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Oral health, hygiene practices and oral cancer

Saúde bucal, práticas de higiene bucal e ocorrência de câncer da cavidade oral

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ABSTRACT

OBJECTIVE: To assess the association between oral health and hygiene practices and oral cancer.

METHODS: Hospital-based case-control study in the metropolitan area of São Paulo, southeastern Brazil, from 1998 to 2002. A total 309 patients with squamous cell carcinoma of the mouth and the pharynx and 468 controls matched by sex and age were included in the study. Cases were recruited in seven reference hospitals and controls were selected in five out of the seven participating hospitals. Detailed information on smoking, alcohol consumption, schooling, oral health status and hygiene practices were obtained through interviews. Odds ratios (OR) and 95% confidence intervals (95% CI), adjusted by sex, age, schooling, smoking, alcohol consumption as well as the variables oral health status and hygiene practices were estimated using unconditional logistic regression analyses.

RESULTS: The use of complete dental prosthesis was not associated with oral cancer but regular gum bleeding showed a strong association (OR 3.1; 95% CI 1.2–7.9). Those who never attended a dental visit were more likely to have oral cancer (OR 2.5; 95% CI 1.3–4.8). Daily mouthwash use showed a stronger association to pharynx (OR 4.7; 95% CI 1.8–12.5) than mouth cancer (OR 3.2; 95% CI 1.6–6.3).

CONCLUSIONS: Gum bleeding, no dental care, and daily mouthwash use were factors associated with oral cancer regardless of tobacco and alcohol consumption.

DESCRIPTORS: Mouth Neoplasms. Oral Hygiene. Oral Health. Risk Factors. Case-Control Studies.

RESUMO

OBJETIVO: Avaliar a associação entre saúde e higiene bucal na ocorrência de câncer oral.

MÉTODOS: Estudo caso-controle de base hospitalar, realizado entre 1998 e 2002 na área metropolitana de São Paulo, SP. Foram incluídos 309 pacientes com carcinoma epidermóide de boca e orofaringe e 468 controles, pareados com os casos por sexo e idade. Os casos foram levantados em sete hospitais que concentram a assistência médica a pacientes com a doença e os controles rastreados em cinco hospitais gerais dentre os sete. Informações pormenorizadas sobre tabagismo, consumo de álcool, escolaridade, saúde bucal e práticas de higiene bucal foram obtidas por entrevista. Por meio de análise de regressão logística não condicional foram calculados odds ratios (OR) e intervalos com 95% de confiança (IC 95%), ajustados por sexo, idade, nível educacional, tabagismo e consumo de álcool, bem como para as demais variáveis de saúde e higiene bucal.

RESULTADOS: Uso de prótese bucal total não se associou a câncer oral, mas sangramento gengival freqüente apresentou alta associação (OR=3,1; IC 95%: 1,2;7,9). Nunca ter consultado dentista mostrou associação com câncer oral (OR=2,5; IC 95%: 1,3;4,8). Uso diário de enxaguatórios bucais apresentou associação mais intensa com tumores de faringe (OR=4,7; IC 95%: 1,8;12,5) do que com tumores de boca (OR=3,2; IC 95%: 1,6;6,3).

CONCLUSÕES: Sangramento gengival, ausência de consultas com dentistas e uso regular de enxaguatórios bucais foram fatores associados com câncer oral, independentemente de tabagismo e consumo de bebidas alcoólicas.

DESCRITORES: Neoplasias Bucais. Higiene Bucal. Saúde Bucal. Fatores de Risco. Estudos de Casos e Controles.

INTRODUCTION

Oral cancer accounts for 7% of all new cancer cases worldwide, around 270,000 cases annually. In developing countries, it is the fifth most common cancer in men and the seventh in women.[15] In South America, Brazil has the highest rates of oral cancer in men.[19] The city of São Paulo has the highest incidence of oral cancer in the Brazil, 25.3 cases per 100,000 males and 4.9 per 100,000 females.[20]

Smoking and alcohol consumption are widely recognized as risk factors for oral cancer,[10,a,b,c] but also nutrition,[6] occupation[1] and metabolic gene polymorphisms[9] seem to have specific roles for the development of oral cancer. Previous epidemiological studies have provided evidence of the effect of oral health status and oral hygiene practices on the development of oral cancer. Poor oral hygiene seems to cause additional cancer risks. Irregular toothbrushing, dental prostheses, and mouthwash use have all been associated with oral cancer.[3,14,17] A case-control study conducted in Puerto Rico[18] reported non-significant risk of frequent mouthwash use for oral cancer in non-smokers and non-alcohol users. Even though associations between mouthwash use and oral cancer have been reported in the literature, there is no conclusive evidence of increased risk.[7] Alcohol is a component of many commercial mouthwash formulations, which could explain the observed increased risk with their use for oral cancer. In Brazil, mouthwash products are freely marketed and some brands may contain as much as 27% alcohol.

