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Índice de massa corporal, resposta ao tratamento e sobrevida no câncer de cabeça e pescoço: fatores relacionados aos desfechos clínicos

Governador Valadares
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Dissertação apresentada ao Programa de Pós-Graduação em Ciências Aplicadas à Saúde, da Universidade Federal de Juiz de Fora, Campus Governador Valadares, como requisito parcial à obtenção do título de Mestre em Ciências Aplicadas à Saúde, área de concentração Biociências.

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Dedico este trabalho

à minha mãe, que me ensinou a contar nos dedos.

Ao meu pai, que me ensinou a fazer conta de cabeça.

À minha avó, que me ensinou a contar com Deus.

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*“*Um professor, uma caneta, um livro e uma criança

podem mudar o mundo”

Malala Yousafz

RESUMO

A incidência e mortalidade por câncer têm aumentado globalmente, com o câncer de cabeça e pescoço (CCP) representando 5% dos casos e cerca de 500.000 mortes anuais. O CCP pode causar desnutrição devido à dificuldade na ingestão de alimentos, efeitos colaterais do tratamento e aumento das necessidades nutricionais. A má nutrição prejudica a eficácia do tratamento, aumenta o risco de complicações e afeta a sobrevida dos pacientes. O objetivo da pesquisa foi avaliar os fatores relacionados aos resultados negativos da terapia antitumoral inicial e a relação entre o estado nutricional pré-tratamento e sobrevida. Foi realizado um estudo de coorte retrospectivo com pacientes maiores de 18 anos diagnosticados com CCP, atendidos em um serviço de oncologia em Minas Gerais, Brasil, entre 2009 e 2014. Os dados sociodemográficos, clínicos e características da doença foram extraídos de prontuários eletrônicos e analisados por regressão logística multinomial e curvas de Kaplan-Meier com regressão de Cox, nos *softwares SPSS Statistics e Jamovi*, respectivamente, com nível de significância de 5%. O estudo incluiu 635 pacientes com CCP, com mediana de idade de 61 anos (33-101 anos). Desses, 31,7% (201) receberam tratamento multimodal, combinando radioterapia e quimioterapia. Ao final da terapia antitumoral inicial, 45,4% (288) dos pacientes apresentaram progressão da doença e 61,0% (126) desenvolveram recidiva loco-regional. A análise de regressão logística indicou que atrasos no início do tratamento ($p < 0.004$), manutenção do tabagismo ($p < .001$) e estadiamento do tumor ($p < 0.033$) e comprometimento dos linfonodos ($p < .001$; $p < 0.032$) foram associados a piores resultados. Os dados de peso e estatura estavam disponíveis apenas para 201 pacientes. Destes, 48% (96) estavam abaixo do peso, 42% (85) tinham peso normal e 10% (20) estavam acima do peso. Na análise univariada, pacientes com sobrepeso apresentaram significativamente melhor sobrevida global (SG) (HR = 0,60; IC 95% = 0,31-1,14; p = 0,035) e sobrevida específica da doença (SED) (HR = 0,45; IC 95% = 0,20-0,99; p = 0,047). No entanto, a significância estatística não foi mantida na análise multivariada. O grupo com excesso de peso teve uma maior mediana (MD) de tempo de sobrevida (SG = MD 32 meses; IC 95% = 6-103; e SED = MD 37 meses; IC 95% = 23-62), comparado aos grupos baixo peso (SG = MD 8 meses; IC 95% = 6-13; e SED = MD = 13 meses; IC 95% = 8-18) e eutrofia (SG = MD 12 meses; IC 95% = 8-20; e SED = MD = 15 meses; IC 95% = 11-23). No entanto, é importante considerar os riscos associados à obesidade na avaliação desses desfechos. Em conclusão, a análise revelou que fatores como o atraso no início do tratamento, a manutenção do tabagismo e o estadiamento avançado estão associados a progressão da doença e mortalidade. Além disso, o estado nutricional pré-tratamento impacta a sobrevivência, com outros fatores também influenciando o desfecho. Esses achados reforçam a importância do diagnóstico e tratamento precoces, a implementação de intervenções nutricionais direcionadas e o monitoramento contínuo dos grupos de risco, com abordagens terapêuticas personalizadas para cada paciente.

Palavras-chave: Carcinoma de Células Escamosas; Estado nutricional; Prognóstico; Sobrevida.

ABSTRACT

The incidence and mortality rates of cancer have been increasing globally, with head and neck cancer (HNC) accounting for 5% of cases and approximately 500.000 deaths annually. HNC can cause malnutrition due to difficulties in food intake, treatment side effects, and increased nutritional requirements. Poor nutrition impairs treatment effectiveness, increases the risk of complications, and affects patient survival. The aim of this study was to evaluate factors associated with negative outcomes of initial antitumor therapy and the relationship between pre-treatment nutritional status and survival. A retrospective cohort study was conducted with patients aged over 18 years diagnosed with HNC, treated at an oncology service in Minas Gerais, Brazil, between 2009 and 2014. Sociodemographic, clinical, and disease characteristics were extracted from electronic medical records and analyzed using multinomial logistic regression and Kaplan-Meier curves with Cox regression in SPSS Statistics and Jamovi software, respectively, with a significance level of 5%. The study included 635 patients with HNC, with a median age of 61 years (range 33–101 years). Of these, 31.7% (201) received multimodal treatment combining radiotherapy and chemotherapy. At the end of initial antitumor therapy, 45.4% (288) of patients showed disease progression, and 61.0% (126) developed locoregional recurrence. Logistic regression analysis indicated that delays in treatment initiation ($p < 0.004$), continued smoking ($p < 0.001$), tumor staging ($p < 0.033$), and lymph node involvement ($p < 0.001$; $p < 0.032$) were associated with worse outcomes. Weight and height data were available for only 201 patients. Of these, 48% (96) were underweight, 42% (85) had normal weight, and 10% (20) were overweight. In univariate analysis, overweight patients had significantly better overall survival (OS) (HR = 0.60; 95% CI = 0.31-1.14; $p = 0.035$) and disease-specific survival (DSS) (HR = 0.45; 95% CI = 0.20-0.99; $p = 0.047$). However, statistical significance was not maintained in multivariate analysis. The overweight group had a higher median (MD) survival time (OS = MD 32 months; 95% CI = 6-103; and DSS = MD 37 months; 95% CI = 23-62), compared to the underweight group (OS = MD 8 months; 95% CI = 6-13; and DSS = MD 13 months; 95% CI = 8-18) and normal weight group (OS = MD 12 months; 95% CI = 8-20; and DSS = MD 15 months; 95% CI = 11-23). However, it is important to consider the risks associated with obesity when evaluating these outcomes. In conclusion, the analysis revealed that factors such as delayed treatment initiation, continued smoking, and advanced tumor staging are associated with disease progression and mortality. Furthermore, pre-treatment nutritional status impacts survival, with other factors also influencing outcomes. These findings emphasize the importance of early diagnosis and treatment, the implementation of targeted nutritional interventions, and continuous monitoring of at-risk groups, with personalized therapeutic approaches for each patient.

Keywords: Squamous Cell Carcinoma; Nutritional Status; Prognosis; Survival.

SUMÁRIO

1 INTRODUÇÃO

As Doenças Crônicas Não Transmissíveis (DCNTs) são a principal causa de morte e incapacidade globalmente, sendo responsáveis por quatro em cada seis óbitos em 2023, com 48% das mortes ocorrendo de forma prematura (1,2). No Brasil, mais de 700.000 mortes anuais são atribuídas às DCNTs, com destaque para as neoplasias malignas, responsáveis por aproximadamente 500.000 óbitos anuais (3). O Brasil apresenta a maior taxa de incidência de câncer na América do Sul e a segunda maior taxa de mortalidade (4). Em 2023, o país estimou 704 mil novos casos de câncer, com a região Sudeste concentrando 48,4% dos casos (5). Segundo a Organização Mundial da Saúde, até 2040, o número de novos casos de câncer pode variar entre 29 e 37 milhões globalmente (6).

O câncer de cabeça e pescoço (CCP) constitui-se como uma preocupação de saúde pública, sendo a sexta neoplasia mais comum, com incidência global em aumento (6). Esse tipo de câncer origina-se nas células que revestem as mucosas da região e pode afetar várias estruturas, como a cavidade oral, faringe, laringe e esôfago (7). Entre esses tipos, o câncer de lábio e cavidade oral é o terceiro mais comum em países com baixo ou médio Índice de Desenvolvimento Humano (8). No território nacional, em 2022, houve 389.846 novos casos de câncer oral (5). Esse aumento na incidência de CCP é impulsionado por fatores como a transição demográfica, epidemiológica e nutricional, além da maior exposição a agentes cancerígenos (9,10). Como esses fatores de risco são passíveis de intervenção, atuar sobre eles pode auxiliar na prevenção, bem como melhorar a qualidade de vida e a saúde da população (11).

Apesar dos esforços substanciais investidos no desenvolvimento terapêutico do CCP, a taxa de sobrevivência em cinco anos permanece baixa, cerca de 40–50% (12). A principal razão é o diagnóstico tardio, a metástase recorrente, resistência terapêutica e a falta de opções eficazes em estágios avançados (13). A sobrevivência depende de vários fatores, como o estadiamento clínico (TNM), hábitos de vida (dieta, uso de álcool e tabaco durante o tratamento e atividade física) (4,14) e o estado nutricional (15). Além disso, as complicações associadas aos tratamentos, como mucosite, disfagia, anorexia e caquexia, agravam frequentemente o quadro clínico, prejudicando a continuidade do tratamento (16-19).

Este cenário evidencia a necessidade urgente de estratégias eficazes de prevenção e diagnóstico precoce, a fim de reduzir os elevados índices de incidência do CCP. Em relação à sobrevivência e mortalidade, é fundamental identificar os grupos de risco

predominantes e adotar tratamentos mais eficazes e personalizados, levando em conta as particularidades de cada paciente. Nesse contexto, intervenções multidisciplinares desempenham papel crucial, aprimorando os protocolos terapêuticos e, consequentemente, os resultados clínicos e a saúde geral dos pacientes. Fatores como o estado nutricional pré-tratamento e outras variáveis clínicas estão associados aos resultados negativos da terapia antitumoral inicial e à sobrevida no câncer de cabeça e pescoço. Assim, este estudo tem como objetivos: 1) analisar os fatores associados aos resultados negativos da terapia antitumoral inicial; e 2) avaliar a relação entre o estado nutricional pré-tratamento e a sobrevida no CCP. Espera-se que os achados proporcionem novas perspectivas para a implementação de protocolos individualizados, com impacto significativo tanto na prática clínica quanto nas políticas de saúde pública voltadas à oncologia.

2 ARTIGO CIENTÍFICO

Artigo científico submetido para publicação no periódico *International Journal of Oral and Maxillofacial Surgery,* qualis CAPES Interdisciplinar A2. A estruturação do artigo baseou-se nas instruções aos autores preconizadas pelo periódico (ANEXO B).

Predictive factors of the efficacy of initial antitumor therapy in patients with head and neck squamous cell carcinoma: a Brazilian cohort

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Abstract

Head and neck squamous cell carcinoma (HNSCC) is an aggressive disease, often diagnosed at advanced stages, with many patients presenting locoregional recurrence after initial treatment. This retrospective cohort study aimed to identify factors associated with recurrence and mortality after initial therapy. We analyzed electronic medical records of 635 patients aged over 18 years diagnosed with HNSCC, treated at an oncology service in Minas Gerais, Brazil, between 2009 and 2014. A multinomial logistic regression model was used to assess predictive factors using SPSS Statistics software. The median age was 61 years (range, 33–101 years). Regarding initial treatment, 31.7% (201) of patients received a combination of radiotherapy and chemotherapy. At the end of treatment, 45.4% (288) showed disease progression and 61,7% (392) developed locoregional recurrence. Significant predictors of disease progression included time to treatment initiation ($p < 0.004$), continued smoking ($p < 0.001$), and advanced nodal involvement ($p < 0.001$). Predictors of mortality included age ($p = 0.031$), clinical T staging ($p = 0.033$), and advanced nodal involvement ($p = 0.032$). These findings emphasize the importance of early screening, especially in older patients. The high rates of progression and recurrence highlight the need for personalized treatments, particularly for those with identified risk factors.

Keywords: Progression-Free Survival, Mortality, Adverse Symptoms; Outcomes.

Introduction/Background

Head and neck cancer (HNC) accounts for 5% of all malignant cancers worldwide, with approximately 600.000 new cases diagnosed annually, resulting in approximately 500.000 deaths (1). Head and neck squamous cell carcinoma (HNSCC) is the most common subtype, characterized by highly aggressive behavior and a significant genetic diversity (2). The average age at diagnosis of non-viral HNSCC is 66 years, with an increase in its incidence observed in younger age groups (≤45 years) (3). HNSCC is more prevalent in men who are two to four times more likely to develop it than women (1). The most common risk factors include smoking and excessive alcohol consumption, both of which are known to have a synergistic effect. Additionally, lifestyle habits, diet, and physical inactivity contribute to an increased risk, as well as viral infections from the human papillomavirus (HPV) (4).

The five-year survival rate for HNSCC is among the lowest of all common cancers and is related to late diagnosis (5). Diagnosis HNSCC remains a concern, as many cases are diagnosed when the disease is locally advanced or metastatic (4). Clinical staging, based on the TNM system, is essential for determining the extent of the disease and guiding the choice of initial therapy. However, the detection of HNSCC at more advanced stages, often diagnosed in stages III and IV, contributes to late diagnosis and the complications associated with treatment (6).

In general, surgery is the first treatment for cancers of the oral cavity, while other regions often require the use of radiotherapy (RT) with or without chemotherapy (CT). Although the addition of CT to RT increases the likelihood of local control in advanced cancers, the associated toxicities remain a significant concern (7). These adverse symptoms can affect patients' oral intake and may compromise treatment continuity (8).

Despite technological advancements in treatments, approximately 60% of patients with HNSCC experience recurrence after initial treatment (9). Recurrence can worsen prognosis, increase treatment costs and complexity, and lead to greater anxiety for patients (10). Identifying the ideal first-line therapy for HNSCC requires an understanding of the patient's medical history, disease burden, and related symptoms (11). The existing literature on the factors influencing the effectiveness of antitumor therapies and HNSCC recurrence has mainly focused on the type of medication used (12), treatment adherence (13), progression-free survival after first- and second-line therapies (14), and factors such as hemoglobin levels (15). However, such studies often do not address early

outcomes, limiting themselves to two-year periods or death, which hampers the identification of predictors that impact short-term outcomes. Therefore, the objective of this study was to fill this gap by characterizing patients with HNSCC and evaluating factors related to recurrence and mortality at the end of the initial antitumor therapy, focusing on early outcomes and variables that are still underexplored, providing a more detailed and updated view of the factors influencing the clinical progression of these patients.

