Are recurrent denture-related sores associated with the risk of oral cancer? A case control study

Há associação entre as feridas bucais por prótese dentária e risco de câncer de boca? Estudo caso-controle

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Abstract

Objectives: This study aimed to assess the hypothesis that recurrent denture-related sores association may be associated with the risk of oral cancer. **Methods:** We conducted a hospital-based case-control study comprising 71 new cases of oral cancer in two hospitals in São Paulo, Brazil, and 240 controls without cancer, recruited from outpatient units of the same hospitals. All cases had histologically confirmed squamous cell carcinoma in anatomic sites of the mouth that may be specifically considered at risk of sores by ill-fitting dentures. Denture-related sores were assessed by the self-report of recurrent oral sores due to the use of ill-fitting complete removable dental prosthesis. Associations were assessed by multivariate logistic regression conditioned on socio-demographic and behavioral characteristics. **Results:** The association between ill-fitting dentures and oral cancer was statistically significant in the multivariate model: odds ratio 3.98; 95% confidence interval 1.06 – 14.96. The specific assessment of association between tumors in the lower jaw and sores by mandibular dentures confirmed this result: odds ratio 6.39; 95% confidence interval 1.49 – 29.52. **Conclusion:** The potential contribution of denture-related sores to oral carcinogenesis still fuels controversies. This study reinforces the hypothesis that recurrent denture-related sores may be associated with the risk of oral cancer. Results reported here also suggest that an appropriate application and monitoring of dental prosthesis represent a non-negligible scope for cancer prevention.

Keywords: Epidemiology. Mouth neoplasms. Dentures. Case-control studies. Risk factors. Oral ulcer.

Resumo

Objetivo: O presente estudo avaliou a associação entre as feridas recorrentes por prótese dentária mal adaptada e o risco de câncer bucal. **Metodologia:** Foi realizado estudo caso-controle de base hospitalar que incluiu 71 pacientes com câncer bucal atendidos em dois hospitais da cidade de São Paulo, Brasil. O grupo controle foi composto por 240 pacientes sem câncer, atendidos em ambulatórios diversos dos mesmos hospitais. Todos os casos receberam diagnóstico histológico de carcinoma epidermoide em localizações anatômicas da boca sujeitas a feridas pelo uso de prótese mal adaptada. As feridas decorrentes do uso de prótese mal adaptada foram avaliadas por meio do autorrelato dos pacientes. A análise utilizou modelos de regressão logística não condicional multivariada. **Resultados:** A associação entre feridas por prótese mal-adaptada e câncer de boca mostrou-se estatisticamente significante no modelo multivariado: OR 3.98; IC95% 1.06 – 14.96. A avaliação específica dos tumores da mucosa inferior confirmou esse resultado (OR 6.39; IC95% 1.49 – 29.52). **Conclusão:** A contribuição do uso de próteses mal-adaptadas para a carcinogênese bucal ainda é controversa. O presente estudo confirma a hipótese de que as feridas recorrentes pelo uso de próteses mal-adaptadas podem estar associadas ao risco de câncer bucal. Os resultados encontrados sugerem que a avaliação profissional regular das próteses dentárias pode ser importante para a prevenção do câncer.

Palavras-chave: Epidemiologia. Neoplasias bucais. Dentaduras. Estudos caso-controle. Fatores de risco. Úlceras orais.

Introduction

Oral cancer incidence is an important problem of public health. About 263,900 new cases of oral cancer and 128,000 deaths were estimated for 2008 worldwide.[1] Tobacco and alcohol are acknowledged to be the main behavioral risk factors for oral cancer[1-3]. Dietary habits, such as a low intake of fruits and raw vegetables, have also been associated with the disease[4]. Gum bleeding, periodontal disease and poor oral hygiene have been assessed as factors that may be associated with tumors of the oral cavity[5-8].

The use of complete dentures by edentulous people has been reported to be safe and unrelated to the risk of intra-oral cancer[5,] but few studies assessing the quality of the denture fitting were perfomed until now[9,10]. In a study performed in Sweden the use of poorly fitting complete dentures was associated with and oral cancer[9]. Also, Vaccarezza et al., in a study performed in Brazil, found associations between the self-report of sores by ill-fitting dentures and oral cancer[10]. In addition, a recent study found that the chronic trauma of the oral mucosa could be a risk factor for oral cancer[11].