The objective of the study was to assess the association between oral health status and hygiene practices and oral and pharynx cancer.

METHODS

Hospital-based case-control study conducted in the metropolitan area of São Paulo (Southeastern Brazil) between November 1998 and March 2002. Cases were recruited in seven reference hospitals in this area. Controls were selected from five out of these seven general hospitals. Cases and controls had to be living in the metropolitan area of São Paulo for at least six months.

Eligible cases were all patients newly diagnosed during the study period and histologically confirmed as oral squamous cell carcinoma, and coded according to the International Classification of Diseases and Related Health Problems – 10th revision (ICD-10): oral cavity (C00, C02, C03, C04, C05.0, C06) and pharynx (C01, C02.4, C05.1, C05.2, C09, C10). Patients with cancers of the vermilion border, parotid gland and other major salivary glands, nasopharynx, paranasal sinus, and hypopharynx, or classified as non-specific sites of the oral cavity, lips, or pharynx, were excluded.

Out of 573 cases recruited, 210 were considered ineligible according to one of exclusion criteria: 74 were living outside the study area; 79 did not have their cancers histologically confirmed; 32 had undergone previous treatment for oral cancer; six had cancer involving pharynx and larynx anatomical areas of unknown origin; seven patients had tumor primary sites other than those established in the study; 12 cases were not confirmed as squamous cell carcinoma. Of 363 eligible cases, 28 were severely ill and unable to undergo an interview and 26 refused to participate in the study. The overall response rate was 85.1%. A total of 309 cases were interviewed and included in the analysis.

Cases and controls were matched by sex and age (5-year age groups). Controls were selected from patients admitted in the participating general hospitals during the study period. Controls had no previous history of oral cavity or pharynx cancer. Patients with diseases associated with oral cancer risk factors (tobacco smoking, alcohol consumption and occupation) such as emphysema, cirrhosis, asthma, ischemic heart diseases, cancers, and chronic sinusitis were excluded.

Of 527 controls selected, 24 were excluded as they were living outside of the study area. Of the remaining patients, 31 were severely ill and unable to undergo an interview; and four refused to participate in the study. A total of 468 controls were interviewed and included in the analysis.

All contacts and interviews with cases and controls were carried out by trained interviewers who were not blinded to the patient status as case or control, but did not have any knowledge on the study hypothesis.

Data were collected through face-to-face interviews using a standardized questionnaire applied to all cases and controls. The questionnaire included items on socioeconomic status, occupation, smoking, alcohol consumption, family history of cancer, infectious diseases, diet, sexual behavior, and oral health and hygiene practices. The questionnaire was piloted on a group of ten cases and ten controls, and few adjustments were made in the instrument before its application.

The study subjects were inquired regarding the period before the diagnosis of the conditions for which they were hospitalized. General oral health/hygiene practices were assessed using standard criteria for the following variables: use of complete dental prosthesis, gum bleeding, frequency of dental visits, tooth brushing and frequency of mouthwash use.

Subjects were classified into the following categories of alcohol consumption: non-drinkers, former drinkers (no alcohol consumption for at least one year prior to the interview), or current drinkers. Additionally, average daily alcohol intake was estimated in grams per liter per day (g/L/day). Subjects' consumption of different beverages was converted into liters of alcohol as follows: beer, 5%; wine, 12%; spirits (*cachaça*, whiskey, vodka, rum), 41%; and liqueurs, 30%. Then they were converted into grams of alcohol (one liter is equivalent to 798 g of alcohol).[a] Five categories were created: <1 g/L/day (non-drinker or drinking at most one glass of wine every ten days); 1 to <40 g/L/day; 40 to <80 g/L/day; 80 to <120 g/L/day; and ≥120 g/L/day.

