

ANA DANIELA SPÍNOLA DA SILVA ANTUNES

**Influence of clinicopathological and psychological factors
on the smoking maintenance in head and neck cancer
patients**

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on the smoking maintenance in head and neck cancer
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Dissertação apresentada à Faculdade de Odontologia de Araçatuba da Universidade Estadual Paulista “Júlio de Mesquita Filho”- UNESP, como parte dos requisitos para obtenção do título de Mestre em Odontologia- Área de concentração em Estomatologia.

Orientador: Professor Titular Glauco Issamu Miyahara

Coorientador: Professor Doutor Daniel Galera Bernabé

Araçatuba - SP
2021

Catálogo na Publicação (CIP)

Diretoria Técnica de Biblioteca e Documentação – FOA / UNESP

A636i

Antunes, Ana Daniela Spínola da Silva.
Influence of clinicopathological and psychological
factors on the smoking maintenance in head
and neck cancer patients / Ana Daniela Spínola
da Silva Antunes. – Araçatuba, 2021
41 f. : tab.

Dissertação (Mestrado) – Universidade Estadual
Paulista, Faculdade de Odontologia de Araçatuba
Orientador: Prof. Glauco Issamu Miyahara
Coorientador: Prof. Daniel Galera Bernabé

1. Head and neck neoplasms 2. Smoking
3. Anxiety 4. Depression I. T.

Black D6
CDD 617.63

Claudio Hideo Matsumoto CRB-8/5550

Às minhas amadas mãe Elzimar Ferreira Spínola (*In memorian*) e madrinha Idamar Ferreira Spínola (*In memorian*). *Obrigada* pelo exemplo de coragem e todo incentivo. Por me ensinarem a importância do estudo, da humildade e da humanidade. Por mesmo de longe continuarem a ser minha de força. E acima de tudo pelo cuidado e amor a mim sempre dedicado por toda vida.

AGRADECIMENTOS

Gostaria de agradecer a todos que tornaram a concretização desse trabalho e da minha jornada acadêmica possível.

A **Universidade Estadual Paulista Júlio de Mesquita Filho - UNESP** por ser meu lar há 19 anos. A **Faculdade de Odontologia de Araçatuba**, ao **Programa de Pós-Graduação** e ao **Centro de Oncologia Bucal (COB)** por oferecer sua estrutura física e o melhor corpo docente e técnico, o que possibilita a realização deste e tantos outros projetos e uma formação de qualidade.

Ao professor titular e orientador **Glauco Issamu Miyahara**, por acreditar em mim, me aceitar como sua orientada. Saiba que é grande exemplo de pessoa e estomatologista, ver como o senhor busca ser correto sempre e como lida com os pacientes com humanidade e profissionalismo é algo inspirador. Ao professor doutor e coorientador **Daniel Galera Bernabé** por me aceitar junto ao NuPPE e confiar pesquisas tão significantes a mim. Minha admiração ao senhor enquanto clínico, pesquisador e docente é imensurável. O senhor é o responsável pela minha paixão na área de diagnóstico. Agradeço ainda a ambos pela paciência, compreensão e apoio nos meus momentos de dificuldades pessoais e acadêmicas.

Ao professor doutor **Rafael Akira Murayama**, por aceitar desprender de seu tempo para compor a minha banca avaliadora e assim participar deste momento tão importante para mim, e por contribuir para o enriquecimento deste trabalho.

Ao amigo **Vitor Bonetti Valente**, por aceitar fazer parte da banca examinadora desse trabalho, e ser um exemplo de profissionalismo e dedicação à carreira acadêmica. Agradeço ainda por cada oportunidade a mim por você oferecida, por cada aprendizado compartilhado, cada conversa e conselho, e pela confiança que sempre teve em mim nas clínicas.