Materials and Methods

Study Population

Retrospective cohort study of all patients over 18 years of age and with a primary diagnosis of HNSCC who underwent oncology treatment between 2009 and 2014 in an oncology service in Minas Gerais, Brazil. Patients without clinical outcomes were excluded. This study was approved by the research ethics committee (5.510.352) and was conducted in accordance with the Declaration of Helsinki (2013).

Data Collection

The baseline data of the patients were obtained through the analysis of electronic medical records at the time of medical admission. The collected information included demographic data (age and sex), clinical data (tumor location, staging, and type of treatment), outcome at the end of the initial treatment (stable disease, disease progression, or death), and recurrence over five years, as well as lifestyle habits (smoking and alcohol consumption) and adverse symptoms during treatment. The five-year recurrence was evaluated in patients who had stable disease after six months of completing initial antitumor therapy, with this period being defined based on previous literature, which suggests this timeframe as a standard for assessing recurrence after treatment completion. Additionally, the six-month period was chosen due to patient follow-up loss beyond this point, making it a practical and consistent reference for evaluating disease stability and recurrence. The patients were characterized by the anatomical location of the tumor, which included the following areas: oral cavity (tongue; floor of mouth; lip; ridge; buccal mucosa; retromolar area; soft palate; lower ridge/gum; parotid; piriform sinus; hard palate; diffuse; submandibular; maxillary sinus; lingual tonsil; main salivary gland; and uvula), upper airways (oropharynx; hypopharynx; larynx; nasopharynx; epiglottis;

thyroid gland; pharynx; and glottis), esophagus, and other anatomical sites. The patients were grouped according to the outcome, assessed six months after the completion of initial antitumor therapy, into three categories: stable disease, progressive disease, or death.

Statistical Analysis

The variables sex, smoking, alcohol use, tumor location, T staging, lymph node involvement, recurrence, and treatment characteristics were evaluated categorically using absolute and relative frequencies. The time between diagnosis and the first medical consultation, termed Time 1, and the time between diagnosis and the initiation of treatment, Time 2, were calculated to analyze the impact of these factors on recurrence and mortality. Both times were analyzed using the median and interquartile range, as well as age, duration of smoking, and alcohol consumption. The prevalence of adverse symptoms was estimated based on the medical report of symptoms from the onset to the completion of treatment. The clinical staging of the tumor was determined based on the 7th edition of the American Joint Committee on Cancer (2017) (6). A multinomial logistic regression model was used to assess the relationship between factors related to recurrence and mortality at the end of the initial treatment, with patients with controlled disease as the reference category. Significant associations were initially identified through univariate analysis and then combined into a multivariate model using the forward method. Collinearity tests were conducted for potential covariates. All statistical analyses were performed using SPSS Statistics software (v. 29.0.2.0, Armonk, New York). All significance levels were set at $p < 0.05$, and all tests were two-tailed.

Result

Based on the defined inclusion criteria, 704 patients were initially identified. 69 were excluded due to missing clinical data, resulting in a final total of 635 patients with HNSCC. The baseline characteristics of these patients are presented in Table 1. The patients' age ranged from 33 to 101 years (median = 61 years), with 77.5% (492) male patients. Among the patients, 76.1% (512) were current or former tobacco users. The patients were diagnosed at more advanced stages, with T3/T4 staging present in 57.5% (357) of the cases, although 63.8% (405) patients did not have lymph node involvement. The most common site of involvement was the esophagus (40.8%).

Table 1. Baseline patient characteristics

Variables	All	
	N = 635	%
Age (years)		
median (range)	635	61 (33-101)
Sex (%)		
Female	142	22,5
Male	492	77.5
Smoking history		
Never	123	19.4
Current	360	56.7
Past	152	23.9
Smoking duration (years)		
median (range)		10 (1-70)
Alcohol use history		
Never	231	36,4
Current	221	34.8
Past	183	28.8
Duration of alcohol use (years)		
median (range)		7 (1-64)
Stage of disease at diagnosis		
Clinical stage T		
T0	115	18.1
T1/T2	155	24.4
T3/T4	365	57.5
Clinical stage N		
N0	413	65.1
N1/N2	189	29.7
N3/N4	33	5.2
Primary tumor location (%)		
Oral cavity	187	29.4
Upper airways	178	28.1
Esophagus	259	40.8
Other anatomical sites	11	1.7
Nutritional Care (%)	256	40.3

Clinical stage T - characteristics of the primary tumor; Clinical stage N - characteristics of the lymph nodes in the lymphatic system

The median time between diagnosis and the first medical consultation in the clinical oncology service (Time 1) was one month, ranging from one to twenty-five months. Treatment initiation occurred between one and twenty months after diagnosis, with a median of two months (Time 2) (Table 2). In this cohort, 31.7% (201) of patients were treated with a combination of radiotherapy and chemotherapy, with cisplatin used in 50.6% (321) of cases. After the completion of the initial antitumor therapy, at six months, 45.5% (288) of patients showed disease progression, 32.4% (206) had the disease controlled, and 22.2% (141) had died. Among the patients with controlled disease, 61%

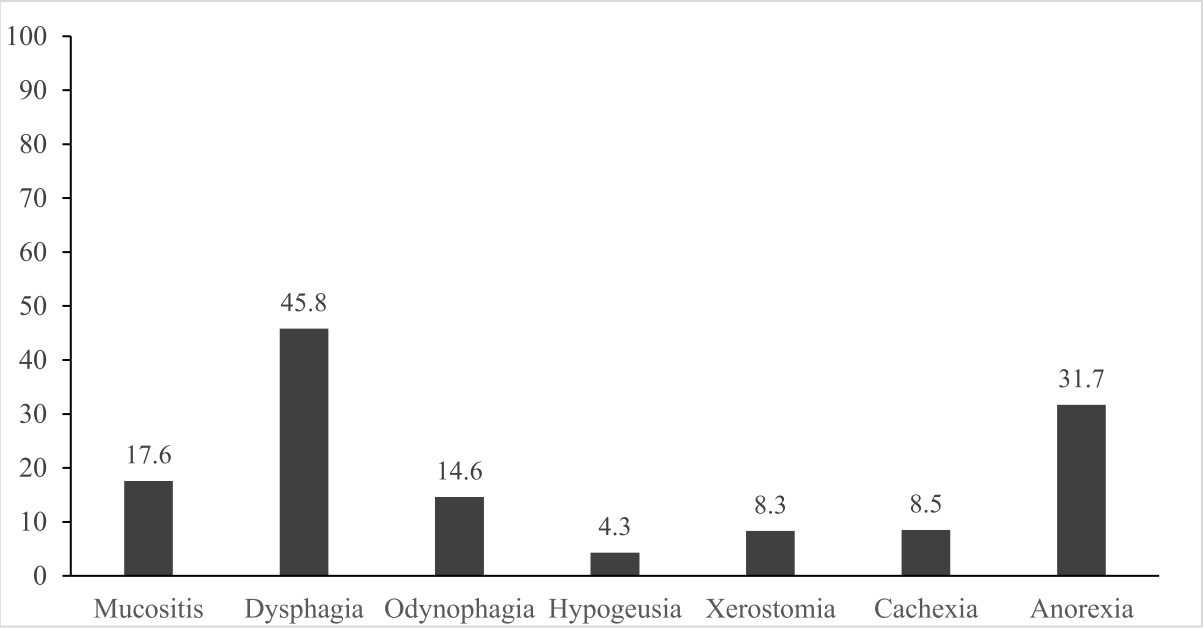
(126) developed loco-regional recurrence within five years. Regarding the adverse symptoms evaluated after the start of treatment, dysphagia was the most common (45.8%), followed by anorexia (31.7%) and mucositis (17.6%) (Figure 1).

Table 2. Treatment characteristics

Variables	All	
	N = 635	%
Time 1 (months)		
median (range)		1 (1-25)
Time 2 (months)		
median (range)		2 (1-20)
Treatment type		
RT	102	16.1
CT	75	11.8
RT/CT	201	31.7
Surgery	17	2.7
Type of medication		
Taxol	184	29.0
Cisplatin	321	50.6
5-Fluorouracil	141	22.2
Outcome of initial antitumor therapy (after six months)		
Controlled disease	206	32.4
Progressive disease	288	45.4
Death	141	22.2
Recurrence (five years)	126	61.0

Time 1 - Time between diagnosis and the first medical consultation; Time 2 - Time between diagnosis and the start of treatment; RT – radiotherapy; CT – chemotherapy

Figure 1. Prevalence of adverse symptoms in patients with HNSCC during the initial treatment



Predictors of outcome at the end of initial antitumor therapy were assessed by multinomial logistic regression. In univariate analysis, sex and lesion site were not significant predictors and were therefore excluded from multivariate analysis. In the final multivariate model, for patients with disease progression, significant predictors included time from the first medical consultation to start of treatment (Time 2) ($p < 0.004$), continued smoking during treatment ($p < .001$), and more advanced lymph node involvement ($p < .001$). Among patients who died, significant predictors were age group ($p = 0.031$), clinical T stage ($p = 0,033$), and lymph node involvement ($p = 0.032$), which was also in advanced stages (Table 3). The model used explained between 36,7% (Cox and Snell R^2) and 41,2% (Nagelkerke R^2) of the variability in the factors influencing treatment efficacy.

Table 3. Multinomial logistic regression

	Exp (β)	S.E.	P value	95% CI for Exp (β)	
Progressive disease x Controlled disease					
Age group	0.96	0.26	0.898	0.57	1.62
Time 2 (months)	1.10	0.03	0.004	1.03	1.17
Smoking	1.30	0.43	<.001	0.55	3.03
Alcohol use	1.03	0.33	0.554	0.42	1.58
Clinical stage T	1.48	0.59	0.507	0.46	4.77
Clinical stage N	1.32	0.68	<.001	0.64	9.46
RT	0.88	0.35	0.055	0.67	0.98

CT	0.45	0.42	0.058	0.17	1.02
RT/CT	0.38	0.52	0.062	0.13	0.61
Taxol	1.15	0.29	0.611	0.65	2.05
Cisplatin	1.42	0.38	0.358	0.66	3.04
5-Fluorouracil	0.80	0.32	0.514	0.42	1.53
Death x Controlled disease					
Age group	0.06	1.26	0.031	0.005	0.78
Time 2 (months)	2.34	1.10	0.685	1.20	9.11
Smoking	1.53	0.39	0.283	0.70	3,36
Alcohol use	1.10	0.98	0.596	0.53	1.78
Clinical stage T	4.85	2.31	0.033	1.20	6.49
Clinical stage N	3.56	2.14	0.032	1.11	11.44
RT	1.05	0.25	0.841	0.64	1.72
CT	2.00	0.36	0.057	0.97	4.11
RT/CT	1.17	0.30	0.117	0.06	1.44
Taxol	0.28	2.83	0.318	1.60	5.00
Cisplatin	1.53	0.40	0.289	0.69	3.38
5-Fluorouracil	0.77	0.30	0.405	0.43	1.40

RT – radiotherapy; CT – chemotherapy; Progressive disease: n= 288; Controlled disease: n= 206; Death: n= 133.

Discussion

In this study, we retrospectively investigated the characteristics of patients with HNSCC to identify factors associated with negative outcomes related to initial antitumor therapy, six months after the completion of treatment. Treatment outcomes were significantly influenced by various factors, including patient age, continued smoking, clinical T staging, and advanced nodal involvement. Additionally, we highlight the importance of other factors, such as delays in treatment initiation, which negatively impact disease recurrence.

Our findings are consistent with those of other retrospective cohorts (14-16). Fisher *et al*. (2018), when evaluating overall survival and progression-free survival, observed that the effectiveness of initial therapy in patients with refractory or recurrent HNC was significantly predicted by sex, age at diagnosis, alcohol and tobacco use, performance status, and treatment modality (14). Similarly, Irawan *et al*. (2022) identified that factors such as smoking have a significant impact on progression-free survival in HNC (15).

Smoking is one of the main risk factors for the development of HNSCC, and its continued use can have a negative impact on disease progression (17). We observed that most patients were current or former smokers. Tobacco is associated with hypoxia

mechanisms at the tissue level. Hypoxia induces the formation of hypoxia-inducible factor 1, whose overexpression can stimulate vascular endothelial growth factor, promoting angiogenesis and increasing tumor aggressiveness (11).

We observed a predominance of male patients and clinical T staging at more advanced stages, as reported in other studies (4,8,18). These data correspond to the epidemiological profile of the disease, which is recognized to be more frequent in men and commonly diagnosed at advanced stages. Additionally, by the end of initial therapy, most patients still exhibited disease progression, and a considerable proportion developed loco-regional recurrence within six months, corroborating other findings (15,19).

Despite advances in therapeutic approaches, recurrence in HNSCC remains high, as also described by Haring *et al*. (2023). In their twenty-year cohort, they found that most patients experienced treatment failure within six months after the completion of therapy (19). The time interval to recurrence is associated with unfavorable clinical outcomes. Early recurrence is primarily attributed to the aggressive biological behavior of the tumor, characterized by a rapid growth rate and resistance to treatment (20).

Identifying barriers to treatment access is crucial for understanding the impact of these factors on disease progression, emphasizing the importance of investigating factors associated with delays. Rutkowska *et al*. (2020) reported that the average time between the onset of symptoms and seeking specialized care is 7.4 months. In contrast, the interval between the pathological diagnosis and the initiation of therapy ranges from two to four months (18), which is consistent with the findings of our study. Although the median time between diagnosis and the first consultation was only one month, the time to treatment initiation varied significantly, indicating possible delays that may influence prognosis. It is widely recognized that prolonged waiting periods lead to tumor progression and can impact local control and patient survival (21).

One factor to consider in this context is the limited availability of oncology support services, as is the case in the region where the study was conducted. Several factors contribute to delayed access to healthcare services. Patient-related factors are multidimensional and include symptoms, treatment toxicities, and the demanding treatment schedules, as well as socioeconomic factors such as education level and the distance traveled to receive treatment (22). These aspects not only impact treatment adherence but also increase the risk of treatment abandonment, as evidenced in various cases (13). Additionally, specialized centers are integrated with other primary care services and operate through referral and counter-referral mechanisms to ensure

continuity of care (23–25). However, this system faces significant barriers to providing universal and timely coverage, which affects waiting times for treatment initiation and contributes to higher treatment abandonment rates, ultimately hindering clinical outcomes for patients (26). In our analysis, we were unable to determine the treatment abandonment rate due to the lack of these data. It is worth noting that abandonment is an important factor for the negative outcomes observed, such as early disease recurrence.