Smoking status was categorized into non-smokers, former smokers (no smoking for at least one year prior to the interview), and current smokers. Cumulative exposure was determined based on the number of daily packs of cigarettes consumed per year (pack-years). The following criteria were used: one cigarette is equivalent to 1 g of tobacco; the content of one pipe is equivalent three cigarettes; and one cigar is equivalent to four cigarettes.[b] One pack contains 20 cigarettes. Five categories were created for tobacco consumption: <1 pack-year (non-smoker or smoker of at most 0.05 cigarettes per day); 1 to <20 pack-years; 20 to <40 pack-years; 40 to <60 pack-years; and ≥60 pack-years.

Use of complete dental prosthesis (both jaws) was considered a dichotomous variable (yes/no). Gum bleeding was ascertained by asking subjects about bleeding during tooth brushing (no; sometimes; always; or almost

[a] International Agency for Research on Cancer. Alcohol drinking. Lyon; 1988. (IARC Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans, 44).
[b] International Agency for Research on Cancer. Tobacco smoking. Lyon; 1986. (IARC Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans, 38)

always). The study hypothesis was that subjects who reported gum bleeding every or almost every time they brushed their teeth would have higher risk of oral cancer than those with no or sporadic gingival bleeding.

Frequency of dental visits in the last twenty years was categorized as never, occasionally (intervals ≥2 years), and regular annual visits. For tooth brushing frequency, subjects were divided into four groups: no brushing; less than once a day; once or twice a day; and three or more times a day. Frequency of mouthwash use was categorized as never; less than once a day; and more than once a day.

Sample size calculation considered the population prevalence of use of complete dental prosthesis, one of the main independent study variables. In a survey conducted by the Health Department of the State of São Paulo in 1998[a] it was estimated that around 29% of the state's adult population used dental prostheses. Then, assuming $\alpha=0.05$ and $\beta=0.20$, 309 cases and an equivalent number of controls, the study would detect an odds ratios (OR) of 1.6.[16]

The association between oral health and hygiene practices and oral cancer was estimated by OR and 95 percent confidence intervals (95% CI) using unconditional logistic regression analysis.[5] For each oral health status or hygiene practice variable the OR was adjusted by all other oral health variables and by sex, age (five age groups), smoking (pack-years), alcohol consumption (g/L/day), and schooling (illiterate, elementary, high school, and college education). Linear trend was estimated for alcohol consumption and smoking by fitting the categorical variable into the logistic regression model as a continuous variable.[10]

The study was approved by the Research Ethical Committees of all participating medical sites and Universidade de São Paulo School of Public Health, as well as by the National Human Research Ethics Committee of the Brazilian Ministry of Health. Cases and controls were informed of the objectives and uses of the research project both in person and through a consent form, which was signed by them.

RESULTS

The study sample included 198 cases of mouth cancer and 111 cases of pharynx cancer. The most common anatomical site of cancer was the tongue (ICD-10 code C01 – base of tongue 5.5%; ICD-10 code C02 – other and unspecified parts of tongue 32%). Digestive conditions were generally reported as the main reason for hospital admission in 24.1% of controls, followed by

Table 1. Sociodemographic characteristics, alcohol consumption and smoking in cases and controls. Metropolitan area of São Paulo, Southeastern Brazil, 1998–2002.

Variable	Case		Control		p-value
	(N=309)	%	(N=468)	%	
Sex					0.036
Female	46	14.9	99	21.2	
Male	263	85.1	369	78.8	
Age (years)					0.028
<40	18	5.8	40	8.5	
40–49	83	26.9	102	21.8	
50–59	107	34.6	135	28.8	
60–69	70	22.7	117	25.0	
≥70	31	10.0	74	15.8	
Skin color					0.546
White	211	71.0	318	69.0	
Nonwhite	86	29.0	143	31.0	
Schooling					0.407
Illiterate	42	13.6	65	13.9	
Elementary school	221	71.5	318	68.1	
High school	36	11.7	57	12.2	
College	10	3.2	27	5.8	
Alcohol status (g/L/day)					<0.001
<1	25	8.1	155	33.5	
1–39	58	18.8	132	28.6	
40–79	55	17.8	65	14.1	
80–119	39	12.6	28	6.1	
120 and more	132	42.7	82	17.7	
Smoking (pack-years)					<0.001
<1	15	5.0	142	31.3	
1–19	36	11.9	54	11.9	
20–39	65	21.5	81	17.8	
40–59	49	16.2	42	9.3	
60 and more	137	45.4	135	29.7	

Skin color: missing information in 12 cases and 7 controls; schooling: missing information in one control; alcohol: 6 missing controls; smoking: 7 missing cases and 14 missing controls.

cardiovascular diseases (21.6%). However, the distribution according to specific diseases was lower than 10% for each diagnosis. For instance, in the great group of chapter XI of ICD-10 (diseases of the digestive system), the most common diagnosed disease among controls was ICD-10 code K40.9 (unilateral or unspecified

inguinal hernia, without obstruction or gangrene). There were 28 patients diagnosed with this disease, only 6.0% of all controls. No patient with alcohol- or tobacco-related digestive or cardiovascular diseases was included as control in the study.

