Lip Cancer: A 10-Year Retrospective Epidemiological Study

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Abstract. *Background: Lip cancer is the most frequent tumor of the oral-maxillary region. A high incidence of lip cancer has been reported among the Italian population over the past decade. Materials and Methods: This retrospective study analyzes epidemiological data and risk factors for lip cancer among patients who presented to our department between 2000-2010. Statistical analysis for this study was calculated employing Student T and χ-square tests. Results: Of 540 cases, most were found among men (82%), and those aged over 45 years (84.8%). The dominant cancer type was squamous cell carcinoma of the external lower lip (predominantly in men). We recorded high rates of chronic solar exposure, and tobacco and alcohol drinking habits in patients with squamous cell carcinoma. Conclusion: Individuals aged over 45 years are at higher risk for lip cancer. The high association of the examined risk factors with the rate of squamous cell carcinoma confirms their role in the development of this type of tumor.*

Oral and pharyngeal cancer, grouped together, are the sixth most common type of cancer worldwide. While the incidence of lip cancer is low (1-2%) (1-4) this is the most frequent tumor of the oral-maxillary region, comprising the 25-30% of all oral cancer. In the head and neck region, squamous cell carcinomas (SCCs) of the lip is second only to skin cancer in terms of frequency (5). SSC is the most represented histological type (more than 90%), while basal cell carcinoma (BCC) is uncommon in this anatomical site (less than 10%). BCCs generally occur in the upper lip and do not usually develop lymph node metastases (3, 6). In contrast, SCCs develop most often in the lower lip, with a possibility of neck metastases. Lip carcinomas frequently appear on top of pre-cancerous lesions, such as radiodermitis, chronic cheilitis and xeroderma pigmentosum. The combination of long-term exposure to ultraviolet (UV) radiation from exposure to sunlight and a fair skin has been proposed as one of the etiological factors in the epidemiology of lip cancer (7). Surgery is the treatment of choice for most of the tumors of the lip and full thickness resection is the surgical procedure indicated. The lips constitute the principal feature of the lower face, playing a major role in facial appearance and function and their reconstruction still represents a significant challenge to the reconstructive surgeon.

The purpose of this study was to provide information about the clinicopathological features of lip cancer in patients in our sample during a 10-year period, and to investigate risk factors associated with the development of this type of tumor.

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Key Words: Lip cancer, squamous cell carcinoma, basal cell carcinoma, risk factors.

Patients and Methods

This retrospective study analyzes 540 (female: 97; male: 443) fully reviewed cases of lip lesions registered from 2000 to 2010 at the Department of Plastic and Reconstructive Surgery of the Umberto I Policlinic of the "Sapienza" University of Rome. The inclusion criteria were an age range between 32 and 92 year and histological diagnosis of SCC or BCC.

Lip cancer incidence distributions were analyzed by available registered data: gender (female and male), age (those aged 45 years or less and older), histological diagnosis (BCCs and SCCs), site of lip cancer (lower and upper lip), chronic solar exposure (exposed and not-exposed), tobacco and alcohol habits (absent and present). Stage of cancer at the diagnosis was not available from the registry. The influence of chronic solar exposure and tobacco and alcohol habits were analyzed. Chronic solar exposure was classified as present or absent. Cases considered exposed to chronic solar exposure had cumulative and intense solar exposure in the workplace such as farmers, construction employees or garbage collectors. Nonexposed was the person that did not report occupational chronic solar exposure, such as teachers or dentists.

Drink habit was also investigated. Alcohol drinking habit was classified as present or absent. In a similar way, tobacco habit was also investigated as present or absent. Ex-drinkers and ex-smokers were those who had abstained from any type of drinking and smoking for at least 10-years. Non-smokers and ex-smokers, like non-drinkers and ex-drinkers were grouped combined.

None of the patients examined presented metastases at the time of diagnosis.

Descriptive analysis of clinical, and morphological variables of the BCC and SCC patients of this study were calculated employing Student's t and χ-square tests. The level of statistical significance was chosen as p-Value<0.05. The statistical processing was conducted employing SPSS (Chicago, Illinois, USA).