The guidelines on new efficacy criteria for solid tumors emphasize that changes in tumor size can be considered an objective indicator in evaluating the efficacy of any anticancer therapy (27). Tumor reduction and disease progression are important outcomes that can reflect treatment response and overall effectiveness (28). Li *et al*. (2024) conducted a study with lung cancer patients using the Response Evaluation Criteria in Solid Tumors (RECIST) to assess tumor response and found no significant differences in progression-free survival between patients with complete or partial response and those with progressive disease (29). Our study was based exclusively on initial clinical staging, specifically tumor size, which may not accurately reflect the status of tumor cells. Additionally, the RECIST system recommends that the evaluation of objective response or future progression be done through a comparison of the overall tumor burden at the beginning of the study with subsequent measurements. Since tumor size was recorded only at the time of diagnosis, it was not possible to establish this comparison (27).

The study results showed variation in therapeutic modalities and medications used in treatment. The platinum-based chemo-radiotherapy multimodal approach was the most used as the initial therapy. Studies conducted over the years have demonstrated advantages in the use of concurrent chemoradiotherapy (30). The combination of chemotherapy and radiotherapy can improve local control and survival rates due to the additive or synergistic effects of chemoradiotherapy (31). However, the tolerability and outcomes of this treatment approach depend on several factors, including the presence of positive cervical lymph nodes. In the study conducted by Zami *et al*. (2024), nodal involvement was identified as a significant predictor of negative treatment response, corroborating our findings (21). Thus, lymph node involvement can affect both treatment and prognosis, as well as being associated with recurrence and reduced overall survival in these patients (32). Identifying lymph node involvement as a significant predictor of treatment failure is a key point, and this information can be incorporated into more accurate risk assessments, contributing to the personalization of therapeutic approaches.

Additionally, a high incidence of adverse symptoms was observed among the patients in the study, which is consistent with previous research (8,33). These symptoms, which have a nutritional impact, can cause pain, inflammation, and malnutrition, reducing treatment tolerance and increasing the risk of toxicity. The multicenter study conducted by Schiessel *et al*. (2022) revealed that the presence of more than three adverse symptoms indicates a significant risk of weight loss (8). Although we did not assess total weight and symptom severity due to the lack of these data, it is evident that these symptoms affect food intake and may require dietary adjustments. The high incidence of these symptoms highlights the need for nutritional intervention, as only 40.3% of patients received this care. In the current context, nutritional monitoring is carried out through medical referrals, although not formally standardized, prioritizes patients with eating difficulties, involuntary weight loss, overweight, or associated metabolic comorbidities. Given that these symptoms are common in patients with HNSCC, it is essential to continuously monitor them to restore food intake, which may require different levels of nutritional intervention (33).

The identification of nodal involvement as a significant predictor of negative treatment response can be incorporated into risk assessments and prognostic evaluations, helping to personalize treatment according to the individual needs of patients Additionally, the high incidence of adverse symptoms and their impact on nutrition and treatment tolerance emphasize the importance of including specific nutritional interventions in therapeutic plans, which could potentially improve both the quality of life of patients and clinical outcomes. The results reinforce the importance of educating patients and healthcare professionals about the risks associated with smoking and the significance of early cancer detection. These contributions not only enhance the understanding of the dynamics of HNSCC treatment but also provide practical guidelines that can be implemented to improve patient care.

Our study has several limitations, including data restrictions typical of retrospective cohort studies, such as missing data in patient records, lack of standardization in documentation, and specific follow-up cut-off points. Additionally, the study was conducted at a single specialized oncology treatment center. The analysis of clinical and demographic characteristics was also limited by the available documentation in the electronic medical records.

Conclusion

The results of this study indicate that advanced age, delays in the initiation of treatment, continued smoking, and starting treatment at more advanced stages in clinical T and N staging are associated with a higher likelihood of negative outcomes at the end of initial anticancer therapy, regardless of the type of treatment used. These factors are also correlated with considerable mortality rates, highlighting the importance of early screening and diagnosis of HNSCC. Furthermore, the findings reveal a high prevalence of adverse symptoms in this population, which can impact both quality of life and treatment continuity. The elevated rates of disease progression and loco-regional recurrence emphasize the need for more effective and personalized therapeutic approaches, particularly for patients with identified risk factors.

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3. ARTIGO 2

Artigo científico publicado no periódico *Oral diseases*, qualis CAPES Interdisciplinar A1. A estruturação do artigo baseou-se nas instruções aos autores preconizadas pelo periódico (ANEXO D).

Santos D. C.; Carvalho, G. Q.; Silvestre, C. C.; de Aquino, S. N. *Body Mass Index as an Indicator of Survival in Oral Cancer.* ***Oral Dieases***. Oct. 2024. Doi: 10.1111/odi.15155.

Oral Diseases

WILEY

ORAL DISEASES

LETTER TO THE EDITOR

Body Mass Index as an Indicator of Survival in Oral Cancer

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Dear Editor,

Oral squamous cell carcinoma (OSCC) is the most prevalent type of head and neck cancer. Despite advancements in early detection and treatment, overall survival (OS) and disease-specific survival (DSS) rates remain low (Bhat, Hyole, and Li 2021; Bray et al. 2024). Additionally, approximately 20% to 70% of patients are malnourished at diagnosis (Chen et al. 2024). While anthropometric indicators are commonly used as prognostic predictors, the role of body mass index (BMI) in OSCC prognosis is not well-defined.

A retrospective cohort study was conducted at a single institution, approved by the research ethics committee (5.510.352), with data collected between 2009 and 2014. Patients aged 18 or older with available BMI data at admission and a histological diagnosis of OSCC were included. Electronic medical records were analyzed for clinical, demographic, anthropometric information, and outcomes. Patients without clinical outcomes were excluded.

Analyses employed χ^2 or Fisher's exact tests and Kruskal–Wallis. Survival was calculated from diagnosis to death or five-year censoring, with survival curves generated using Kaplan–Meier. Hazard ratios (HR) for OS and DSS were determined for BMI using univariate and multivariate Cox models, including variables that were clinically relevant or had univariate associations ($p \leq 0.2$). Analyses were conducted using the IAMGVI software.

A total of 201 patients with OSCC were included, of whom 48% were underweight, 42% had a normal weight, and 10% were overweight. The median (MD) age at diagnosis was 61 years (34–97 years). The BMI ranged from 11.9 to 31.6 kg/m^2 (MD = 20.4 kg/m^2). No significant differences were found in the baseline characteristics between the groups (Table S1).

In the Cox regression, OS and DSS were significantly better in the overweight group in the univariate analysis, OS (HR = 0.60; CI = 0.31–1.14; $p = 0.035$) and DSS (HR = 0.45; CI = 0.20–0.99; $p = 0.047$), but this significance did not persist in the multivariate analysis (Table S2). Overweight patients showed better clinical outcomes and 5-year survival (Figure S1), consistent with previous studies (Pastorino et al. 2022; Wu et al. 2022; Yang et al. 2024). It has been suggested that a higher BMI represents a reserve of nutrients, providing greater protection (Ferrão et al. 2020). However, the protective effect of being overweight loses significance when BMI exceeds 30 kg/m^2 due to its association with an increased risk of developing cardiovascular diseases (Hobday et al. 2022). The patients in the sample did not exhibit severe obesity, resulting in a lower risk and better survival.

The study observed a higher prevalence of underweight individuals, possibly related to tumor location and disease progression. Patients in this condition may represent a risk group for treatment tolerance or indicate the presence of a more aggressive tumor (Gama et al. 2017).

The results reinforce that pretreatment BMI is a significant prognostic factor for OS and DSS in patients with OSCC. Furthermore, a higher BMI at diagnosis has a protective effect on OS and DSS. However, patients with obesity require greater attention due to the risk of developing other diseases. Thus, assessing BMI at diagnosis may help identify more vulnerable patients.

Author Contributions

Deysimara de Cássia Santos: conceptualization, investigation, writing – original draft, methodology, project administration, formal analysis. **Gisele Queiroz Carvalho:** writing – review and editing, methodology, data curation. **Carina Carvalho Silvestre:** writing – review and editing. **Sibele Nascimento de Aquino:** writing – review and editing, supervision, project administration.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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Carina Carvalho Silvestre
Sibele Nascimento de Aquino

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Supporting Information

Additional supporting information can be found online in the Supporting Information section.

4. CONCLUSÃO

As DCNTs, em especial as neoplasias malignas, representam uma das principais causas de mortalidade global, com o CCP emergindo como uma preocupação significativa no contexto de saúde pública. A elevada prevalência desse tipo de câncer em países de baixo e médio desenvolvimento humano ressalta a urgência de intervenções preventivas que visem reduzir a incidência e promover a conscientização sobre fatores de risco modificáveis, como tabagismo e consumo de álcool.

Os resultados desta pesquisa enfatizam que a desnutrição se relaciona diretamente ao prognóstico de indivíduos com CCP, afetando sua qualidade de vida dos pacientes. Além disso, o diagnóstico precoce e a minimização dos atrasos no tratamento são cruciais, uma vez que esses fatores influenciam significativamente a evolução da doença e a sobrevivência dos pacientes. Ainda, a relação entre o IMC e a sobrevivência dos pacientes revela uma complexa interação entre estado nutricional e prognóstico, sugerindo que um IMC elevado pode ter um efeito benéfico na sobrevida, embora seja essencial monitorar os riscos associados à obesidade. A implementação de intervenções nutricionais adequadas é fundamental, podendo contribuir para a melhoria dos desfechos clínicos e manejo dos sintomas adversos evidenciados.

A descoberta de que atrasos na iniciação do tratamento e a prevalência de sintomas adversos impactam significativamente o prognóstico dos pacientes sugere que melhorar o acesso ao tratamento e fornecer suporte nutricional adequado devem ser prioridades. Políticas de saúde pública que visem reduzir as barreiras ao tratamento, como a falta de recursos ou de centros especializados, são essenciais para melhorar os desfechos clínicos. Em perspectiva, há uma necessidade de mais pesquisas que explorem a interrelação entre fatores de risco, intervenções nutricionais e resultados clínicos. O fortalecimento das estratégias de saúde pública é essencial para enfrentar o aumento do câncer e melhorar a vida dos pacientes afetados.

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APÊNDICE A – Material suplementar Artigo 2 - *Body Mass Index as an Indicator of Survival in Oral Cancer*

Table S1. Demographic, Clinical, and Nutritional Characteristics of Patients with OSCC

Characteristic	All		Underweight		Normal weight		Overweight		p
	N = 201	%	N = 96	%	N = 85	%	N = 20	%	
Age									
median (range)	61 (34 - 97)		96	64,5 (36 - 86)	85	56 (40 - 97)	20	55 (34 - 78)	0,002[a]
≤ 60 years	93	46,3	29	30,2	52	61,2	12	60,0	< .001[ϐ]
≥ 60 years	108	53,7	67	69,8	33	38,8	8	40,0	
BMI									
median (range)	20,4 (11,9 - 31,6)		17,9 (11,9 - 19,1)		22 (18,6 - 26,6)		28,4 (25,4 - 31,6)		< .001[a]
Gender									
Woman	36	17,9	16	16,7	15	17,6	5	25	0,674[ϐ]
Man	165	82,1	80	83,3	70	82,4	15	75	
Race/ethnicity									
White	18	9,0	6	6,3	7	8,2	5	25,0	
Black	56	27,9	24	25,0	26	30,6	6	30,0	0,094[ϐ]
Brown	115	57,2	7	7,3	3	3,5	2	10,0	
Not available	12	6,0	59	61,5	49	57,6	7	35,0	
Smoker									
Never smoker	23	11,4	11	11,5	11	12,9	1	5,0	
Current	117	58,2	60	62,5	49	57,6	8	40,0	0,177[ϐ]
Former smoker	61	30,3	25	26,0	25	29,4	11	55,0	
Smoking duration (years)									
median (range)	147	10 (1 - 60)	72	10 (2 - 44)	62	10 (1 - 60)	13	20 (3 - 50)	0,742[a]
Etilist									
Never etilist	34	16,9	18	18,8	11	12,9	5	25,0	
Current	82	40,8	42	43,8	36	42,4	4	20,0	0,204[ϐ]
Ex-etilist	85	42,3	36	37,5	38	44,7	11	55,0	
Alcoholism duration (years)									
median (range)	80	8 (1 - 47)	33	6 (1 - 47)	38	8 (1 - 40)	9	8 (3 - 20)	0,233[a]

T staging	30	15,0	14	14,6	13	15,5	3	15,0	
T0	8	4,0	0	0,0	8	4,0	2	10,0	
T1	40	20,0	12	12,5	23	27,4	5	30,0	0,007ᵟ
T2	84	42,0	49	51,0	32	36,9	4	20,0	
T3	38	19,0	21	21,9	11	13,1	6	25,0	
T4									
N staging									
N0	136	68,0	63	65,6	58	69,0	15	75,0	0,089ᵟ
N1	25	12,5	8	8,3	15	17,9	2	10,0	
N2	28	14,0	20	20,8	7	8,3	1	10,0	
N3	11	5,5	5	5,2	4	4,8	2	5,0	
N4	0	0	0	0	0	0	0	0	
Site of the lesion									
Oral cavity	47	23,5	21	21,9	20	23,8	6	30,0	0,100ᵟ
Upper airways	54	27,0	21	21,9	25	29,8	8	40,0	
Intestine	94	47,0	50	52,1	39	46,5	5	25,0	
Other anatomical sites	5	2,5	4	4,2	0	0	1	5,0	
Treatment									
RT	29	14,4	12	12,5	17	20,0	0	0	0,046ᵟ
CT	30	14,9	15	15,6	30	14,9	11	12,9	0,703ᵟ
RTCT	58	28,9	23	24,0	33	38,8	2	10,0	0,013ᵟ
Outcome									
Death	163	81,1	85	88,5	64	75,3	14	70,1	0,031ᵟ
Death due to OSCC	134	66,7	89	71,9	57	67,1	8	40,0	0,023ᵟ

Data expressed in absolute and relative frequency; BMI - Body mass index; CT – Chemotherapy; RT – Radiotherapy; RTCT – Chemotherapy + Radiotherapy; OSCC - Oral squamous cell carcinoma; [a]Kruskal Wallis; [ᵟ]Chi-square or fisher

Table S2. Univariate and multivariate analyses of prognostic factors associated with OS in patients with OSCC using BMI as the dependent variable

Characteristic	Category	HR	Univariate Cox IC 95%	p	HR	Multivariate Cox IC 95%	p
	Normal weight		-	-	-	-	-
BMI	Underweight	1.29	0.92-1.82	0.155	1.28	0.84-1.96	0.256
	Overweight	0.60	0.31-1.14	0.035	0.57	0.28-1.14	0.114
Gender	Woman		-	-	-	-	-
	Man	1.20	0.74-1.94	0.464			
Age (years)	≤ 60		-	-	-	-	-
	≥ 60	0.64	0.09-0.84	0.009	0.73	0.48-1.10	0.129
T staging	I	0.28	0.27-0.86	0,024	0.35	0.110-1.08	0,067
	II	0.48	0.27-0.86	0,014	0.42	0.23-0.77	0.005
	III	0.77	0.46-1.38	0,314	0.62	0.36-1.05	0.073
	IV	1.26	0.71-2.22	0,432	0.87	0.44-1.69	0,673
	I	0.98	0.58-1.65	0.945	1.06	0.61-1.82	0.845
	II	1.88	1.18-3.00	0.008	1.38	0.77-2.46	0.281
N staging	III	3.43	1.57-7.49	0.002	2.41	1.01-5.73	0.046
Smoker	Current		-	-	-	-	
	Never smoker	0.70	0.40-1.21	0,199			
	Former smoker	0.83	0.57-1.20	0,312			
Etilist	Current		-	-	-	-	-
	Etilist	0.55	0.34-0.90	0,017	0.74	0.43-1.26	0.263
	Ex-elitist	0.83	0.58-1.19	0,311	0.98	0.66-1.45	0.904
RT		1.20	0.74-1.95	0.455			
CT		1.17	0.75-1.82	0.486			
RT/CT		0.93	0.64-1.35	0.701			

20.