Male-to-female ratio was 5.7:1 and 84.2% aged between 40 and 69 years. About 70% of both cases and controls were classified by interviewers as white skin. Schooling was slightly higher among controls, but this difference was not statistically significant (Table 1).

Current drinkers showed higher risk of oral cancer than former drinkers and current smokers had higher risk compared to former smokers. Although a clear dose-response effect was seen in both tumor sites, increased alcohol consumption was associated to higher risk of pharynx than mouth cancer. As for tobacco smoking, no clear risk differences were seen between pharynx and mouth cancers. Only in those in the strata of tobacco

smoking of 40 to 59 pack-years the risk was higher for pharynx than mouth cancer (Table 2).

The use of complete dental prosthesis was not associated with increased risk of oral cancer (Table 3). The risk of oral cancer was higher among subjects who reported regular gingival bleeding during tooth brushing. Those who reported never attending dental visits had a statistically significant oral cancer risk of 2.5 compared to those who attended annual dental visits. In the crude analysis, those who reported never brushing their teeth showed higher risk of oral cancer compared to those who brushed their teeth three times a day (OR=2.6, 95% CI: 1.1;5.9), but the association lost its statistical significance after adjustment. Subjects who reported using mouthwash products more than once a day showed a statistically significant 3-fold increase in the risk of oral cancer compared to those who never used them.

Table 2. Association of smoking and alcohol consumption with oral cancer (mouth + pharynx), and mouth and pharynx cancers separately. Metropolitan area of São Paulo, Southeastern Brazil, 1998–2002.

Variable	Oral OR (95% CI)	Mouth OR (95% CI)	Pharynx OR (95% CI)
Alcohol status*			
Non-drinkers	1	1	1
Former drinkers	4.9 (2.3;10.3)	3.2 (1.4;7.1)	30.2 (3.6;250.7)
Current drinkers	7.5 (3.5;15.8)	5.2 (2.3;11.4)	38.4(4.6;319.0)
Alcohol consumption (g/L/day)**			
<1	1	1	1
1–39	3.1 (1.5;6.2)	2.4 (1.1;5.3)	6.4 (1.6;26.3)
40–79	6.2 (2.8;13.8)	4.7 (1.9;11.5)	13.1 (2.9;59.1)
80–119	8.9 (3.6;22.0)	7.3 (2.7;20.0)	18.3 (3.7;90.6)
≥120	11.1 (5.2;23.9)	7.7 (3.3;18.1)	30.2 (7.2;126.9)
Linear trend	p<0.001	p<0.001	p<0.001
Smoking status***			
Non-smokers	1	1	1
Former smokers	2.4 (1.2;5.1)	2.7 (1.2;6.3)	2.1 (0.6;7.2)
Current smokers	10.5 (5.3;20.6)	10.5 (4.8;23.0)	12.0 (3.8;37.4)
Smoking (pack-years)****			
<1	1	1	1
1–19	4.2 (1.9;9.1)	4.8 (2.0;11.4)	3.8 (0.9;15.3)
20–39	4.4 (2.1;9.2)	5.0 (2.2;11.8)	4.5 (1.3;15.9)
40–59	6.8 (3.0;15.5)	5.3 (2.0;13.9)	11.2 (3.0;41.2)
≥ 60	5.3 (2.6;10.7)	5.7 (2.5;13.0)	5.7 (1.7;19.0)
Linear trend	p<0.001	p<0.001	p= 0.002

Missing values: for oral (mouth + pharynx) cancer analysis = 104 (42 cases and 62 controls); for mouth cancer analysis = 92 (30 cases and 62 controls); for pharynx cancer analysis = 74 (12 cases and 62 controls).
* OR adjusted for sex, age, schooling, smoking status, oral health/hygiene
** OR adjusted for sex, age, schooling, smoking (pack-years), oral health/hygiene
*** OR adjusted for sex, age, schooling, alcohol status, oral health/hygiene
**** OR adjusted for sex, age, schooling, alcohol consumption (g/L/day), oral health/hygiene

Table 3. Association of self-reported oral health status and hygiene practices with oral cancer (mouth + pharynx). Metropolitan area of São Paulo, Southeastern Brazil, 1998–2002.

