Next came oral cavity and larynx, with incidence of 5.6/100,000 in females and 16.1/100,000 in males, close to the figures for cancers of the kidney, pancreas and uterus and melanoma [1]. Cancer of the larynx had the lowest incidence, at 0.96/100,000 in females and 5.62/100,000 in males, close to the figure for testicular cancer [1]. These data were derived from 21 local registries: 11 general, 10 specialized, totaling 925,242 cases; Réunion Island, however, was not included, although it has had its own registry since 1988. In view of this gap in the data, we performed a retrospective study of epidemiological characteristics of patients with cancer of the oral cavity, pharynx (other than nasopharynx) or larynx diagnosed between 2009 and 2013, and compared data for this cohort with French national and local data, particularly in terms of prevalence of alcohol and nicotine dependence and HPV infection, according to gender, cancer location and sublocation; we also specified the standardized worldwide incidences for males and females.

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Table 1
Study population characteristics.

	All		Female		Male	
	n	%	*n*	%	*n*	%
Oropharynx	225	37.6	23	33.8	202	38
Nicotine dependence	121/135	89.6	11/16	68.7	110/119	92.4
Alcohol dependence	113/135	83.7	6/16	37.5	107/119	89.9
HPV infection	22/68	32.4	4/10	40	18/58	31
Larynx	159	26.5	10	14.7	149	28
Nicotine dependence	95/98	96.9	4/5	80	91/93	97.8
Alcohol dependence	94/113	83.1	2/6	33.3	92/107	85.9
HPV infection	1/44	2.3	0/0	0	1/44	2.3
Oral cavity	129	21.5	31	45.6	98	18.5
Nicotine dependence	53/69	76.8	4/11	36.4	49/58	84.5
Alcohol dependence	48/67	71.6	3/11	27.3	45/56	80.3
HPV infection	5/41	12.2	0/6	0	5/35	14.3
Hypopharynx	86	14.4	4	5.9	82	15.5
Nicotine dependence	95/98	96.9	1/2	50	51/55	92.8
Alcohol dependence	54/60	90	1/2	50	53/58	91.4
HPV infection	3/31	9.7	1/1	100	2/30	6.7
Total	599	100	68	11.4	531	88.6
Nicotine dependence	309/359	86.1	20/34	58.8	301/325	92.6
Alcohol dependence	340/375	81.25	12/35	34.3	297	87.3
HPV infection	31/184	16.9	5/17	29.4	26/167	15.6

2. Material and method

A retrospective study, approved by the French data protection commission (Commission Nationale d'Informatique et Liberté: CNIL), analyzed files for 599 patients with cancer of the oral cavity, pharynx or larynx diagnosed between January 1, 2009 and December 31, 2013 in public ($n = 3$) or private ($n = 3$) health-care structures and followed up by an ENT or maxillofacial surgeon, radiotherapist or oncologist in Réunion Island. No other medical centers on the Island manage this kind of pathology, due to absence of relevant specialists. Inclusion was based on lists provided by the Island's 3 multidisciplinary ENT meetings, which were compared to data in the local registry. To optimize exhaustiveness, the Réunion ENT Society (Société des ORL de la Réunion: SORLOI), of which all ENT specialists in Réunion Island are members, was asked to provide data for patients who had left the Island for treatment following or without a local multidisciplinary team meeting. Exclusion criteria comprised: residence outside Réunion Island, precancerous pathology (dysplasia, in situ carcinoma), recurrence, involvement by extension of a contiguous tumor, and cancerous cervical lymph-nodes of unknown primary cancer.

Epidemiological data comprised: histology, location and sublocation, TNM stage on the 2010 UICC classification [2], age, gender, smoking status (pack-years: data for 359 patients), alcohol status (threshold of 2 glasses of wine equivalent per day: data for 375 patients), and Human Papilloma Virus (HPV) status (data for 184 patients) assessed by p16 protein expression on immunohistochemistry, with a threshold of > 10% on strong diffuse cytoplasmic and nuclear labeling. (HPV screening was not intended to establish a causal relation with cancer, for which p16 protein is insufficient [3]). Prevalences of alcohol and nicotine dependence and HPV infection were reported according to gender, cancer location (Table 1) and sublocation, and compared to standardized worldwide incidence for both genders.