21. **Table S2.** Univariate and multivariate analyses of prognostic factors associated with DSS in patients with OSCC using BMI as the dependent variable

Characteristic	Category	HR	Univariate Cox IC 95%	p	HR	Multivariate Cox IC 95%	p
	Normal weight		-	-	-	-	-
BMI	Underweight	1.15	0.79-1.68	0.462	1.05	0.66-1.68	0.826
	Overweight	0.45	0.20-.099	0.047	0.49	0.21-1.13	0.095
Gender	Woman		-	-	-	-	-
	Man	0.95	0.58-1.55	0.824			
Age (years)	≤ 60		-	-	-	-	-
	≥ 60	0.75	0.52-1.08	0,123	0.87	0.55-1.38	0.550
	I	0.30	0.09-1.03	0,056	0.35	0.10-1.25	0,106
T staging	II	0.46	0.24-0.87	0,018	0.46	0.19-0.76	0.006
	III	0.80	0.46-1.38	0,426	0.80	0.37-1.15	0.138
	IV	1.06	0.56-2.38	0,861	1.06	0.32-1.44	0,316
N staging	I	0.98	0.55-1.73	0.939	1.02	0.56-1.86	0.940
	II	1.70	1.00-2.88	0.051	1.70	0.88-3.27	0.114
	III	4.03	1.83-8.86	0.001	3.81	1.55-9.36	0.004
	Current		-	-	-	-	
Smoker	Never smoker	0.69	0.38-1.28	0,243			
	Former smoker	0.87	0.58-1.30	0,492			
Etilist	Current		-	-	-	-	-
	Etilist	0.65	0.38-1.11	0,116	0.73	0.40-1.31	0.289
	Ex-elitist	0.92	0.70-1.37	0,694	1.04	0.67-1.61	0.869
RT		1.43	0.87-2.37	0.161	1.70	0.98-293	0.058
CT		1.24	0.77-2.00	0.367			
RT/CT		1.07	0.72-1.59	0.736			

CI – Confidence Interval; HR – Hazard Ratio; BMI – Body Mass Index; CT – Chemotherapy; RT – Radiotherapy

Figure 1a: Kaplan-Meier curves for overall survival adjusted for body mass index

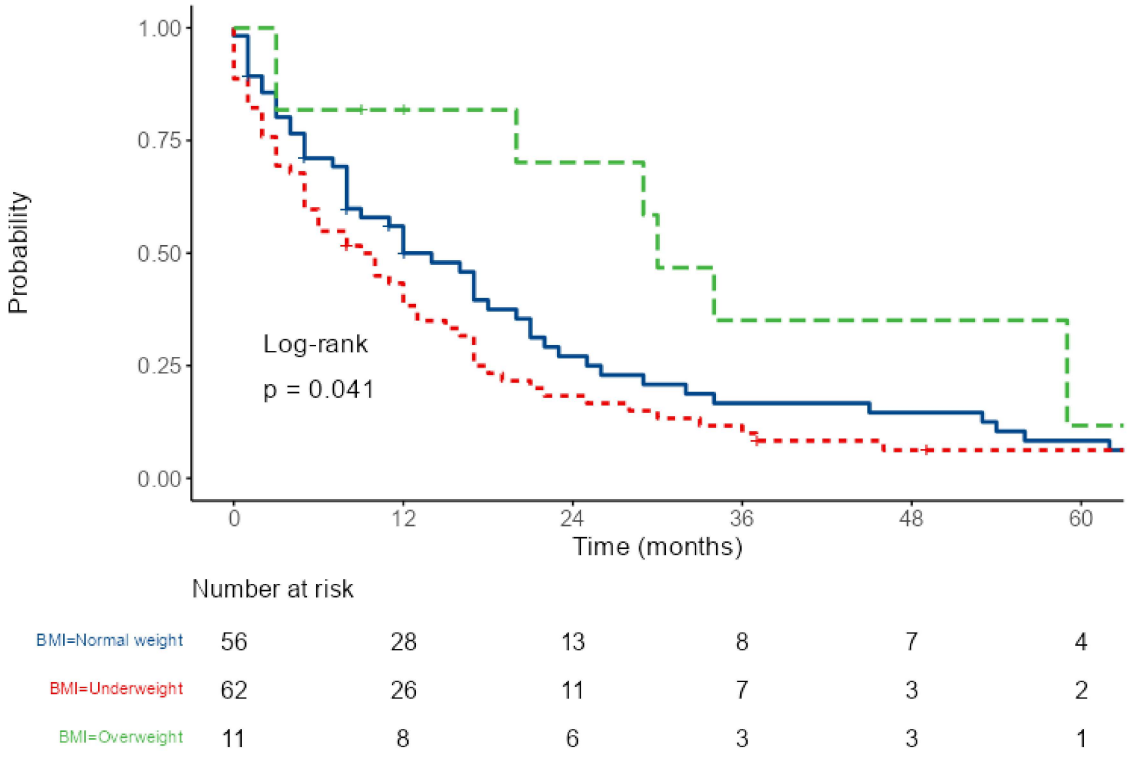
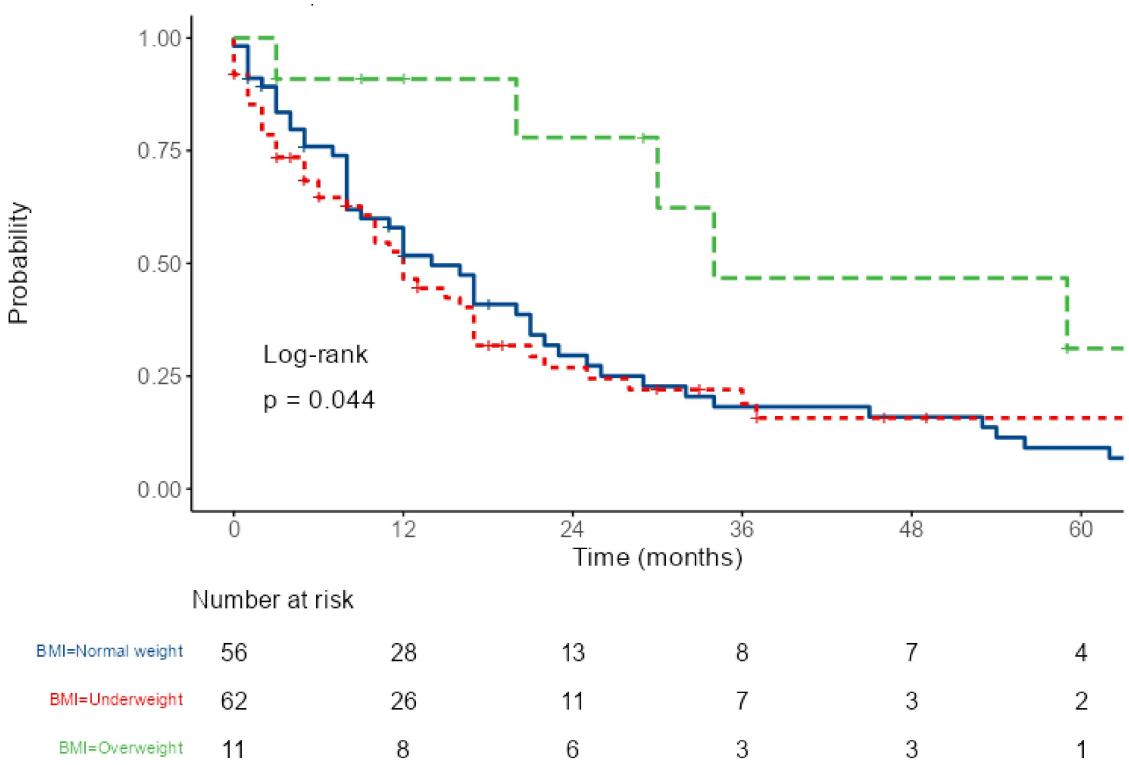


Figure 1b: Kaplan-Meier curves for disease-specific survival adjusted for body mass index



APÊNDICE B – Ficha de coleta de dados

Identificação do paciente
Nome: Iniciais - digitar iniciais sem ponto **Data de nascimento** DN Ex:DD/MM/AA **Idade:** (digitar idade em anos) **Local de nascimento:** NATURAL (código cidade IBGE cidades) **Sexo:** SEXO 1= masculino 2=feminino **Local de moradia:** CIDADE (código cidade IBGE cidades) **Zona: Z**ONA (1=urbana 2 = rural) **Ocupação:** OCUPA (código)
Estado civil: CIVIL 1.( )solteiro 2.( )casado/vive com companheiro 3. ( ) divorciado 4.( )viúvo 5. S/informação
Cor da pele: PELE 1.( ) branco 2.( ) negro 3.( )amarelo 4.( )pardo 5.( )indígena
Grau de instrução: ESCOL 1.( )analfabeto 2.( )fundamental 3.( )médio 4.( )superior 5.( )sem informação
Hábitos e vícios: **Fumo** 1.( )Sim 0.( )Não 2.( )ex-fumante **Tipo de tabaco** 1. Cigarro 2. Palha 3. Charuto 4. Cachimbo 5. Palha + Cachimbo **Quantidade de** cigarros/dia NCIGARRO **Bebida alcóolica** 1.( )Sim 0.( )Não 2. ( )ex-etilista **Tipo de bebida** 1. Fermentados 2. Destilados 3. Outros, 4 (fermentados + destilados) **Quantidade/dia NBEBIDA** **Outro OUTROVICIO** 0=não 1=sim
Informações sobre a doença
Procedência (encaminhamento) PROCEDÊNCIA: 1.( )SUS/UBS 2.( )SUS/Hospital 3. ( )Privado 4. ( ) SUS 5. ( ) Sem informação **Profissional PROFISSIONAL** 1. ( )Cirurgião Dentista 2. ( ) Médico 3. ( )Outro_____ 4. ( ) Sem informação
Data do diagnóstico DATADIAGNOSTICO dd/mm/aa (Laudo) **Tipo histológico do tumor primário TIPOHISTOL**
História familiar de câncer HISTFAM 1.( )Sim 2.( )Não Parentesco (PARENTESCO 1 - Pai, mãe, irmãos; 2 - Avô, avó, tios; 3- outros.) **Local de câncer_ LOCALFAM**
Presença de sintomas SINTOMA 0. ( ) não 1. ( ) sim 1. ( )Dor 0=não 1=sim 2. ( ) Trismo 0=não 1=sim 3. ( ) Dificuldade fala (fala) 0=não 1=sim 4. ( ) Dificuldade Alimentação (alimenta) 0=não 1=sim 6. ( ) Outros 0=não 1=sim

Aspecto clínico da lesão inicial (CLINICO) CLINICO2
1. ( ) Úlcera 2. ( ) Leucoplasia 3. ( ) Eritroplasia 4. ( ) Leucoeritroplasia 5. ( ) Nódulo 6. ( ) Outro_____

Aspectos imaginológicos
_____

Margens cirúrgicas (MARGEM)
1.( )Negativas 2.( )Positiva 3.( )não se aplica/sem tto cirúrgico

Estadiamento clínico: T_____N_____M_____ (digitar valores separados) TNM (digitar valores juntos) EC_____

Nodos (linfonodos) 0. não 1. sim
1. ( ) nodoN 1. Unilateral 2. Bilateral

Metástases à distância 0. não 1. sim Número NMETASTASE
Local e data de definição:
0.( )Sem metástases
1.( )Pulmão 0. ( ) Não 1 . ( ) Sim
2.( )Fígado 0. ( ) Não 1. ( ) Sim
3.( )Ossos 0. ( ) Não 1. ( ) Sim
4.( ) Cérebro 0. ( ) Não 1. ( ) Sim
5. ( ) pelve/abdome 0. ( ) Não 1. ( ) Sim
6. ( ) Outros 0. ( ) Não 1. ( ) Sim

Data 1ª consulta no NEO (DATACONSUL) dd/mm/aa Data do início do tratamento no NEO (DATATRAT): dd/mm/aa

Primeiro tratamento recebido no NEO TRATAMENTO 0=não 1=sim, Se marcar não, deixe opções em branco. (Ordenar) 0. não 1.primeiro 2.segundo
1.( )Nenhum 2.( )Cirurgia 3.( )Radioterapia 4.( )Quimioterapia 5.( )Sem inform.
( )Outros_____

Estado da doença após tratamento ESTADODOEN
1.( )Remissão completa 2.( )Remissão parcial 3.( )Doença estável 4.( )Doença em progressão 5.( )Sem possibilidade terapêutica 6.( )Sem informação 7.( )Abandono do tto
Óbito 1. ( )Sim 0.( ) Não
Data: dd/mm/aa Causa básica da morte CÓDIGO

Avaliação odontológica
Estomatologia 0=não 1=sim
Preencha abaixo quando marcar SIM, quando marcar NÃO deixe em branco. Exceção edentulismo. Exame clínico
1. Cárie 0. ( ) Não 1. ( ) Sim
2. Gengivite 0. ( ) Não 1. ( ) Sim
3. Periodontite 0. ( ) Não 1. ( ) Sim
4. Edentulismo 0. ( ) Não 1. ( ) Sim 2. ( ) Parcial

2º Tumores primários

0. ( ) Não 1. ( ) Sim

Data da identificação dd/mm/aa

Localização (LOCALSEG) Tipo da lesão (TIPOSEG)

Tratamento executado

Tratamento oncológico

Drogas: Taxol 0=não 1=sim
CDDP 0=não 1=sim
5FU 0=não 1=sim
Docetaxel 0=não 1=sim
Flutamida 0=não 1=sim
Aredia 0=não 1=sim

Manifestações bucais de tratamento quimio/radioterápico

( ) Mucosite Grau_____ 0. ( ) Não 1. ( ) Sim
( ) Xerostomia 0. ( ) Não 1. ( ) Sim
( ) Candidíase 0. ( ) Não 1. ( ) Sim
( ) Cárie por radiação 0. ( ) Não 1. ( ) Sim
( ) Outra (outramani)

Atendimento nutricional:

0 =não 1 = sim
Nº de consultas = Nconsul
Peso no 1º atendimento: peso kg
Data do 1º atendimento: DD/DD/DDDD
Peso relatado no 1º atend. Nutricional: peso em Kg
Data do 1º atend. Nutricional:
Peso no último atendimento
Utilizou sonda: 0 =não 1 = sim
Localização: 1 nasogastrica 2 Nasojejunal 3 Gastrostomia 4 Jejunostomia
Tipo de dieta: 1 artesanal 2 Industrializada 3 Artesanal + industrializada
Usou suplemento alimentar: 0 =não 1 = sim
Intercorrências: 0 =não 1 = sim
Anorexia: 0 =não 1 = sim
Hipogeusia: 0 =não 1 = sim
Caquexia: 0 =não 1 = sim
Disfagia: 0 =não 1 = sim

ANEXO A – Parecer consubstanciado do CEP

DADOS DA EMENDA

Título da Pesquisa: PERFIL EPIDEMIOLÓGICO DE CASOS INCIDENTES DE CÂNCER DE BOCA E OROFARINGE DIAGNOSTICADOS NO MUNICÍPIO DE GOVERNADOR VALADARES - MG.