This study was undertaken to assess the association between recurrent denture-related sores and cancer in anatomic sites of the mouth that may be specifically considered at risk of developing sores due to ill-fitting dentures.

Methods

We conducted a case-control study assessing the odds of oral cancer between patients who do and who do not complain of recurrent denture related sores (either because they do not use dentures or because their denture is not ill adjusted). Participants were enrolled among patients who had been admitted to two major hospitals in the city of São Paulo (Hospital Heliópolis and Hospital A. C. Camargo) from 2006 to 2008. The study enrolled 71 new cases of histologically-confirmed squamous cell carcinoma in anatomic sites of the mouth

that may be specifically considered at risk of developing sores due to ill-fitting dentures: lateral border of tongue (coded C02.1 in the International Classification of Diseases, 10th Revision): 16 patients; floor of mouth (C04): 25 patients; hard palate (C05.0): 16 patients; gum (C03): 7 patients; retromolar area (C06.2): 6 patients; and cheek mucosa (C06.0): 1 patient.

The control group comprised 240 individuals, frequency matched with cases by gender and age. To avoid the selection of hospital controls with a unique disease, controls were enrolled among persons that were accompanying patients without cancer, or had been attended at outpatient units (except dental or stomatology units) of the same hospitals for a wide spectrum of health complaints. Since some cancers are associated with the same risk factors of oral cancer (e.g. lung cancer is also related to tobacco smoking), individuals who presented with previous or current experience of cancer were not included as controls

Five experienced and specifically trained interviewers administered a 30-minute structured questionnaire to cases and controls. The participants were interviewed in a separate room of the health unit immediately after their clinical consultation. The questionnaire elicited information about socioeconomic status and behavioral exposures. No proxy respondents were allowed; patients with impaired speech function were not included. This study observed Brazilian and international statutes on ethics in research involving human beings. Ethical clearance was given by the research committees of the participating institutions.

Socioeconomic status was assessed by family income and measured in multiples of the Brazilian minimum wage, a national standard for measuring income, which was roughly equivalent to US$ 200 per month during the study period.

The assessment of diet used an extensive food frequency questionnaire that originally had been devised for a previous study[12]. Two food items, fruits and deep fried foods, stratified by categories of frequency of intake, were chosen as indicative of diet quality. The assessment of fruit consumption was unspecific. Bananas, apples and oranges are some of the most frequently consumed fruits in Brazil. Deep fried foods referred to different items that are common in the Brazilian diet and rich in saturated fat. These include French fries, manioc or cassava, deep fried pastries and stuffed tidbits, high-fat hors d'oeuvres that contain animal protein.

Patients who reported that they had not smoked one or more cigarettes daily for an entire year were classified as non-smokers. The assessment of tobacco smoking considered sequential patterns of frequency, duration, and type of products consumed during the lifetime, according to a methodology that was standardized by the International Agency for Research in Cancer (IARC)[13]. A cigar was considered to be equivalent to four cigarettes; each pipe serving was considered to be equivalent to three cigarettes. The cumulative exposure to tobacco was measured in pack-years (number of packs of 20 cigarettes smoked per day multiplied by the number of smoking years) and subsequently stratified into three categories: non-smokers and two groups of smokers who were classified by the median value of pack-years that were consumed in the control group.

Patients who reported that they had not consumed one or more drinks on a regular monthly basis were classified as non-drinkers. The assessment of alcohol consumption also considered sequential patterns of frequency, volume, duration, and type of beverages consumed during the lifetime, according to a methodology that was standardized by the IARC[14]. The cumulative exposure to alcohol was measured in grams of ethanol, considering that one liter of ethanol weighs 798 grams, and that the ethanol content by volume in beer is 5%, 12% in wine, 30% in liqueurs, and 40% in distilled spirits. The variable was expressed in gram-years (grams of ethanol per day multiplied by the number of

drinking years) and subsequently stratified into three categories: non-drinkers and two groups of drinkers who were classified by the median value of gram-years consumed in the control group.

Participants were asked if they had ever worn dentures until a year before the diagnosis. Those who had worn complete dentures for less than six months prior to the diagnosis of the tumor were considered to be non-wearers, because this time interval was considered too reduced to be referred to recurrent sores of oral mucosa. Denture-related sores were assessed by the self-report of recurrent oral sores due to the use of ill-fitting complete removable dental prosthesis.