Results

The total number of new malignant cases diagnosed as lip cancer between 2000 and 2010 was 540, which comprised 443 male (82%) and 97 (18%) female. The male-to-female ratio was 4.6:1. The majority of individuals were older patients [458 (84.8%)] with a mean age±SD of 65.4±13.6. The external lower lip was affected in 426 cases (78.9%) while the external upper lip in 114 cases (21.1%).

The most common histological type was SCC, with 436 (80.7%) of the total number of cases. Tobacco and drink habits were present in 394 cases (73%) and 375 cases (69.4%) respectively, and 389 (72%) patients had a history of chronic exposure to solar radiation. Table I shows tobacco and drink habits and solar radiation exposures among gender: there was a significant difference in habits and solar radiation exposures among men and women (p-Value<0.001) with a major incidence in men.

The diameter of the tumor was less than 0.5 cm in 149 (27.6%) of patients, between 0.5 cm and 1 cm in 232 (43%) patients, between 1 cm and 2 cm in 83 (15.4%) patients and more than 2 cm in 27 (5%) patients.

The descriptive statistics of lip cancer distribution in our study and its association with investigated risk factors are presented in Tables II and III. The SCCs involved mainly the lower lip [423 cases (99.3%)] and BCCs occurred principally in the upper one [101 cases (88.6%)]. There was also a significant difference in SCCs and BCCs among men and women. SCCs was more frequent in males [410 cases (92.5%)] while BCCs were typically found in females [71 cases (73.2%)].

A significant association between work-related chronic solar exposure and incidence of cancer in the lower lip, and also with tobacco and alcohol habits, and in these cases, SCC was the most frequent histological type (Table II).

Table III shows the association between the analyzed risk factors and tumor position; there was a significant association between them and the incidence of lower lip tumors (p-Value<0.001).

Discussion

Approximately 25% of all oral tumors are carcinomas of the lip, although some reports claim a tendency of this percentage to decrease (1, 4, 8). The lip is the most prevalent site of oral cancer in some geographical areas, *e.g.* Australia, Canada and Spain (4, 7, 9). The major histological types of lip cancer are SCC and BCC.

The tumor, in its initial phase, usually appears as a papule or a plate which tends to progress into a vegetative or ulcerative form. In these cases, a biopsy is indispensable to confirm the diagnosis of carcinoma. Although in the case of T1 or T2 lesions, the percentage of patients with lymph node metastases at the time of diagnosis is 8%, this figure increases considerably in advanced-stage tumors, making it necessary to search for possible cervical metastatic adenopathies (2).

Different risk factors have been associated with lip tumors such as age, chronic exposure to solar radiation and tobacco and alcohol habits. Several reports suggested the pathogenic role of some viral factors, such as Human Papilloma Virus (HPV) 16 and 24 and Herpes Virus (HSV) 1 and 2, especially in immune-depressed individuals (10, 11). In particular, the association of HSV2, exposure to UV rays and chemical factors can considerably increase the risk of these tumors (8).

In our retrospective analysis of a large number of cases, we were able to characterize the two most common lip cancer types and to correlate these with age, sex, anatomical site and risks factors of solar radiation exposure and tobacco and alcohol drinking habits.

In accordance to the literature data, we found an increase in lip cancer incidence with increasing age (12). In our sample, lip carcinomas were most frequent in those aged 60-70 years, with a mean age of 65.4±13.6 years. This could be a result of accumulation of molecular changes due to exposure to factors such as tobacco and other carcinogens, or as part of the biological ageing process that has been shown to be linked to accumulation of DNA damage (13, 14).

SCC is the most frequent histological type of malignant tumor of the lip region, as shown in our sample, while BCC is uncommon in this area. Some authors doubt that this histological type is a primary lesion of the lip and suggest that it probably arises in the skin from where it subsequently infiltrates the vermillion border and labial mucosa.

Another important feature is the difference in incidence and tumor type distribution according to sex. We found a higher number of lip cancer cases among men than women, with a male to female ratio of 4.6:1. These differences might be due to occupational and behavioral differences between the sexes: a higher percentage of men working outdoors or taking part in outdoor leisure activities. Some investigators have also suggested the value of women's lipstick, a known protector against solar exposure of the lip (15). Carcinomas of the lower lip most frequently occur in male smokers working in the open air, such as sailors, fishermen and farmers. It occurs especially among Caucasians. Dark skinned people are probably protected against UV rays by their natural skin pigment (16).