Pesquisador: Clarice Lima Alvares da Silva **Área Temática:**

Versão: 5

CAAE: 49855815.4.0000.5147

Instituição Proponente: Universidade Federal de Juiz de Fora UFJF

Patrocinador Principal: Financiamento Próprio

DADOS DO PARECER

Número do Parecer: 6.431.766

Apresentação do Projeto:

Trata-se da segunda versão de emenda a projeto anteriormente aprovado, emenda que é apresentada com a seguinte justificativa: "Justificativa da Emenda:

A emenda está sendo proposta com objetivo de ampliar a coleta de dados de participantes tratados a partir do ano de 2015 e até o ano de 2023. Assim, nessa emenda os pesquisadores propõem a alteração do cronograma do projeto, considerando a ampliação dos anos de coleta de dados (extensão para dados a partir de 2015 até 2023). Justifica-se a emenda pela necessidade de análises adicionais dos casos a partir de 2015 já que não há dados publicados sobre os casos de câncer de boca e orofaringe para a região, sendo de extrema importância o seguimento do estudo e da excelente parceria com o serviço no intuito de gerar dados adicionais para os serviços de saúde regional e nacional, que possibilitem melhoria da qualidade de vida, diagnóstico precoce e tratamento dos pacientes".

Objetivo da Pesquisa:

Foi mantida inalterada a redação dos objetivos do projeto aprovado.

Avaliação dos Riscos e Benefícios:

A redação de riscos e benefícios da pesquisa aprovada não sofreu alteração.

Comentários e Considerações sobre a Pesquisa:

A emenda apresentada é considerada pertinente e em conformidade com as normas pertinentes.

Considerações sobre os Termos de apresentação obrigatória:

Os termos de apresentação obrigatória do projeto aprovado não sofreram alterações.

Recomendações:

Sem recomendações a acrescentar.

Conclusões ou Pendências e Lista de Inadequações:

Inexistindo inconsistências ou inadequações, a emenda está em condições de ser aprovada.

Considerações Finais a critério do CEP:

Este parecer foi elaborado baseado nos documentos abaixo relacionados:

Tipo Documento	Arquivo	Postagem	Autor	Situação
Informações Básicas do Projeto	PB_INFORMAÇÕES_BÁSICAS_2201956_E3.pdf	02/10/2023 09:38:32		Aceito
Cronograma	CronogramaEmenta2023CEC.pdf	24/08/2023 11:32:40	Sibele Nascimento de Aquino	Aceito
Projeto Detalhado / Brochura Investigador	PROJETOEmenta2023.pdf	24/08/2023 11:32:27	Sibele Nascimento de Aquino	Aceito
Outros	cartaesclarecimentoprojetoca.pdf	29/09/2015 09:54:56	Clarice Lima Alvares da Silva	Aceito
Declaração de Pesquisadores	assinadotermoconfidencialidade.pdf	20/08/2015 11:52:14	Clarice Lima Alvares da Silva	Aceito
TCLE / Termos de Assentimento / Justificativa de Ausência	assinadodispensatcle.pdf	20/08/2015 11:51:27	Clarice Lima Alvares da Silva	Aceito
Declaração de Instituição e Infraestrutura	assinadoconvenioneo.pdf	20/08/2015 11:50:30	Clarice Lima Alvares da Silva	Aceito
Brochura Pesquisa	FICHACOLETADEDADOS.pdf	20/08/2015 11:48:28	Clarice Lima Alvares da Silva	Aceito
Folha de Rosto	AssinadoFolhadeRosto.pdf	20/08/2015 11:46:40	Clarice Lima Alvares da Silva	Aceito

Situação do Parecer:
Aprovado
Necessita Apreciação da CONEP: Não

JUIZ DE FORA, 17 de Outubro de 2023

Assinado por:
Jubel Barreto
(Coordenador(a))

ANEXO B – Author Guidelines *International Journal of Oral and Maxillofacial Surgery*

Guide for authors

Authors wishing to submit their work to the journal are urged to read this detailed guide for authors and comply with all the requirements, particularly those relating to manuscript length and format. This will speed up the reviewing process and reduce the time taken to publish a paper following acceptance.

Online Submission

Submission and peer-review of all papers is conducted entirely online, increasing efficiency for editors, authors, and reviewers, and enhancing publication speed. Authors requiring further information on online submission are strongly encouraged to view the system, including a tutorial, at https://www.editorialmanager.com/IJOMS/default.aspx . For additional enquiries please visit our Support Center. Once a paper has been submitted, all subsequent correspondence between the Editorial Office (ijoms@elsevier.com) and the corresponding author will be by e-mail.

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A paper is accepted for publication on the understanding that it has not been submitted simultaneously to another journal, has been read and approved by all authors, and that the work has not been published before. The Editors reserve the right to make editorial and literary corrections. Any opinions expressed or policies advocated do not necessarily reflect the opinions and policies of the Editors.

Declarations

Upon submission you will be required to complete and upload the declarations page (pdf version or word version) to declare funding, conflict of interest and to indicate that ethical approval was given – all studies involving patients must have patient consent and ethical committee approval or exemption in writing, please refer to the section on 'Ethics' below. Patient consent is required for the publication of any clinical photographs, and all single case reports, including those where the data is anonymised. This information must also be inserted into your manuscript under the acknowledgements section with the headings below. Upon submission you will be required to complete and upload this form (pdf version or word version) to declare funding, conflict of interest, and to indicate whether ethical approval and patient consent were given and you must also upload with it the IRB approval or exemption letter. This applies to original research articles carried out on humans, including observational studies and case series. Ethical committee approval or exemption is not needed for systematic review articles or articles that are not based on humans or animals. Research on animal studies should be uploaded with the appropriate ethical approval for the study. If the ethical approval or exemption letter is not in English please provide the text in English. Lastly you must confirm that all authors have agreed to the submission.

PLEASE NOTE that all funding must be declared at first submission, as the addition of funding at acceptance stage may invalidate the acceptance of your manuscript.

Authorship

All authors should have made substantial contributions to all of the following: (1) the conception and design of the study, or acquisition of data, or analysis and interpretation of data

(2) drafting the article or revising it critically for important intellectual content

(3) final approval of the version to be submitted.

Upon submission, you will be required to complete and upload the Author contribution form to show the contribution of each author to the paper.

Normally a maximum of four authors should appear on a case report or technical note, and six authors on all other article types. If there is a requirement to include additional authors please request this in your cover letter and include the authors in the author contribution form. Minor contributors and non-contributory clinicians who have allowed their patients to be used in the paper should be acknowledged at the end of the text before the references. Please note, a request for exceeding the number of authors is not automatically accepted. The Editor-in-Chief may disagree and require an adjustment.

Co-first authorship is permitted on request of the corresponding author and must be agreed to by all co-authors.

Please note that we can only allow for one corresponding author. The corresponding author is responsible for ensuring that all authors are aware of their obligations. The corresponding author is responsible for the content and integrity of the data that is ultimately published in the accepted manuscript.

Changes to Authorship

Authors should consider carefully the list and order of authors before submitting their manuscript and provide the full list of authors at the time of the original submission. Any amendment to the author list (including addition and deletion) should be made only prior to acceptance of the manuscript. Please note that any change must be approved by the Editor-in-Chief. If you require to make a change to the authorship, please email IJOMS@elsevier.com with the reasons for the change in authorship.

If the Editor-in-Chief agrees to the change, we must receive an email from each author including the manuscript number, the original author list, the new author list and their agreement to the change. Requests to add or delete, or rearrange the author list after the manuscript has been accepted will only be considered in exceptional circumstances. While the Editor considers the request, publication of the manuscript will be suspended.

If the manuscript has already been published in an online issue, no requests for authorship amendment will be considered.

Before a paper is accepted all the authors of the paper must sign the Confirmation of Authorship form. This form confirms that all the named authors agree to publication if the paper is accepted and that each has had significant input into the paper. Please download the form and send it to the Editorial Office. (pdf version or word version) It is advisable that to prevent delay this form is submitted early in the editorial process.

Acknowledgements

All contributors who do not meet the criteria for authorship as defined above should be listed in an acknowledgements section. Examples of those who might be acknowledged include a person who provided purely technical help, writing assistance, or a department chair who provided only general support. Authors should disclose whether they had any writing assistance and identify the entity providing the assistance (upload the certificate of editing if appropriate)

and the funding source for this assistance. Professional language editing service may not be acknowledged in the acknowledgement section if it is a paid service.

Conflict of interest

At the end of the main text, all authors must disclose any financial and personal relationships with other people or organisations that could inappropriately influence (bias) their work. Examples of potential conflicts of interest include employment, consultancies, stock ownership, honoraria, paid expert testimony, patent applications/registrations, and grants or other funding. If an author has no conflict of interest to declare, this should be stated.

Role of the funding source

All sources of funding should be declared as an acknowledgement at the end of the text. Authors should declare the role of study sponsors, if any, in the study design, in the collection, analysis and interpretation of data; in the writing of the manuscript; and in the decision to submit the manuscript for publication. If the study sponsors had no such involvement, the authors should so state.

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Ethics

Any manuscript concerned with human subjects, medical records, or human tissue that is submitted to the International Journal of Oral and Maxillofacial Surgery should comply with the principles stated in the Declaration of Helsinki “Ethical Principles for Medical Research Involving ‘Human Subjects”, adopted by the 18th World Medical Assembly, Helsinki, Finland, June 1964, and as amended most recently by the 64th World Medical Assembly, Fontaleza, Brazil, October 2013.

The manuscript should contain a statement that the work has been approved by the appropriate Ethical Committee related to the institution(s) in which the work was performed, and that subjects gave informed consent to the work. The International Journal of Oral and Maxillofacial Surgery requires institutional Ethics Committee approval for all human studies. For retrospective studies of records either a statement of approval or a statement of exemption from the Committee is appropriate. This statement should be provided upon submission of the manuscript.

Studies involving experiments with animals must state that their care was in accordance with institution guidelines.

It is important that ethics committee oversight is independent, as stated by the ICMJE guidelines: http://www.icmje.org/recommendations/browse/roles-and-responsibilities/protection-of-research-participants.html

Reporting sex- and gender-based analyses

Reporting guidance

For research involving or pertaining to humans, animals or eukaryotic cells, investigators should integrate sex and gender-based analyses (SGBA) into their research design according to funder/sponsor requirements and best practices within a field. Authors should address the sex and/or gender dimensions of their research in their article. In cases where they cannot, they should discuss this as a limitation to their research's generalizability. Importantly, authors should explicitly state what definitions of sex and/or gender they are applying to enhance the precision, rigor and reproducibility of their research and to avoid ambiguity or conflation of terms and the constructs to which they refer (see Definitions section below). Authors can refer to the Sex and Gender Equity in Research (SAGER) guidelines and the SAGER guidelines checklist. These offer systematic approaches to the use and editorial review of sex and gender information in study design, data analysis, outcome reporting and research interpretation - however, please note there is no single, universally agreed-upon set of guidelines for defining sex and gender.

Definitions

Sex generally refers to a set of biological attributes that are associated with physical and physiological features (e.g., chromosomal genotype, hormonal levels, internal and external anatomy). A binary sex categorization (male/female) is usually designated at birth ("sex assigned at birth"), most often based solely on the visible external anatomy of a newborn. Gender generally refers to socially constructed roles, behaviors, and identities of women, men and gender-diverse people that occur in a historical and cultural context and may vary across societies and over time. Gender influences how people view themselves and each other, how they behave and interact and how power is distributed in society. Sex and gender are often incorrectly portrayed as binary (female/male or woman/man) and unchanging whereas these constructs actually exist along a spectrum and include additional sex categorizations and gender identities such as people who are intersex/have differences of sex development (DSD) or identify as non-binary. Moreover, the terms "sex" and "gender" can be ambiguous-thus it is important for authors to define the manner in which they are used. In addition to this definition guidance and the SAGER guidelines, the resources on this page offer further insight around sex and gender in research studies.