A previous study had concluded that the proportion of patients who complains of poorly fitting dentures is higher for mandibular than to maxillary dentures[15]. Taking this information into account, we performed a complementary assessment, specifically focusing on tumors in the lower jaw and sores that were related to the use of mandibular dentures.

The statistical analysis used unconditional logistic regression models. The fitting of multivariate models observed a conceptual framework[16], in which denture wearing and the self-record of denture-related sores (predictors) were adjusted for gender and age group, and for other exposures such as covariates on socioeconomic status, tobacco and alcohol consumption, and diet (frequency of fruit and bacon intake). Categories of alcohol and tobacco consumption, as well as fruit and bacon intake, were based in the median values of controls. The subsequent assessment of patients who were wearing mandibular dentures exclusively considered patients who were affected by mandibular tumors (i.e., cancer in the floor of mouth and mandibular gum).

Associations were assessed in terms of odds ratio (OR) point and interval estimates. Two-sided p-values lower than 0.05 were considered to be indicative of a significant association between covariates and the outcome. The statistical analysis used the Stata 11.0 2009 software (Stata Corporation, College Station, TX, USA).

Results

The case group comprised 18 women and 53 men, with a mean age of 56.4 ± 9.7 (standard deviation) years. Fifteen patients had tumors in the lateral border of the tongue, 26 in the floor of the mouth, 16 in the palate, seven in the gum, five in the retromolar area and two in the cheek mucosa. More than one third (33.8%) of cases reported the use of removable dental prosthesis.

The control group comprised 56 women and 184 men with a mean age of 55.9 ± 10.7 years. They were enrolled in the outpatient units of both hospitals: 118 participants were accompanying other patients than those included as cases, and have not reported any health complaint of their own. The remaining participants were undergoing treatment related to the skin (79), cardiovascular system (26), genito-urinary tract (25), endocrine disorders (15), respiratory diseases (9), orthopedic conditions (8), infectious diseases (8), rheumatoid arthritis (6), plastic surgery (4) and neurological conditions (2). Near four out of each 10 (40.8%) controls reported the use of removable dental prosthesis.

Table 1 summarizes the distribution of cases and controls according to income, tobacco and alcohol consumption, diet, use of complete dentures and self-report of denture-related sores. Five percent of controls and 9.9% of cases complained about denture-related sores. Crude ORs and 95% confidence interval (95%CI) estimates are reported in Table 2. Although no association between sores from ill-fitting dentures and cancer was found in the crude analysis (OR 2.09; 95%CI 0.79 – 5.50); this association was considered to be statistically significant when the multivariate model was adjusted for behavioral exposures (OR 3.98; 95%CI 1.06 – 14.96).

The multivariate model confirmed the statistical association between mouth

Table 1 - Distribution of cases and controls by covariates on socioeconomic status, tobacco smoking and alcohol consumption, dietary habits and denture condition. São Paulo, Brazil, 2008.
Tabela 1 - *Distribuição de casos e controles segundo condição socioeconômica, tabagismo, consumo de álcool, hábitos alimentares e uso de prótese bucal. São Paulo, Brasil, 2008.*

Covariates	Controls	Cases
	n (%)	n (%)
Socioeconomic status		
Family income per month: MW (1)		
Less than 1.00	14 (5.8)	14 (19.7)
From 1.00 to 2.99	103 (42.9)	27 (38.0)
3.00 or more	110 (45.8)	27 (38.0)
Not informed	13 (5.4)	3 (4.2)
Lifestyle exposures		
Smoking: daily packs × year		
Non-smokers	93 (38.7)	8 (11.3)
Less than 21.0	73 (30.4)	7 (9.9)
21.0 or more	74 (30.8)	56 (78.9)
Alcohol drinking: daily g ethanol × year		
Non-drinkers	71 (29.6)	15 (21.1)
Less than 500	85 (35.4)	4 (5.6)
500 or more	84 (35.0)	52 (73.2)
Dietary habits		
Fruit: weekly frequency		
Less than 4 times	122 (50.8)	48 (67.6)
4 times or more frequently	118 (49.2)	23 (32.4)
Deep fried foods: weekly frequency		
Less than once	131 (54.6)	24 (33.8)
Once or more	109 (45.4)	47 (66.2)
Oral status		
Use of removable dentures		
No	143 (59.6)	47 (66.2)
Yes	97 (40.4)	24 (33.8)
Recurrent sores by ill-fitting removable dentures		
No	228 (95.0)	64 (90.1)
Yes	12 (5.0)	7(9.9)