In accordance to the literature data, we also found that SCC is the most frequent histological type among men, while BCC is more frequent in women.

The lower lip is the most affected anatomical site (2, 6, 17) and SCCs are the most frequent in these patients. The higher occurrence of disease of the lower lip has been attributed to its position, which usually means that it receives a higher exposure to solar radiation and is also more subjected to the action of the other factors such as tobacco and alcohol (16).

Table I. *Statistical analysis of variables and gender.*

Variables	Male, n	Female, n	*p*-Value
Smoking (no/yes)	83/360	63/34	<0.001
Alchol (no/yes)	107/336	58/39	<0.001
Solar radiation (no/yes)	79/364	72/25	<0.001

Table II. *Statistical analysis of variables and tumor histology.*

Variable	SCC, n	BCC, n	*p*-Value
Sex (male/female)	410/13	33/71	<0.001
Position(upper/lower)	13/423	101/3	<0.001
Smoking (no/yes)	60/376	86/18	<0.001
Solar radiation (no/yes)	53/383	98/6	<0.001
Alchol (no/yes)	88/348	77/27	<0.001

SCC: Squamous Cell Carcinoma; BCC: Basal Cell Carcinoma.

Table III. *Statistical analysis of variables and tumor anatomical site.*

Variables	Lower lip, n	Upper lip, n	*p*-Value
Gender (male/female)	399/27	44/70	<0.001
Smoking (no/yes)	51/375	19/95	<0.001
Solar radiation (no/yes)	43/383	108/6	<0.001
Alchol (no/yes)	78/348	87/27	<0.001

As reported in the literature data (3, 17, 18), in our study, nearly all cases of SCC occurred in the lower lip, while BCCs were generally located in the upper lip. Interestingly, this finding gives credit to many authors that suggested that the etiology of upper lip cancer could be regarded as a separate entity and different from that of the lower lip (19).

In our series, there is evidence to confirm the independent effect of exposure factors related to lip carcinoma. We found a significant association between lip cancer and risk factors such as solar radiation exposure and tobacco and alcohol drinking. Chronic exposure to solar ultraviolet radiation is the most widely accepted cause of lip cancer. UVB radiation, together with UVA, produces mutations in DNA. Tumor development is the result of failure to repair these mutations (10, 20). Exposure to UV radiation is measured by lifelong cumulative exposure to sunlight. Accumulated solar exposure during work is associated with a constant level of exposure over the years. This is consistent with the greater frequency of lip cancer in males and with previous findings concerning the prevalence of agricultural, forest and fishery professions in relation to this type of cancer. It is also coherent with the fact that lip cancer is rare on the upper lip.

As suggested above (21, 22), the occurrence of tobacco and alcohol drinking habits were significant in our sample: 72.96% of patients were smokers and 72.04% had an alcohol habit. Smoking is an important factor in lip SCC and the malignant lesion will occur in the location where the cigarette, cigar or pipe is placed (7, 23). We found a significant association between tobacco habit and SCC of the lower lip. The same finding was made for alcohol drinking habit. It is probable that tobacco and alcohol beverage products might also be associated with occurrence of the disease in the lower lip.

Some authors found an interaction between alcohol consumption and the habit of leaving the cigarette on the lip while smoking, which is independent of the cumulative amount of tobacco smoked (7). So, according to them, the effect of alcohol is more important in those with this habit.

Conclusion

In conclusion, we have reported higher levels of lip cancer among men and those above 65 years of age. In the external lower lip, most cases were SCC, more commonly among men. In the external upper lip tumors were more common among women and most cases were BCC. The low incidence of external upper lip cancer, BCCs and the absence of a significant association with solar exposure, and tobacco and alcohol use may indicate that this histological type of lip cancer is not associated with these risk factors in the present population.

Our findings showed that SCC patients exhibited typical epidemiological and clinical profiles as noted in other studies. These findings can be useful for stimulating the creation of health promotion strategies.

Acknowledgements

The Authors have no financial interest to declare in relation to the content of this manuscript.

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Received February 21, 2012
Revised March 16, 2012
Accepted March 19, 2012