Variable	Case	Control	OR* (95% CI)
Oral health status			
Complete dental prosthesis			
No	162	211	1
Yes	105	195	0.7 (0.5;1.0)
Gum bleeding			
None	208	325	1
Occasional	40	69	0.9 (0.6;1.5)
Always or almost always	19	12	3.1 (1.2;7.9)
Oral hygiene practices			
Frequency of dental visits			
Annual	26	63	1
Occasional**	128	233	1. 5 (0.8;2.8)
Never	113	110	2.5 (1.3;4.8)
Tooth brushing frequency			
3 or more times a day	67	120	1
Once or twice a day	166	244	0.7 (0.5;1.2)
Less than once a day	24	35	0.7 (0.3;1.5)
Never	10	7	1.3 (0.4;4.5)
Mouthwash use frequency			
Never	199	324	1
Less than once a day	27	54	1.0 (0.6;1.9)
One or more times a day	41	28	3.3 (1.7;6.1)

Missing values: 104 (42 cases and 62 controls)
* OR adjusted for sex, age, schooling, smoking, alcohol consumption and all other oral health/hygiene variables
** Interval between visits ≥ 2 years

The effect of distinct oral health status and health care variables on mouth and pharynx cancer was assessed separately. For those with frequent gingival bleeding, no dental visits, and mouthwash use, the risk of pharynx cancer was greater than mouth cancer (Table 4).

DISCUSSION

A possible limitation of the present study includes the risk of misclassification of exposure history. The sensitivity of self-reported oral health status is lower than objective bucal examination. However, mouth examination in patients with oral cancer could be compromised in order to obtain information on gingival bleeding previously to the disease. However, self-reported oral health status and practices may have introduced a nondifferential misclassification that would dilute risk estimates.

There is no simple explanation for the high incidence of cancer of oral cavity and oropharynx found in São Paulo,[20] since the prevalence of tobacco smoking and alcohol consumption seems not be different from other Brazilian regions.[13] The results in the present study for the effect of tobacco smoking and alcohol consumption confirm what is long known, that these two exposures are the main risks for oral cavity and oropharynx cancers.[10]

No association was seen between complete dental prosthesis and oral cancer, corroborating other studies.[8,11,12] On the other hand, high association of frequent gum bleeding during toothbrushing and oral cancer was found. Maier et al[12] reported among oral cancer cases that 40.9% had 3 mm or more dental calculus or tartar and 28% had chronic gingival inflammation, thus indicating that patients with oral cancer could have poorer oral care and health. Other studies carried out in Brazil[8] and India[2] showed increased oral cancer risk among subjects with poor oral hygiene practices. In the present study, information on missing and decayed teeth (DMF index) and the index of periodontal disease were not used; instead, oral health status was assessed through the variables dental prostheses and frequency of gum bleeding during toothbrushing, as self-reported by interviewees.

Table 4. Association of self-reported oral health status and hygiene practices with mouth and pharynx cancer. Metropolitan area of São Paulo, Southeastern Brazil, 1998–2002.

Variable	Mouth cancer	Control	OR* (95% CI)	Pharynx cancer	Control	OR* (95% CI)
Oral health status						
Complete dental prosthesis						
No	104	211	1	58	211	1
Yes	64	195	0.7 (0.4;1.1)	41	195	0.7 (0.4;1.3)
Gum bleeding						
No	130	325	1	78	325	1
Occasional	25	69	0.9 (0.5;1.5)	15	69	1.1 (0.5;2.2)
Always or almost always	13	12	3.0 (1.0;8.5)	6	12	4.7 (1.2;17.9)
Oral hygiene practices						
Frequency of dental visits						
Annual	23	63	1	3	63	1
Occasional**	72	233	1.0 (0.5;2.0)	56	233	7.3 (1.7;30.0)
Never	73	110	2.0 (1.0;4.2)	40	110	9.1 (2.1; 40.0)
Tooth brushing frequency						
3 or more times a day	50	120	1	17	120	1
Once or twice a day	98	244	0.7 (0.4;1.1)	68	244	0.8 (0.4;1.8)
Less than once a day	12	35	0.6 (0.2;1.4)	12	35	1.1 (0.4;3.1)
Never	8	7	1.5 (0.4;5.6)	2	7	1.0 (0.2; 6.6)
Mouthwash use frequency						
Never	123	324	1	76	324	1
Less than once a day	16	54	0.9 (0.4;1.8)	11	54	1.4 (0.6;3.4)
One or more times a day	29	28	3.2 (1.6;6.3)	12	28	4.7 (1.8;12.5)