Statistical analysis used SAS software, version 9.2 (SAS Institute, Cary, NC, USA), with Chi^2, Fisher exact, Student and Mann–Whitney U tests, with a significance threshold of $P < 0.05$. Standardized incidences were based on estimates of the Réunion Island population on July 1st of the year in question according to the National Statistics and Economic Studies Institute (Institut National de la Statistique et des Études Économiques: INSEE) for the period 2009–2013 [4], and on the world population according to the International Agency for Research on Cancer (IARC) [5]. Standardized incidence according to cancer location in the worldwide population for both genders was calculated based on the two anatomic classifications of the French National Cancer Institute (INCA) [6] and of the IARC [7] using the International Classification of Diseases (ICD-10) [8] within the Programme de Médicalisation des Systèmes d'Information (PMSI) medical information system used in France to record cancer patients' data in the local registries. In both the INCA and the IARC classifications, any new location non-contiguous with the index cancer (e.g., for the larynx: cancer of the laryngeal side of the epiglottis following vocal fold cancer) is not taken into account, even with onset more than 5 years later; likewise, any new location occurring within the same anatomic category (e.g., tonsillar cancer following cancer of the lips, both of which come under the INCA lip/mouth/pharynx category). Data from the present cohort for nasopharynx and salivary gland cancer were used to calculate incidence for the respective anatomic categories (lines 1 and 4 in Table 2), although the corresponding sublocation incidences in Réunion Island are not shown in Table 2, for the sake of oncologic homogeneity.

We thus calculated incidence per anatomic category following the IARC and INCA, but also according to the locations actually used by clinicians (oral cavity, oropharynx, hypopharynx, larynx), so as to have more specific data.

3. Results

3.1. Population and risk factors

The sex ratio was 7.77: 531 male (88.6%) and 68 female patients (11.4%). Mean age was 60 years (range, 28–88 years) for males and 62 years (range, 38–90 years) for females. Among the patients, 18.56% (99/531) were born outside of Réunion Island.

Among the patients, 81.25% of whichever gender (340/375), were alcoholic, with significant male predominance: 297 male vs. 14 female; $P < 0.0001$; 86.1% (309/359) were smokers, with a mean consumption of 37 pack-years (range, 2–120 pack-years, for males and females), and once again significant male predominance: 301 male vs. 20 female; $P < 0.00001$. Sixteen percent (31/184) had HPV infection: 26 male, 5 female (NS); 22 of the 31 patients with HPV infection were nicotine-dependent.

Table 1 shows prevalence of alcohol and nicotine dependence and HPV infection according to gender and cancer location. There were significantly fewer smokers among patients with oral cavity cancer than for other locations: $P = 0.021$ vs. oropharynx, $P = 0.031$ vs. hypopharynx, and $P < 0.001$ vs. larynx. There were significantly fewer alcoholics among patients with oral cavity cancer than for the hypopharynx ($P = 0.009$). HPV infection was detected in 31 of the 184 patients who were screened (16.8%): 26 male, 5 female (NS). HPV rates were significantly higher ($P = 0.0007$) in cancer of the oropharynx (32.4%; 22/68) than for other locations: oral cavity (12.2%; 5/41), hypopharynx (9.7%; 3/31), or larynx (2.3%; 1/43). In oropharyngeal cancer, the palatine tonsils were significantly more often the sublocation infected by HPV (43.3%; 22/68; $P = 0.01$). Seventy-one percent of HPV-positive patients (22/31) were also nicotine-dependent.

3.2. Topography, type of cancer and standardized incidences

Of the cancers, 99.1% (594/599) consisted of squamous cell carcinoma. The other 5 comprised: 2 cystic adenoid carcinomas, 1 adenocarcinoma, 1 accessory salivary gland cystadenocarcinoma, and 1 undifferentiated nasopharyngeal carcinoma exclusively involving the tonsils. There were 10 primary tumors synchronous to the ENT cancer (1.67% of cases): 6 involving the esophagus, 2 the lungs and 2 the liver. Table 2 shows the distribution of loca-

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