Patient confidentiality

Patients have a right to privacy. Therefore identifying information, including patients' images, names, initials, or hospital numbers, should not be included in videos, recordings, written descriptions, photographs, and pedigrees unless the information is essential for scientific purposes and you have obtained written informed consent for publication in print and electronic form from the patient (or parent, guardian or next of kin where applicable). If such consent is made subject to any conditions, The Editor and Publisher must be made aware of all such conditions. Written consents must be provided to the Editorial Office on request. Even where consent has been given, identifying details should be omitted if they are not essential. If identifying characteristics are altered to protect anonymity, such as in genetic pedigrees, authors should provide assurance that alterations do not distort scientific meaning and editors should so note. Patient consent is required for the publication of any clinical photographs, and all single

case reports, including those where the data is anonymised. *If consent for publication has not been obtained, personal details of patients included in any part of the paper and in any supplementary materials (including all illustrations and videos) must be removed before submission.*

Registration of clinical trials

Registration in a public trials registry is a condition for publication of clinical trials in this journal in accordance with International Committee of Medical Journal Editors recommendations. Trials must register at or before the onset of patient enrolment. The clinical trial registration number should be included at the end of the abstract of the article. A clinical trial is defined as any research study that prospectively assigns human participants or groups of humans to one or more health-related interventions to evaluate the effects of health outcomes. Health-related interventions include any intervention used to modify a biomedical or health-related outcome (for example drugs, surgical procedures, devices, behavioural treatments, dietary interventions, and process-of-care changes). Health outcomes include any biomedical or health-related measures obtained in patients or participants, including pharmacokinetic measures and adverse events. Purely observational studies (those in which the assignment of the medical intervention is not at the discretion of the investigator) will not require registration.

Supplementary Data

For ease of download, the recommended upper limit for the size of a single video/animation file is 150 MB, otherwise users may experience problems when downloading the file. Please see https://www.elsevier.com/authors/author-schemas/artwork-and-media-instructions/media-specifications for further information.

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The below guidance only refers to the writing process, and not to the use of AI tools to analyse and draw insights from data as part of the research process.

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This declaration does not apply to the use of basic tools for checking grammar, spelling, references etc. If there is nothing to disclose, there is no need to add a statement.

Language Editing Services

Papers will only be accepted when they are written in an acceptable standard of English. Authors, particularly those whose first language is not English, who require information about

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Article Types

The following contributions will be accepted for publication. *Please take careful note of the maximum length where applicable*. Overlength articles will be returned to the authors without peer review:

• editorials (only if commissioned by the editor)

• clinical papers: no more than 3000 words and 30 references

• research papers: no more than 3000 words and 40 references

• review papers - no limit on length or number of references

• technical notes (surgical techniques, new instruments, technical innovations) - no more than 1500 words, 10 references and 2 figures

• case reports - no more than 1500 words, 10 references and 2 figures

• book reviews

• letters to the editor - please see detailed guidelines provided at the end of the main guide for authors

• IAOMS announcements

• general announcements.

Please note: Case reports will be considered for publication only if they add new information to the existing body of knowledge or present new points of view on known diseases.

All authors must have contributed to the paper, not necessarily the patient treatment. Technical notes and case reports are limited to a maximum of 4 authors, in exceptional circumstances, 5.

Criteria for Publication

Papers that will be considered for publication should be: • focused

• based on a sound hypothesis and an adequate investigation method analysing a statistically relevant series, leading to relevant results that back the conclusion

• well written in simple, scientific English grammar and style

• presented with a clear message and containing new information that is relevant for the readership of the journal

• Note the comment above relating to case reports. • Please include a paragraph in your cover letter where you explain what is new about your study and why it will have an impact on your field of research.

Following peer-review, authors are required to resubmit their revised paper within **3 months;** in exceptional circumstances, this timeline may be extended at the editor's discretion. Please note below instructions on how to present revised manuscripts.

Presentation of new Manuscripts

General points

Papers should be submitted in journal style. Failure to do so will result in the paper being immediately returned to the author and may lead to significant delays in evaluation and eventual publication. Spelling may follow British or American usage, but not a mixture of the two. Papers should be double-spaced with a margin of at least 3 cm all round. Each line must be numbered.

Keywords

Please include a minimum of 5 keywords that are most relevant to the content of your article using the US National Library of Medicine MeSH terms. You can check whether your keywords are MeSH terms here: https://meshb.nlm.nih.gov/search.

Including keywords with your article will ensure that your article will be found during PubMed, Scopus and other searches.

Format

Observational or Case Cohort Studies, as well as Case Series must be presented in conformance with STROBE guidelines: http://www.strobe-statement.org

Randomized Controlled Trials must be presented in conformance with CONSORT guidelines

Systematic Reviews and Meta-Analyses must be presented according to PRISMA guidelines: http://www.prisma-statement.org

Papers should be set out as follows, with each section beginning on a separate page: • title page

• abstract

• text

• acknowledgements

• references

• tables

• captions to illustrations.

Please note that the qualifications of the authors will not be included in the published paper. Also, only the surname and initials of authors will appear in the article.

Title page

The title page should give the following information: • title of the article

• full name, relevant qualifications and affiliations of each author

• name and address of the department or institution to which the work should be attributed

• name, address, telephone and fax numbers, and e-mail address of the author

responsible for correspondence and to whom requests for offprints should be sent

• sources of support in the form of grants

• key words.

If the title is longer than 40 characters (including spaces), a short title should be supplied for use in the running heads.

Abstract

200 words maximum. Do not use subheadings or abbreviations; write as a continuous paragraph. Must contain all relevant information and follow the sequence: background, methods, results and conclusion without including sub-headings.

Text

Please ensure that the text of your paper conforms to the following structure: Introduction, Materials and Methods, Results, Discussion. There is no separate Conclusion section.

Introduction

• Present first the nature and scope of the problem investigated

• Review briefly the pertinent literature

• State the rationale for the study by briefly presenting the knowledge gap

• Explain the purpose in writing the paper

• Complete this section with an "aims of the study" sentence

•; Should be written in the present tense

Materials and Methods

• Give the full details, limit references • Include exact technical specifications, quantities and generic names • Limit the number of subheadings, and use the same in the results section • Mention statistical method under a sub heading • Do not include results in this section

Should be written in past tense

Avoid using the first person (We,I). Use the impersonal form when forming sentences. For example: instead of "we performed the following procedures", use "the following procedures were performed."

Results

• Do not describe methods

• Present results in the past tense, also using non personal form of sentences

• Present representations rather than endlessly repetitive data

• Use tables where appropriate, and do not repeat information in the text

Discussion

• Discuss - do not recapitulate results • Point out exceptions and lack of correlations. Do not cover up data. • Show how results agree/contrast with previous work • Discuss the implications of your findings • State your conclusions very clearly

Sub-Headings: Sub-Headings enhance readability but should be appropriate to the nature of the paper. They should be kept to a minimum and may be removed by the Editors.

Quantitative analysis: If any statistical methods are used, the text should state the test or other analytical method applied, basic descriptive statistics, critical value obtained, degrees of freedom, and significance level, e.g. (ANOVA, F=2.34; df=3,46; P<0.001). If a computer data analysis was involved, the software package should be mentioned. Descriptive statistics may be presented in the form of a table or included in the text.

Please follow the Cochrane style manual for statistical and mathematical presentation. P values should be expressed with two significant figures and to three decimal places: e.g. P = 0.051, P = 0.003, P = 0.001. P values should be stated exactly, apart from values less than 0.001, which should be expressed as P < 0.001. Do not use inappropriate hedge terms such as “marginal significance” or “trend toward significance” for results that are not statistically significant. Failure to follow these rules will result in a manuscript returned to authors with request for revisions.

Abbreviations, symbols, and nomenclature: Only standardized terms, which have been generally accepted, should be used. Unfamiliar abbreviations must be defined when first used. For further details concerning abbreviations, see Baron DN, ed. Units, symbols, and abbreviations. A guide for biological and medical editors and authors, London, Royal Society of Medicine, 1988 (available from The Royal Society of Medicine Services, 1 Wimpole Street, London W1M 8AE, UK).

The minus sign should be -.

If a special designation for teeth is used, a note should explain the symbols. Scientific names of organisms should be binomials, the generic name only with a capital, and should be italicised in the typescript. Microorganisms should be named according to the latest edition of the Manual of Clinical Microbiology, American Society of Microbiology.

Drugs: use only generic (non-proprietary) names in the text. Suppliers of drugs used may be named in the Acknowledgments section. Do not use 'he', 'his' etc where the sex of the person is unknown; say 'the patient' etc. Avoid inelegant alternatives such as 'he/she'. Patients should not be automatically designated as 'she', and doctors as 'he'.

References

References should be numbered consecutively throughout the article, beginning with 1 for the first-cited reference. References should be listed at the end of the paper in the order in which they appear in the text (not listed alphabetically by author).

The accuracy of references is the responsibility of the author. References in the text should be numbered with superscript numerals inside punctuation: for example, "Kenneth and Cohen14 showed..."; "each technique has advantages and disadvantages5-13." Citations in the text to papers with more than two authors should give the name of the first author followed by "et al."; for example: "Wang et al37 identified..."

All references cited in the text must be included in the list of references at the end of the paper. Each reference list must include the names of all authors. Please see section "Article Types" for guidance on the maximum number of references for each type of article.

Titles of journals should be abbreviated according to Index Medicus (see www.nlm.nih.gov.uk) . When citing papers from monographs and books, give the author, title of chapter, editor of book, title of book, publisher, place and year of publication, first and last page numbers. Internet pages and online resources may be included within the text and should state as a minimum the

author(s), title and full URL. The date of access should be supplied and all URLs should be checked again at proof stage.

Data References This journal encourages you to cite underlying or relevant datasets in your manuscript by citing them in your text and including a data reference in your Reference List. Data references should include the following elements: author name(s), dataset title, data repository, version (where available), year, and global persistent identifier. Add [dataset] immediately before the reference so we can properly identify it as a data reference. The [dataset] identifier will not appear in your published article.

Examples:

Journal article: Halsband ER, Hirshberg YA, Berg LI. Ketamine hydrochloride in outpatient oral surgery. J Oral Surg 1971: 29: 472-476.

When citing a paper which has a Digital Object Identifier (DOI), use the following style: Toschka H, Feifel H. Aesthetic and functional results of harvesting radial forearm flap. Int J Oral Maxillofac Surg 2001: 30: 45-51. doi: 10.1054/ijom.2000.0005

Book/monograph: Costich ER, White RP. Fundamentals of oral surgery. Philadelphia: WB Saunders, 1971: 201-220.

Book chapter: Hodge HC, Smith FA. Biological properties of inorganic fluorides. In: Simons JH, ed.: Fluorine chemistry. New York: Academic Press, 1965: 135.

Internet resource: International Committee of Medical Journal Editors. Uniform requirements for manuscripts submitted to biomedical journals. http://www.icmje.org [Accessibility verified March 21, 2008]

Tables

Tables should be used only to clarify important points. Double documentation in the form of tables and figures is not acceptable. Tables should be numbered consecutively with Arabic numerals. They should be double-spaced on separate pages and contain only horizontal rules. Do not submit tables as photographs. A short descriptive title should appear above each table, with any footnotes suitably identified below. Care must be taken to ensure that all units are included. Ensure that each table is cited in the text. Tables should not be too large or crowded. Tables which exceed one printed page or portions thereof, should be divided into two separate tables, and given separate labels such as `1A? and `1B?.

Figures

All illustrations (e.g. graphs, drawings or photographs) are considered to be figures, and should be numbered in sequence with Arabic numerals. Each figure should have a caption, typed double-spaced on a separate page and numbered correspondingly. **The minimum resolution for electronically generated figures is 300 dpi. Figures should not have thin borders around the outside.**

Line illustrations: All line illustrations should present a crisp black image on an even white background (127 x 178 mm (5 x 7 in), or no larger than 203 x 254 mm (8 x 10 in). The size of the lettering should be appropriate, taking into account the necessary size reduction.

Photographs and radiographs: Photomicrographs should show magnification and details of any staining techniques used. **The area(s) of interest must be clearly indicated with arrows or other symbols.**

Colour images are encouraged, but the decision whether an illustration is accepted for reproduction in colour in the printed journal lies with the editor-in-chief. Figures supplied in colour will appear in colour in the online version of the journal.

Size of photographs: The final size of photographs will be: (a) single column width (53 mm), (b) double column width (110 mm), (c) full page width (170 mm). Photographs should ideally be submitted at the final reproduction size based on the above figures.

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Please use this proof only for checking the typesetting, editing, completeness and correctness of the text, tables and figures. Significant changes to the article as accepted for publication will normally not be accepted. Exceptionally, changes may be considered at this stage with permission and approval from the Editor. We will do everything possible to get your article published quickly and accurately. Therefore, it is important to ensure that all of your corrections are sent back to us in one communication: please check carefully before replying, as inclusion of any subsequent corrections cannot be guaranteed. Proofreading is solely your responsibility. Note that Elsevier may proceed with the publication of your article if no response is received.

Offprints

The corresponding author will be provided, at no cost, with a customize Share Link providing 50 days free access to the final published version of the article on Science Direct. The Share Link can be used for sharing the article via any communication channel, including email and social media. For an extra charge, paper offprints can be ordered via the offprint order form which is sent once the article is accepted for publication. Both corresponding and co-authors may order offprints at any time via Elsevier's Webshop. Corresponding authors who have published their article open access do not receive a Share Link as their final version of the article is available open access on Science Direct and can be shared through the article DOI link.

Accepted Articles

For the facility to track accepted articles and set email alerts to inform you of when an article's status has changed, visit: http://authors.elsevier.com/TrackPaper.html There are also detailed artwork guidelines, copyright information, frequently asked questions and more. Contact details

for questions arising after acceptance of an article, especially those related to proofs, are provided after registration of an article for publication.

Instructions for Letters to the Editor

The IJOMS welcomes Letters to the Editor. To facilitate submission of the highest quality of Letters to the Editor, the following guidelines should be followed:

1. Letters are meant to be focus pieces and, therefore, are limited to no more than 600 words, 6 references and a maximum of 2 figures. One reference (normally the first) should be a reference to the IJOMS article being addressed.

2. The letter should be concerned with only one recently published article in IJOMS.

3. Please ensure all Letters to the Editors begin with `comment on:' followed by the IJOMS article being addressed. Please ensure any replies to Letters to the Editor also begin with `In reply to:' followed by the Letter to the Editor being addressed.

4. It is recommended that you limit your letter to one or two important and critical points to which you wish to provide a clear and precise discussion regarding the previously published article.

5. Please include any financial disclosures at the end of the letter. This would include the potential conflicts of interest not just related to the specific content of your letter but also the content of the IJOMS article and other related areas.

6. Please recognize that letters that are essentially in agreement with the author's findings and offer no additional insights provide little new information for publication. Likewise, letters that highlight the writer's own research or are otherwise self promotional will receive a low publication priority or may not be accepted.

7. There may be a need for additional editing. Should editing be required the letter will be sent back to the author for final approval of the edited version.

8. It is important to use civil and professional discourse. It is not advisable that one adopt a tone that may be misconstrued to be in anyway insulting.

9. Finally, it is not advisable to provide a letter that is anecdotal. While personal experiences can have great value in patient care, it is generally not strong evidence to be placed in a letter to the editor.