MW: minimum wage in Brazil, approximately US$ 200 during the gathering of data.
SM: Salário mínimo no Brasil, aproximadamente US$ 200 durante a coleta dos dados.

cancer and covariates of the study (Table 2). Family income was inversely related to disease, whereas tobacco smoking, alcohol drinking, and frequent intake of deep fried foods were associated with an increased risk. The use of dentures (irrespective of the quality of fit) was not associated with oral cancer (OR 0.67; 95%CI 0.31 – 1.42); recurrent sores by ill-fitting dentures was directly associated with oral cancer (OR 3.98; 95%CI 1.06 – 14.96).

The stratified assessment for tumors in the lower jaw confirmed the direct association between the disease and the self-report of sores from ill-fitting dentures. Table 3 presents the distribution of cases and controls according to all covariates. In spite of the reduced sample, the self-report of mandibular denture-related sores was associated with tumors in the lower jaw in the multivariate model (OR 6.39; 95%CI 1.49 – 29.52) (Table 4). Conversely, only one patient in the case group complained of sores due to maxillary dentures, which prevented the specific assessment of the upper jaw.

Table 2 - Effect of denture use and sores by ill-fitting dentures on oral cancer. São Paulo, Brazil, 2008.
Tabela 2 - *Efeito do uso de próteses totais e feridas bucais por próteses dentárias na etiologia do câncer de boca. São Paulo, Brasil, 2008.*

Covariates	OR (95%CI) (1)	p-value	OR (95%CI) (2)	p-value
Socioeconomic status (2a)				
Family income per month: MW (3)				
Less than 1.00	1.00	Reference	1.00	Reference
From 1.00 to 2.99	0.26 (0.11 – 0.62)	0.002	0.23 (0.10 – 0.56)	0.001
3.00 or more	0.25 (0.10 – 0.58)	0.001	0.21 (0.09 – 0.51)	0.001
Not informed	0.23 (0.05 – 0.99)	0.049	0.21 (0.05 – 0.91)	0.036
Lifestyle exposures (2b)				
Smoking: daily packs × year				
Non-smokers	1.00	Reference	1.00	Reference
Less than 21.0	1.11 (0.39 – 3.22)		0.94 (0.30 – 2.93)	0.915
21.0 or more	8.80 (3.95 – 19.60)	< 0.001	7.55 (2.83 – 20.15)	< 0.001
Alcohol drinking: daily g ethanol × year				
Non-drinkers	1.00	Reference	1.00	Reference
Less than 500	0.22 (0.07 – 0.70)		0.32 (0.09 – 1.14)	0.078
500 or more	2.93 (1.52 – 5.64)	< 0.001	2.70 (1.00 – 7.25)	0.050
Dietary habits (2c)				
Fruits: weekly frequency				
Less than 4 times	1.00	Reference	1.00	Reference
4 times or more	0.50(0.28 – 0.87)	0.014	0.48 (0.24 – 0.93)	0.031
Deep fried foods: weekly frequency				
Less than once	1.00	Reference	1.00	Reference
Once or more	2.35 (1.35 – 4.09)	0.002	2.34 (1.1 – -4.60)	0.014
Oral status (2d)				
Use of removable dentures				
No	1.00	Reference	1.00	Reference
Yes	0.75 (0.43 – 1.31)	0.316	0.67 (0.31 – 1.42)	0.293
Recurrent sores by ill-fitting removable dentures				
No	1.00	Reference	1.00	Reference
Yes	2.09 (0.79 – 5.50)	0.140	3.98 (1.06 – 14.96)	0.041

(1) Crude Odds Ratio; (2) Odds Ratios and 95% Confidence Intervals adjusted by sex, age group and covariates in the same and more distal levels; (2a) Adjusted by sex and age group; (2b) Adjusted by themselves and by sex, age group and socioeconomic status; (2c) Adjusted by themselves and by sex, age group, socioeconomic status and lifestyle exposures; (2d) Adjusted by sex, age group, socioeconomic status, lifestyle exposures and dietary habits; (3) MW: minimum wage in Brazil ≈ US$ 200 during the gathering of data.
(1) Odds Ratio sem ajuste; (2) Odds Ratio e Intervalo de Confiança ajustados por sexo, faixa etária e covariáveis do mesmo nível e de niveis mais distais - (2a) Ajustada por sexo e faixa etária; (2b) Ajustados entre si e por sexo, faixa etaria e condição socieconomica; (2c) Ajustados entre si e por sexo, faixa etária, condição socieconomica e estilo de vida; (2d) Ajustados entre si e por sexo, faixa etária, condição socieconomica, estilo de vida e habitos alimentares; (3) SM: Salario minimo brasileiro ≈ US$ 200 durante a coleta dos dados.