Missing values: for mouth cancer analysis = 92 (30 cases and 62 controls); for pharynx cancer analysis = 74 (12 cases and 62 controls)
* OR adjusted for sex, age, schooling, smoking, alcohol consumption and all other oral health/hygiene variables
** Interval between visits ≥ 2 years

In regard to oral hygiene practices, a non-significant association for oral cancer was seen among subjects that never brushed their teeth compared to those who brushed them three or more times a day. Patients who had never attended dental visits had a higher risk of oral cancer than subjects who reported attending a visit at least once a year. This finding is similar to that found in studies in Germany[12] and Poland.[11] Those who have frequent dental visits are generally more careful about their oral hygiene, and this behavior could be considered an indicator of good oral care, which can help eliminate or prevent mucosa exposure to certain carcinogens.

There seems to be collinearity between the variables frequency of gingival bleeding and frequency of dental visits, since subjects with poor oral health are probably those who do not often attend dental visits. On the other hand, the findings for toothbrushing could be downplayed, considering that subjects with gingival diseases are less likely to brush their teeth because of gingival bleeding during this procedure.

In the present study, the proportion of cases who reported using mouthwash products one or more times a day was a little over twice that of controls (15.4% vs. 6.9%, respectively). Association with oral cancer was 3-fold higher in subjects who frequently used mouthwash products than among those who never used them. This finding confirms in Brazil the results from Winn et al[18] (2001) that found higher risk, though not statistically significant, among a small number of non-smoking and non-drinking subjects mouthwash users. There is no available data on mouthwash use in Brazilian population. The prevalence among controls in this study (6.9%) could be assumed as a rough estimate, even though a higher prevalence of mouthwash use could be found among those hospitalized, since they could use mouthwash only because their diseases. There are several brands of mouthwash products marketed in Brazil, some of them with alcohol in their formulae. Alcohol is used in mouth rinses as a solvent of other ingredients and a preservative. Certain brands of mouthwash agents commercially available contain

as much as 27% alcohol, and these products are sold over the counter. Mouthwash products are in contact with the oral mucosa as much as alcoholic beverages and may cause chemical aggression of the cells. Similarly to the findings of alcohol consumption, subjects who reported frequent use of mouthwash products also showed higher risk of pharyngeal than mouth cancer. In general, when washing their mouth, people gargle the mouthwash product and the substances of these products come into direct contact with the pharynx mucosa. Special attention should be paid to the differences that may exist between mouth and pharynx mucosas, and to the consequently distinct effects of alcohol, present in beverages and mouthwash formulas, on cancers in these anatomical sites. Also, the mechanisms of alcohol carcinogenesis and the role of acetaldehyde, as a solvent for other carcinogens, and ethanol in DNA damage, or reduced immune surveillance carcinogenicity of non-ethanol compounds, need to be further explored,[4] as they could provide better understanding on cancer development in the head and neck.

The potential bias related to the fact that subjects may use mouthwash to reduce the aftertaste left by smoking or drinking was controlled for in the multiple logistic regression analysis adjusted for smoking and alcohol consumption.

Although it was stressed to the interviewers to ask cases and controls information on oral health status and practices before disease diagnosis (oral cancer for cases and other diseases for controls), the occurrence of reversed causality cannot be excluded. Particularly, patterns of gingival bleeding and mouthwash use could be different after oral cancer patients perceived their disease. Oral neoplasia could make oral care difficult and contribute for the development of gingivitis and, consequently, gingival bleeding. On the other hand, more advanced oral cancers can cause bad breath and make patients try to minimize this inconvenience using mouthwash.

In conclusion, frequent gum bleeding, no dental visits and mouthwash use more than once a day are highly associated with oral cancer. However, reverse causation should be also taken in consideration as a potential alternative explanation.

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