Guidelines for Revised Manuscripts

In addition to general instructions on what is to be uploaded with a revised manuscript which will be included in the editor's decision letter advising revision, the following is what is required from the editors' and reviewers' point of view to facilitate re-evaluation. Adherence to these guidelines will facilitate and speed up the review process of revised manuscripts.

1. Response letter. Authors are required to write a Response to Reviewers that indicates how each reviewer and editor comment was addressed in the revision: a point-by-point response.

2. Each point made by each reviewer and editor is to be consecutively numbered and for each number copied, it should be followed by authors' response (different colour or underlined), and then a clear indication (page and line numbers) of where the change to the manuscript was made as a relevant response. This is to be followed by a copy of the actual changes made to the text (in another colour or highlight).

3. The above point-by-point approach has to be followed for every point made by every reviewer and editor.

4. In their response, authors should avoid entering into a discussion with the reviewer alone in an attempt to answer the point made by the reviewer. Almost every point made by the reviewer implies a need to revise the text as well as answer the reviewer. Reviewers are in a sense test readers and any reviewer remark implies that the reader would need the same clarification in the manuscript itself.

5. Authors may certainly rebut reviewer remarks on occasion and no revision of the text implemented for a particular point. This may be encountered when a reviewer might misunderstand a specific issue within the manuscript, however, this is not the norm. Reviewers are volunteers trying to help and not adversaries of authors even when they are critical.

6. Revised manuscript (Track version) is required and should show the original manuscript with the changes made in response to reviewer and editor critique in Track (showing deletions as deleted text with a line across sentences, not removed) and newly added text in another colour. A comment flag has to be inserted behind every substantial modification of the text with a referral to the point number of the response letter, to show the reviewer which comment of the response letter was addressed.

7. Revised manuscript (Clean Version) is required and should show only the latest clean text without any of the old deleted text but including the newly added text but without highlighting the new content.

8. For tables and figures, track and clean versions must be included. Track tables and figures follow the track version. Clean tables and figures must follow the clean version so as to facilitate editors' re-evaluation.

ANEXO C – Comprovante de submissão *International Journal of Oral and Maxillofacial Surgery*

Dear Mrs Santos,

We acknowledge, with thanks, the receipt of your manuscript submitted to International Journal of Oral & Maxillofacial Surgery.

You may check on the progress of your paper by logging on to the Editorial Manager as an author. The URL is https://www.editorialmanager.com/ijoms/.

Your manuscript will be given a reference number once an Editor has been assigned. Your paper will then be forwarded to the expert reviewers of the Editorial Board for review. Once the results of the reviewing process are available we will advise you.

Thank you for showing your interest in publishing in the International Journal of Oral and Maxillofacial Surgery.

Kind regards,

Jacqui Merrison
IJOMS Editorial Office

ANEXO D - Author Guidelines *Oral Diseases*

Content of Author Guidelines:

Relevant Documents: Open Access Order Form, Standard Release Form for photographic consent
Useful Websites: Submission Site, Articles Published in Oral Diseases, Author Services, Author Services, Guidelines for Figures

SUBMISSION
Once the submission materials have been prepared in accordance with the Author Guidelines, manuscripts should be submitted online at https://wiley.atyponrex.com/journal/ODI.
Click here for more details on how to use ScholarOne.
For technical help with the submission system, please review our FAQs or contact submissionhelp@wiley.com.
For general assistance, please contact odiedoffice@wiley.com.

1. GENERAL
The editors encourage submissions of original articles, review articles, reports of meetings, book reviews and correspondence in the form of letters to the editor. *Oral Diseases* does not accept case reports.
Please read the instructions below carefully for details on the submission of manuscripts, the journal's requirements and standards as well as information concerning the procedure after a manuscript has been accepted for publication in *Oral Diseases*. Authors are encouraged to visit Wiley Author Services for further information on the preparation and submission of articles and figures.

Preprint Policy
Please find the Wiley preprint policy here. *Oral Diseases* accepts articles previously published on preprint servers. *Oral Diseases* will consider for review articles previously available as preprints. Authors are requested to update any pre-publication versions with a link to the final published article. Authors may also post the final published version of the article immediately after publication.

Data Sharing and Data Accessibility
Oral Diseases expects data sharing. All accepted manuscripts will need to publish a data availability statement to confirm the presence or absence of shared data. The journal expects authors to share the data and other artefacts supporting the results in the paper by archiving it in an appropriate public repository. Authors should include a data accessibility statement, including a link to the repository they have used, in order that this statement can be published alongside their paper. Review Wiley's Data Sharing policy where you will be able to see and select the data availability statement that is right for your submission. If you have shared data, this statement will describe how the data can be accessed, and include a persistent identifier (e.g., a DOI for the data, or an accession number) from the repository where you shared the data. Sample statements are available here. If published, statements will be placed in the heading of your manuscript.

2. ETHICAL GUIDELINES
Oral Diseases adheres to the ethical guidelines given below for publication and research.

2.1. Authorship and Acknowledgements
Authorship: *Oral Diseases* adheres to the International Standards for Authors published by the Committee on Publication Ethics (COPE). All authors named on a paper should agree to be named on the paper, and all authors so named should agree to the submission of the paper to *Oral Diseases* and approve the submitted and accepted versions of the publication. Any change to the author list should be approved by all authors, including any author who has been removed from the list.
Oral Diseases also adheres to the definition of authorship set up by The International Committee of Medical Journal Editors (ICMJE). According to the ICMJE authorship criteria should be based on 1) substantial contributions to conception and design of, or acquisition of data or analysis and interpretation of data, 2) drafting

the article or revising it critically for important intellectual content and 3) final approval of the version to be published. Authors should meet conditions 1, 2 and 3.
It is a requirement that the corresponding author submit a short description of each individual's contribution to the research and its publication. Upon submission of a manuscript all co-authors should also be registered with a correct e-mail addresses. If any of the e-mail addresses supplied are incorrect, the corresponding author will be contacted by the Journal Administrator.
For all articles, the journal mandates the CRediT (Contribution Roles Taxonomy), for more information please see Author Services.
Acknowledgements: Authors must acknowledge individuals who do not qualify as authors but who contributed to the research. Authors must acknowledge any assistance that they have received (e.g. provision of writing assistance, literature searching, data analysis, administrative support, supply of materials). If/how this assistance was funded should be described and included with other funding information. "Acknowledgements" should be brief and should not include thanks to anonymous referees and editors. Where people are acknowledged, a cover letter demonstrating their consent must be provided.

2.2. Ethical Approvals

Human Subjects: Experimentation involving human subjects will only be published if such research has been conducted in full accordance with ethical principles, including the World Medical Association Declaration of Helsinki (version 2002) and the additional requirements, if any, of the country where the research has been carried out. Manuscripts must be accompanied by a statement that the experiments were undertaken with the understanding and written consent of each subject and according to the above mentioned principles. A statement regarding the fact that the study has been independently reviewed and approved by an ethical board should also be included.
Photographs of People: Oral Diseases follows current HIPAA guidelines for the protection of patient/subject privacy. If an individual pictured in a digital image or photograph can be identified, his or her permission is required to publish the image. The corresponding author must either submit a letter signed by the patient authorizing Oral Diseases to publish the image/photo, or complete the 'Standard Release Form for photographic consent' available at the top of this page or by clicking the "instructions and Forms" link on the submission site. The approval must be received by the Editorial Office prior to final acceptance of the manuscript for publication. Otherwise, the image/photo must be altered such that the individual cannot be identified (black bars over eyes, tattoos, scars, etc.). Oral Diseases will not publish patient photographs that will in any way allow the patient to be identified, unless the patient has given their express consent.
Editors reserve the right to reject papers if there are doubts as to whether appropriate procedures have been used.
Animal Study: When experimental animals are used the methods section must clearly indicate that adequate measures were taken to minimize pain or discomfort. Experiments should be carried out in accordance with the Guidelines laid down by the National Institute of Health (NIH) in the USA regarding the care and use of animals for experimental procedures or with the European Communities Council Directive of 24 November 1986 (86/609/EEC) and in accordance with local laws and regulations.

2.3 Clinical Trials

Clinical Trials should be reported using the CONSORT guidelines available at www.consort-statement.org. A CONSORT checklist and flowchart should also be included in the submission material. Clinical trials can be registered in any free, public clinical trials registry such as http://www.clinicaltrials.gov or http://isrctn.org/. A list of further registries is available at http://www.who.int/ictrp/network/primary/en/. As stated in an editorial published in *Oral Diseases* (12:217-218), 2006), all manuscripts reporting results from a clinical trial must indicate that the trial was fully registered at a readily accessible website. The clinical trial registration number and name of the trial register will be published with the paper.

2.4 DNA Sequences and Crystallographic Structure Determinations

Papers reporting protein or DNA sequences and crystallographic structure determinations will not be accepted without a Genbank or Brookhaven accession number, respectively. Other supporting data sets must be made available on the publication date from the authors directly.

2.5 Conflict of Interest and Source of Funding

All sources of institutional, private and corporate financial support for the work within the manuscript must be fully acknowledged, and any potential grant holders should be listed. Authors are also required to disclose any possible conflict of interest. These include financial (for example patent, ownership, stock ownership, consultancies, speaker's fee). Information on sources of funding and any potential conflict of interest should be disclosed at submission under the heading "Acknowledgements".

2.6 Appeal of Decision
The decision on a paper is final and cannot be appealed.
2.7 Avoiding allegations of plagiarism
The journal to which you are submitting your manuscript employs text matching software (iThenticate) to ensure against plagiarism. By submitting your manuscript to this journal you accept that your manuscript may be screened for plagiarism against previously published work. Authors should consider whether their manuscript may raise concerns via iThenticate, which will signal whether a paper is likely in any way to be plagiarized in a formal sense. iThenticate will also, however, signal whether a paper may be plagiarized by repeating work of the submitting authors and thus be regarded as duplicate or redundant publication. Experience shows that, on occasion, large sections of submitted manuscripts can be close to verbatim in word choice from that seen in other papers from the authors' group. This has nothing to do with simple repetition of names/affiliations, but does involve common (not necessarily "standard") phrases that are more appropriately referenced instead of repeating. Alternatively, they can be rephrased differently. Previously published results, including numerical information and figures or images, should be labeled to make it clear where they were previously reported. Papers that present new analyses of results that have already been published (for example, subgroup analyses) should identify the primary data source, and include a full reference to the related primary publications. *Oral Diseases* will review and publish accepted mansucripts that report data included in conference proceedings in abstract form. In such cases, authors must be clear to readers that part of all of the manuscript's data have already been published in abstract form by so indicating using a footnote to the title that states the confrence proceedings in which the relevant abstract was published. For full guidance on text matching and plagiarism, please refer to Section 3 ('Research Integrity') of Wiley's Ethics Guidelines at https://authorservices.wiley.com/ethics-guidelines/index.html.
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If all or parts of previously published illustrations are used, permission must be obtained from the copyright holder concerned. It is the author's responsibility to obtain these in writing and provide copies to the Publishers.

3. MANUSCRIPT SUBMISSION PROCEDURE
Oral Diseases only accepts online submission of manuscripts. Manuscripts should be submitted at the online submission site: https://wiley.atyponrex.com/journal/ODI. Complete instructions for submitting a manuscript are available at the site upon creating an account. Assistance for submitting papers can be sought with the editorial assistant at: odiedoffice@wiley.com.
Data protection: By submitting a manuscript to or reviewing for this publication, your name, email address, and affiliation, and other contact details the publication might require, will be used for the regular operations of the publication, including, when necessary, sharing with the publisher (Wiley) and partners for production and publication. The publication and the publisher recognize the importance of protecting the personal information collected from users in the operation of these services and have practices in place to ensure that steps are taken to maintain the security, integrity, and privacy of the personal data collected and processed. You can learn more at https://authorservices.wiley.com/statements/data-protection-policy.html.

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3.1. Manuscript Files Accepted
Manuscripts should be uploaded as Word (.doc/.docx) or Rich Text Format (.rft) files (not write-protected) plus separate figure files. GIF, JPEG, PICT or Bitmap files are acceptable for submission, but only high-resolution TIF or EPS files are suitable for printing. The files will be automatically converted to HTML and PDF on upload and will be used for the review process. The text file must contain the entire manuscript including title page, abstract, text, references, acknowledgements, tables, and figure legends, but no embedded figures. In the text file, please reference figures as for instance 'Figure 1', 'Figure 2' etc to match the tag name you choose for individual figure files uploaded. Manuscripts should be formatted as described in the Author Guidelines below.
3.2. Transparent Peer Review
This journal is participating in a Peer Review Transparency initiative. By submitting to this journal, authors agree that the reviewer reports, their responses, and the editor's decision letter will be linked from the published article to where they appear on Publons in the case that the article is accepted. Authors have the opportunity to opt out

during submission, and reviewers may remain anonymous unless they would like to sign their report. Read more about this initiative here.

3.3. Suggest a Reviewer

Oral Diseases attempts to keep the review process as short as possible to enable rapid publication of new scientific data. In order to facilitate this process, you must suggest the names and current e-mail addresses of from 2-4 potential reviewers whom you consider capable of reviewing your manuscript in an unbiased way.

3.4. Suspension of Submission Mid-way in the Submission Process

You may suspend a submission at any phase before clicking the 'Submit' button and save it to submit later. The manuscript can then be located under 'Unsubmitted Manuscripts' and you can click on 'Continue Submission' to continue your submission when you choose to.

3.5. E-mail Confirmation of Submission

After submission you will receive an e-mail to confirm receipt of your manuscript. If you do not receive the confirmation e-mail after 24 hours, please check your e-mail address carefully in the system. If the e-mail address is correct please contact your IT department. The error may be caused by some sort of spam filtering on your e-mail server. Also, the e-mails should be received if the IT department adds our e-mail server (uranus.scholarone.com) to their whitelist.

3.6. Manuscript Status

The average time from submission to first decision for manuscripts submitted to *Oral Diseases* is 20 days. You can access ScholarOne Manuscripts any time to check your 'Author Centre' for the status of your manuscript. The Journal will inform you by e-mail once a decision has been made.

3.7. Submission of Revised Manuscripts

To upload a revised manuscript, locate your manuscript under 'Manuscripts with Decisions' and click on 'Submit a Revision'. Please remember to delete any old files uploaded when you upload your revised manuscript.

3.8. Refer and Transfer Program

Wiley believes that no valuable research should go unshared. This journal participates in Wiley's Refer & Transfer program. If your manuscript is not accepted, you may receive a recommendation to transfer your manuscript to another suitable Wiley journal, either through a referral from the journal's editor or through our Transfer Desk Assistant.