Discussion

This study reinforces the hypothesis that recurrent oral sores that are related to the use of ill-fitting dentures may be associated with an increased risk of malignant neoplasm in the mouth when behavioral exposures are considered. This observation is in agreement with the findings of previous studies that have been undertaken in Brazil[11,17] and worldwide[10].

Denture-related sores involve chronic traumatic ulcers of the mouth epithelium. It is recognized that chronic inflammation contributes to cancer promotion[18]. Persistent trauma and

Table 3 - Distribution of controls and cases with tumors in the lower portion of the mouth according to socioeconomic status, tobacco smoking and alcohol consumption, dietary habits and denture condition. São Paulo, Brazil, 2008.
Tabela 3 - *Distribuição de controles e casos com tumores na região inferior da boca segundo condição socioeconômica, tabagismo, consumo de bebidas alcoólicas, hábitos alimentares e uso de prótese dentária. São Paulo, Brasil, 2008.*

Covariates	Controls	Cases
	n (%)	n (%)
Socioeconomic status		
Family income per month: MW (1)		
Less than 1.00	14 (5.8)	7 (19.4)
From 1.00 to 2.99	103 (42.9)	15 (41.7)
3.00 or more	110 (45.8)	11 (30.6)
Not informed	13 (5.4)	3 (8.3)
Lifestyle exposures		
Smoking: daily packs × year		
Non-smokers	93 (38.7)	3 (8.3)
Less than 21.0	73 (30.4)	3 (8.3)
21.0 or more	74 (30.8)	30 (83.3)
Alcohol drinking: daily g ethanol × year		
Non-drinkers	71 (29.6)	7 (19.4)
Less than 500	85 (35.4)	1 (2.8)
500 or more	84 (35.0)	28 (77.8)
Dietary habits		
Fruit: weekly frequency		
Less than 4 times	122 (50.8)	24 (66.7)
4 times or more	118 (49.2)	12 (33.3)
Deep fried foods: weekly frequency		
Less than once	131 (54.6)	13 (36.1)
Once or more	108 (45.4)	23 (63.9)
Oral status		
Use of removable dentures		
No	143 (59.6)	24 (66.7)
Yes	97 (40.4)	12 (33.3)
Recurrent sores by ill-fitting removable dentures		
No	228 (95.0)	30 (83.3)
Yes	12 (5.0)	6 (16.7)

MW: Minimum wage in Brazil approximately US$ 200 during the gathering of data.
SM: Salário mínimo brasileiro aproximadamente US$ 200 durante a coleta dos dados.

secondary chronic infections may induce chronic inflammation, and reactive oxygen and nitrogen species released from leukocytes and phagocytes can interact with DNA. This can result in permanent genomic damage in proliferating cells of the repeatedly damaged and regenerated tissue[19]. Furthermore, the recurrent physical irritation of oral mucosa may contribute to the topical carcinogenic effect of tobacco, alcohol drinking and some food compounds in the mouth.

Denture-related sores also involve *Candida*-related stomatitis[20]. *Candida* adherence and colonization of denture-base materials may induce stomatitis, which is associated with epithelial dysplasia[21]. In addition, oral infection by *Candida sp* was related to candidal leukoplakia, premalignant lesions with possibly a higher potential of malignization than other types of leukoplakia[22]. The hypothesis that enzymes developed by yeasts of *Candida albicans* are capable of producing

Table 4 - Effect of mandibular denture use and sores by ill-fitting mandibular dentures on oral cancer (tumors in the lower portion of the mouth). São Paulo, Brazil, 2008.

Tabela 4 - *Efeito de prótese dentária inferior e de feridas por prótese dentária inferior mal ajustada sobre o risco de câncer bucal (tumores na região inferior da boca).*

Covariates	OR (95%CI) (1)	p-value	OR (95%CI) (2)	p-value
Socioeconomic status (2a)				
Family income per month: MW (3)				
Less than 1.00	1.00	Reference	1.00	Reference
From 1.00 to 2.99	0.29 (0.10 – 0.84)	0.022	0.40 (0.08 – 1.92)	0.010
3.00 or more	0.20 (0.07 – 0.60)	0.004	0.17 (0.06 – 0.53)	0.002
Not informed	0.46 (0.10 – 2.17)	0.328	0.40 (0.08 – 1.92)	0.252
Lifestyle exposures (2b)				
Smoking: daily packs × year				
Non-smokers	1.00	Reference	1.00	Reference
Less than 21.0	1.27 (0.25 – 6.50)	0.771	0.84 (0.15 – 4.75)	0.847
21.0 or more	12.57 (3.69 – 42.80)	< 0.001	9.40 (2.25 – 39.20)	0.002
Alcohol drinking: daily g ethanol × year				
Non-drinkers	1.00	Reference	1.00	Reference
Less than 500	0.12 (0.02 – 0.99)	0.049	0.19 (0.02 – 1.87)	0.156
500 or more	3.38 (1.39 – 8.20)	0.007	5.18 (1.23 – 21.89)	0.025
Dietary habits (2c)				
Fruits: weekly frequency				
Less than 4 times	1.00	Reference	1.00	Reference
4 times or more	0.52 (0.25 – 1.08)	0.080	0.52 (0.22 – 1.26)	0.149
Deep fried foods: weekly frequency				
Less than once	1.00	Reference	1.00	Reference
Once or more	2.13 (1.03 – 4.40)	0.042	1.93 (0.78 – 4.79)	0.157
Oral status (2d)				
Use of removable dentures				
No	1.00	Reference	1.00	Reference
Yes	0.74 (0.35 – 1.54)	0.419	1.06 (0.31 – 3.69)	0.922
Recurrent sores by ill-fitting removable dentures				
No	1.00	Reference	1.00	Reference
Yes	3.8 (1.33–10.87)	0.013	6.39 (1.49–29.52)	0.013

(1) Crude Odds Ratio; (2) Odds Ratios and 95% Confidence Intervals adjusted by sex, age group and covariates in the same and more distal levels; (2a) Adjusted by sex and age group; (2b) Adjusted by themselves and by sex, age group and socioeconomic status; (2c) Adjusted by themselves and by sex, age group, socioeconomic status and lifestyle exposures; (2d) Adjusted by sex, age group, socioeconomic status, lifestyle exposures and dietary habits; (3) MW: minimum wage in Brazil ≈ US$ 200 during the gathering of data.

(1) Odds Ratio sem ajuste; (2) Odds Ratio e Intervalo de Confiança ajustados por sexo, faixa etária e covariáveis do mesmo nível e de niveis mais distais; (2a) Ajustada por sexo e faixa etária; (2b) Ajustados entre si e por sexo, faixa etaria e condição socieconomica; (2c) Ajustados entre si e por sexo, faixa etária, condição socieconomica e estilo de vida; (2d) Ajustados entre si e por sexo, faixa etária, condição socieconomica, estilo de vida e habitos alimentares; (3) SM: Salario minimo brasileiro ≈ US$ 200 durante a coleta dos dados.

chemical carcinogens by nitrosination has also been raised[23,24].

Ill-fitting dentures, especially mandibular dentures, are associated with reduced chewing performance[25]. This fact could lead to a reduced effect of the mechanical cleaning of oral mucosa, which occurs while chewing some foods, mainly those rich in dietary fiber[26], thus allowing carcinogens from diet, tobacco and alcohol to remain adhering to the oral mucosa for longer periods.

Case-control studies provide an important tool to assess hypotheses about

retrospective risk factors, which would otherwise remain unaccounted for in public health. Nevertheless, selection bias and recall bias are the main limitations for this type of study[27].

In order to minimize selection bias among controls, we only enrolled individuals who went to the hospital as an accompanying person of other patients then those included in the group of cases, and patients who were admitted in the hospital by health complaints unrelated to the mouth (i.e., no patients were enrolled in the dental or stomatology section of the hospital). We considered patients under treatment at the dental or stomatology unit of the hospital as ineligible as controls because this group might be comprised by a higher proportion of patients with oral sores in comparison to the base population, thus reinforcing selection bias. Among the cases, we only enrolled patients who were affected by tumors that were located in the anatomic sites of the mouth that are most likely to be affected by denture-related sores (oral cavity and lateral border of tongue). In addition, we only assessed patients in two hospitals; our sample cannot be considered representative for the city as a whole. As these criteria resulted in a limited number of patients, data from a larger number of controls were collected in an effort to have more stable measures in the multivariate analysis.