4. MANUSCRIPT TYPES ACCEPTED

Original Research Articles: Manuscripts reporting laboratory investigations, well-designed and controlled clinical research, and analytical epidemiology are invited. Studies related to aetiology, pathogenesis, diagnosis, prevention and treatment are all of interest, but all papers must be based on rigorous hypothesis-driven research. Areas of interest include diseases affecting any structures of the mouth; cancer and pre-cancerous conditions; saliva and salivary glands; bone and hard tissues; relationship between oral, periodontal, and dental conditions and general health; pain; behavioral dentistry; chemosensory, developmental, geriatric, and motor disorders.

Randomised trials must adhere to the CONSORT guidelines, and a CONSORT checklist and flowchart must be submitted with such papers. Please also refer to the notes under section 2.3 above.

Oral Diseases supports the ALLTRIALS initiative and encourages authors submitting manuscripts reporting a clinical trial to register the trials in any of the following free, public clinical trials registries: www.clinicaltrials.gov, http://clinicaltrials.ifpma.org/clinicaltrials/, http://isrctn.org/. The clinical trial registration number and name of the trial register will then be published with the paper.

Observational studies must adhere to the STROBE guidelines, and a STROBE checklist must be submitted with such papers. Diagnostic accuracy studies must adhere to the STARD guidelines, and a STARD checklist must be submitted with such papers.

Review Papers: *Oral Diseases* commissions review papers and also welcomes uninvited reviews. Systematic reviews with or without meta-analyses must adhere to the PRISMA guidelines, and a PRISMA checklist and flowchart must be submitted with such papers. The word limit for Review Papers is 4,000 words, with a maximum of two tables or images and 50 references.

Clinical Image: Clinical Images illustrate a brief presentation of a peculiar case. These include a clinical description, excellent clinical pictures, a multiple choice quiz on the putative diagnosis (no more than 4-5 options), the final diagnosis and a brief discussion, followed by the patient outcome. Clinical Images should be structured as follows:

1. TITLE describing the case without mentioning the diagnosis
2. CASE REPORT: 120 words
3. CASE IMAGE(S): No more than 2 clinical pictures of the case (the legend must not mention the diagnosis). Label image(s) Figure 1 or Figure 1A and 1B.
4. QUIZ: Provide no more than 4 possible answers. See example here:

WHAT IS YOUR DIAGNOSIS?

Based on the patient's history, physical examination, and laboratory findings, which one of the following is the most suspicious diagnosis?

1. Answer A
2. Answer B
3. Answer C
4. Answer D

5. DIAGNOSIS: Provide the answer along with a 1-2 sentence explanation followed by subsequent discussion. (350 words).
6. DIAGNOSIS IMAGE: One picture clarifying the diagnosis (i.e. a histological picture, images, micro, blood tests, ...). Label this Figure
7. OUTCOME: 1-2 sentences.
8. AUTHOR CONTRIBUTION section: Required.
9. PATIENT CONSENT section: Use standard wording, “The patient reported in this manuscript provided written informed consent for the publication of the case details."
10. CONFLICT OF INTEREST STATEMENTS (COIS): Required section. Default text whenno conflicts exist reads “All authors have no conflicts of interest to disclose.”
11. ACKNOWLEDGEMENTS: Optional section.
12. KEYWORDS: Not required as they may give away the answer.
13. FUNDING: Not required for this article type.
14. REFERENCES: Maximum 10.

Letters to the Editors:
Letters, if of broad interest, are encouraged. They may deal with material in papers published in *Oral Diseases* or they may raise new issues, but should have important implications. Only one letter may be submitted by any single author or group of authors on any one published paper. Letters to the Editors should not include an abstract and are limited to 500 words, with a maximum of 1 figure and 10 references.
Case Reports: *Oral Diseases* does not accept case reports and instead recommends that authors submit to Clinical Case Reports an open access journal published by Wiley.
Meeting Reports: Will be considered by the editors for publication only if they are of wide and significant interest.
Short Communications: These are brief papers of any topic within the scope of *Oral Diseases*about significant and novel advances that are complete in research endeavor but not suitable for full publications. Short Communications should not include an abstract and are limited to 1000 words, with a maximum of 3 figures and 20 references. Short Communications **should not** be structured into sections.
Invited Reviews: These may be submitted by invitation of the Senior Editors only, and consist of around 2500-2750 words, with a maximum of one table or image and 25 references.
Commentaries: These may be submitted by invitation of the Senior Editors only.
Invited Editorials: These may be submitted by invitation of the Senior Editors only.
Invited Book Reviews: These may be submitted by invitation of the Senior Editors only.

5. MANUSCRIPT FORMAT AND STRUCTURE
Oral Diseases now offers Free Format submission for a simplified and streamlined submission process.
Before you submit, you will need:

- Your manuscript: this should be an editable file including text, figures, and tables, or separate files – whichever you prefer. All required sections should be contained in your manuscript, including abstract, introduction, methods, results, and conclusions. Figures and tables should have legends. Figures should be uploaded in the highest resolution possible. References may be submitted in any style or format, as long as it is consistent throughout the manuscript. Supporting information should be submitted in separate files. If the manuscript, figures or tables are difficult for you to read, they will also be difficult for the

editors and reviewers, and the editorial office will send it back to you for revision. Your manuscript may also be sent back to you for revision if the quality of English language is poor.

- An ORCID ID, freely available at https://orcid.org. *(Why is this important? Your article, if accepted and published, will be attached to your ORCID profile. Institutions and funders are increasingly requiring authors to have ORCID IDs.)*
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        - data availability statement
        - funding statement
        - conflict of interest disclosure
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        - permission to reproduce material from other sources
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If you are invited to revise your manuscript after peer review, the journal will also request the revised manuscript to be formatted according to journal requirements as described below.

5.1. Page Charge

IMPORTANT:
Please note that articles exceeding 8 published pages, including title page, abstract, references, table/figure legends and tables and figures, are subject to a charge of GBP 70 per additional page. As a guide, one published page amounts approximately to 850 words, or two to four small tables/figures. Additional supplementary material (including text and figures), which does not fit within the page limits, can be published online only as supporting information.

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Language: Authors should write their manuscripts in British English using an easily readable style. Authors whose native language is not English should have a native English speaker read and correct their manuscript. Spelling and phraseology should conform to standard British usage and should be consistent throughout the paper. A list of independent suppliers of editing services can be found at http://authorservices.wiley.com/bauthor/english_language.asp. All services are paid for and arranged by the author, and use of one of these services does not guarantee acceptance or preference for publication.
Presentation: Authors should pay special attention to the presentation of their findings so that they may be communicated clearly. The background and hypotheses underlying the study as well as its main conclusions should be clearly explained. Titles and abstracts especially should be written in language that will be readily intelligible to any scientist.
Technical jargon: should be avoided as much as possible and clearly explained where its use is unavoidable.
Abbreviations: Oral Diseases adheres to the conventions outlined in Units, Symbols and Abbreviations: A Guide for Medical and Scientific Editors and Authors. Non-standard abbreviations must be used three or more times and written out completely in the text when first used.
5.3. Structure: All papers submitted to *Oral Diseases* should include:

- Title Page

- Structured Abstract
- Main text
- References
- (Figures)
- (Figure Legends)
- (Tables)

Title Page: should be part of the manuscript uploaded for review and include:

- A title of no more than 100 characters including spaces
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- Complete names and institutions for each author
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- Date of submission (and revision/resubmission)

Abstract: is limited to 200 words in length and should contain no abbreviations. The abstract should be included in the manuscript document uploaded for review as well as separately where specified in the submission process. The abstract should convey the essential purpose and message of the paper in an abbreviated form. Structured abstract is an abstract divided into distinct sections such as Objective, Methods, Results, and Conclusions. It is typically maximum 250 words containing no abbreviations. The abstract should be included in the manuscript document uploaded for review as well as separately where specified during the submission process.

The Main Text of Original Research Articles should be organised as follows

Introduction: should be focused, outlining the historical or logical origins of the study and not summarize the results; exhaustive literature reviews are inappropriate. It should close with the explicit statement of the specific aims of the investigation.

Materials and Methods must contain sufficient detail such that, in combination with the references cited, all clinical trials and experiments reported can be fully reproduced. As a condition of publication, authors are required to make materials and methods used freely available to academic researchers for their own use. This includes antibodies and the constructs used to make transgenic animals, although not the animals themselves. Other supporting data sets must be made available on the publication date from the authors directly.

(i) Clinical trials: As noted above, these should be reported using the CONSORT guidelines available at www.consort-statement.org. A CONSORT checklist should also be included in the submission material. Clinical trials can be registered in any of the following free, public clinical trials registries: www.clinicaltrials.gov, http://clinicaltrials.ifpma.org/clinicaltrials/, http://isrctn.org/.As stated in an editorial published in *Oral Diseases* (12:217-218), 2006), all manuscripts reporting results from a clinical trial must indicate that the trial was fully registered at a readily accessible website. The clinical trial registration number and name of the trial register will be published with the paper.

(ii)Experimental subjects: As noted above, experimentation involving human subjects will only be published if such research has been conducted in full accordance with ethical principles, including the World Medical Association Declaration of Helsinki (version 2002) and the additional requirements, if any, of the country where the research has been carried out. Manuscripts must be accompanied by a statement that the experiments were undertaken with the understanding and written consent of each subject and according to the above mentioned principles. A statement regarding the fact that the study has been independently reviewed and approved by an ethical board should also be included.Editors reserve the right to reject papers if there are doubts as to whether appropriate procedures have been used. When experimental animals are used the methods section must clearly indicate that adequate measures were taken to minimize pain or discomfort. Experiments should be carried out in accordance with the Guidelines laid down by the National Institute of Health (NIH) in the USA regarding the care and use of animals for experimental procedures or with the European Communities Council Directive of 24 November 1986 (86/609/EEC) and in accordance with local laws and regulations.

***(iii) Suppliers*:** Suppliers of materials should be named and their location (town, state/county, country) included.

Results: should present the observations with minimal reference to earlier literature or to possible interpretations.

Discussion: may usually start with a brief summary of the major findings, but repetition of parts of the abstract or of the results sections should be avoided. The section should end with a brief conclusion and a comment on the potential clinical relevance of the findings. Statements and interpretation of the data should be appropriately supported by original references.

Acknowledgements: Should be used to provide information on sources of funding for the research, any potential conflict of interest and to acknowledge contributors to the study that do not qualify as authors. All sources of institutional, private and corporate financial support for the work within the manuscript must be fully acknowledged, and any potential grant holders should be listed. Acknowledgements should be brief and should not include thanks to anonymous referees and editors. Where people are acknowledged, a cover letter demonstrating their consent must be provided.

5.4. References

References should be prepared according to the *Publication Manual of the American Psychological Association* (6th edition). This means in-text citations should follow the author-date method whereby the author's last name and the year of publication for the source should appear in the text, for example, (Jones, 1998). For references with three to five authors, all authors should be listed only on the first occurrence of the in-text citation, and in subsequent in-text occurrences only the first author should be listed followed by '*et al.*'. The complete reference list should appear alphabetically by name at the end of the paper.

A sample of the most common entries in reference lists appears below. Please note that a DOI should be provided for all references where available. For more information about APA referencing style, please refer to the APA website. Please note that for journal articles, issue numbers are not included unless each issue in the volume begins with page one.

Journal article

Example of reference with 2 to 7 authors

Beers, S. R., & De Bellis, M. D. (2002). Neuropsychological function in children with maltreatment-related posttraumatic stress disorder. *The American Journal of Psychiatry, 159*, 483–486. doi: 10.1176/appi.ajp.159.3.483

Ramus, F., Rosen, S., Dakin, S. C., Day, B. L., Castellote, J. M., White, S., & Frith, U. (2003). Theories of developmental dyslexia: Insights from a multiple case study of dyslexic adults. *Brain, 126*(4), 841–865. doi: 10.1093/brain/awg076

Example of reference with more than 7 authors

Rutter, M., Caspi, A., Fergusson, D., Horwood, L. J., Goodman, R., Maughan, B., … Carroll, J. (2004). Sex differences in developmental reading disability: New findings from 4 epidemiological studies. *Journal of the American Medical Association, 291*(16), 2007–2012. doi: 10.1001/jama.291.16.2007

Book edition

Bradley-Johnson, S. (1994). *Psychoeducational assessment of students who are visually impaired or blind: Infancy through high school* (2nd ed.). Austin, TX: Pro-ed.

5.5. Tables, Figures and Figure Legends

Figures: All figures and artwork must be provided in electronic format. Please save vector graphics (e.g. line artwork) in Encapsulated Postscript Format (EPS) and bitmap files (e.g. half-tones) or clinical or in vitro pictures in Tagged Image Format (TIFF).

Detailed information on our digital illustration standards can be found at http://authorservices.wiley.com/bauthor/illustration.asp.

Check your electronic artwork before submitting it: http://authorservices.wiley.com/bauthor/eachecklist.asp.

Unnecessary figures and parts (panels) of figures should be avoided: data presented in small tables or histograms, for instance, can generally be stated briefly in the text instead. Figures should not contain more than one panel unless the parts are logically connected.

Figures divided into parts should be labelled with a lower-case, boldface, roman letter, a, b, and so on, in the same type size as used elsewhere in the figure. Lettering in figures should be in lower-case type, with the first letter capitalized. Units should have a single space between the number and unit, and follow SI nomenclature common to a particular field. Unusual units and abbreviations should be spelled out in full or defined in the legend. Scale bars should be used rather than magnification factors, with the length of the bar defined in the legend rather than on the bar itself. In general visual cues (on the figures themselves) are preferred to verbal explanations in the legend (e.g. broken line, open red triangles etc).

Guidelines for Cover Submissions

If you would like to send suggestions for artwork related to your manuscript to be considered to appear on the cover of the journal, please follow these general guidelines.

ANEXO E - Decision on Manuscript *Oral diseases*

27-Sep-2024

Dear Dr Santos,

It is a great pleasure to accept your manuscript entitled "Body Mass Index as an Indicator of Survival in Oral Cancer" in its current form for publication in the journal Oral Diseases. Please note, articles also cannot be published until the publisher has received the appropriate signed licence agreement. Therefore, within the next few days the corresponding author will receive an email from Wiley's Author Services system asking them to log in and presenting them with the appropriate licence for completion.

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If your article contains any colour figures, when your article is published in Early View in Wiley Online Library, you will be emailed a link to RightsLink for Author Services allowing you to select optional colour printing and to pay the associated fee.
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On behalf of the Senior Editors of Oral Diseases, we thank you again for your fine contribution, and we look forward to your continued contributions to the journal and its increasing global reputation.

Yours sincerely,
Prof. Stefano Petti, DMD, PhD
Deputy Editor
Oral Diseases
Comments to the Author:
(There are no comments.)