In order to reduce recall bias, interviewers were specifically trained to ask patients about the occurrence of oral sores related to dentures prior to the diagnosis of cancer. However, patients who had oral cancer may have spent some time pondering which habits or events would have contributed to the disease, and would be more likely to recall oral sores than the controls. Then, cohort studies, which would be able to clinically assess oral sores related to dentures, are needed. In our study, nearly 40% of controls and one third of cases reported having worn dentures; however, only a low proportion complained of recurrent oral sores in both groups. This suggests that recall bias may have not been a systematic error source.

Recall bias is a limitation that is difficult to overcome in the scope of a case-control study. The experience of oral sores caused by ill-fitting dentures does not generate effective registries at population level, and clinical examinations of oral mucosa after the diagnosis of cancer cannot be considered in the assessment of etiological factors. Nonetheless, recall bias also affects the recollection of tobacco smoking and alcohol drinking (cancer patients may be more likely to recall deleterious behaviors), and the identification of such exposures as cancer risk factors relied extensively on case-control studies.

Potential confounding biases were reduced by adjusting the multivariate regression model for covariates whose association with oral cancer has been consistently reported. These covariates were socioeconomic status, tobacco smoking and alcohol drinking[1-3,28]. In particular, there is a complex relationship between chronic alcohol abuse and oral disease which may not be explored fully here; thus, alcoholism can lead to neglect which may manifest itself in ill-fitting dentures that cause ulcers. Studies assessing larger samples may contribute to elucidate how the association between oral cancer and recurrent oral sores relate to tobacco and alcohol consumption, by comparing groups of patients who have and who have not had previous exposure to each of these factors.

Data collection observed frequency matching for cases and controls. We were not able to perform individual pairing, which would demand the selection of one or more reference subjects with the same matching-factors (sex and age) whereas frequency matching involves the selection of an entire stratum of reference subjects with analogous matching-factors. Taking into consideration that matching by frequency requires to be controlled in the analysis, we adjusted all regression models by sex and age group.

Dietary patterns have also been associated with oral cancer.[11,12] Thus, it is important to include the intake of food items in covariates. The frequency of fruit intake is a marker of an antioxidant, fiber-rich diet, whereas the frequency of deep fried food intake is a marker of saturated fat in diet. In any event, the assessment of diet is complex, and the possibility of residual confounding due to unacquainted effects of diet on the association between oral cancer and denture-related sores cannot be ruled out.

Although it was statistically significant in the multivariate model, the association between recurrent denture sores and oral cancer was not significant in the direct, non-adjusted assessment. This observation suggests that the potential contribution of recurrent oral sores by ill-fitting dentures in carcinogenesis may be adjuvant to the concurrent exposure to tobacco, alcohol and poor dietary habits.

When the mandible was specifically assessed, the association had analogous results to those obtained in the overall analysis. This observation is consistent with the hypothesis that most of the association between oral cancer and denture-related sores may be attributed to the use of ill-fitting dentures in the lower jaw.

This study observed a higher frequency of oral sores among mandibular denture wearers. Indeed, the anatomical characteristics of the lower jaw may explain the poorer retention of a dental prosthesis. Complaints about denture stability, discomfort and pain from traumatic ulcers more commonly concern the mandible than the maxilla, and the chance of ill-adjustment has already been reported to be higher for mandibular than for maxillary dentures, whether assessed by the patient or by the dentist[15].

This study supplied further evidence of the association between oral cancer and recurrent sores that are caused by ill-fitting dentures in an assessment that has been adjusted for the most relevant cancer covariates. Chronic inflammation of the oral mucosa by sore spots, *Candida*-related stomatitis in denture wearers and lower chewing performance due to pain may provide plausible explanations of these results. Therefore, this study reinforces the importance of dental services for adults and the elderly.

The success of prosthetic dental treatment is multi-factorial and depends on psychological factors of the patient, the quality of denture making, and the previous status of oral, denture-bearing mucosa. Most of these factors can be achieved if adequate oral rehabilitation and patient follow-up are offered to edentulous patients[29,30]. In addition to improving mouth function and quality of life, the appropriate application and monitoring of dental prosthesis represent a non-negligible scope for cancer prevention.

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