Ao professor **Eder Ricardo Biasoli** por todo ensinamento compartilhado a cada clínica de estomatologia durante a monitoria da graduação e o mestrado. É sempre uma honra aprender com o senhor, que é pra mim, um grande exemplo de cirurgião. Agradeço também por a cada ambulatório médico, o seu respeito para comigo, o cuidado em me mostrar e explicar cada detalhe. Poder ver como o senhor lida com os pacientes oncológicos e suas famílias foi fundamentais para a minha

formação. A professora **Kellen Cristine Tjioe**, por toda vivência durante a pós-graduação, por cada ensinamento passado de forma leve e delicada, por toda preocupação e cada palavra de otimismo. Obrigada por me mostrar como eu gostaria de ser.

A todos os professores das disciplinas do Programa de Pós Graduação em Odontologia por todos os ensinamentos compartilhados minha gratidão. Em especial ao professor **Wilson Roberto Poi** por ministrar uma disciplina fundamental para a formação acadêmica de forma incrível, leve e humana. E ao professor **Fernando Yamamoto Chiba** por todo cuidado ao ministrar disciplina tão complexa e importante para nossa formação enquanto pesquisadores, em especial toda paciência e atenção para comigo quando eu tinha dúvidas sobre estatística. Sou grata a todos os funcionários desta Faculdade, em especial **Sueli Yamada, Gustavo Henrique, Cristiane Matos e Ana Claudia Manzatti**, sem vocês eu nem sei o que seria de mim na FOA. Agradeço aos professores **Ana Paula Farnezi Bassi, Leonardo Perez Faverani e Tania Adas Saliba**, por toda amizade, preocupação, cuidado, amor e carinho. Por notarem na minha voz ou olhar possíveis angústias e medos, desprendendo sempre do tempo escasso de vocês para uma palavra amiga, um abraço e um café. Vocês são raros.

Aos **pacientes do Centro de Oncologia Bucal**, sem o qual esse trabalho e todos que realizei desde a minha graduação não seriam possíveis, e por quem fazemos tudo isso. Agradeço a confiança em compartilhar sentimentos tão lindos, dolorosos e pessoais. Este trabalho é feito na minha expectativa de contribuir para um melhor entendimento das suas peculiaridades, levando assim a um atendimento mais individualizado e maior qualidade de vida para com vocês e os que estão por vir. Vocês são fonte de aprendizado clínico e humano.

Agradeço a **Equipe do COB: Jane Fatima Mendes Fernandes da Silva, Adriana de Paula E S Rahal Leal, Grazielle Dourado, Anne Cristina de Faria Cocato, Daniene Tesoni Cavassara Ribeiro, Regiane Mazzarioli Pereira Nogueira, Gabrielle Dias Duarte, Sebastião Conrado Neto, Francisco Urbano Collado, Daniella Michalenni e Aline Satie Takamiya** pela convivência sempre harmoniosa nesses 7 anos, as experiências trocadas e por estarem dispostos a ajudar prontamente sempre que precisei. Em especial a **Gabrielle Dias Duarte** que se tornou uma amiga especial, sempre cuidadosa, preocupada e acolhedora,

alguém com que eu amo conversar, que tem uma visão do mundo muito parecida com a minha e sempre me desafia, me retira da minha zona de conforto, fazendo com que eu enfrente meu interior e evolua.

A todos os professores e funcionários que passaram pela minha vida nesses longos anos de estudo nas instituições CEI Jardim Monjolo (SP-SP), EMEI Manoel Bandeira (SP-SP), EMEF Érico Veríssimo (SP-SP), EE Clóvis de Arruda Campos (Araçatuba-SP), FCT-Unesp (Presidente Prudente-SP), em especial: **Maria Aparecida, Lucelena, Ana Maria, Gláucia, Maria Julieta, Junior, Júlio, Márcia, Fernando (*In Memoriam*), Beatriz, Caetano, Marcia**. Vocês são parte da base que tenho hoje, e co-responsáveis por cada vitória!

À **Jéssica Soares Bugiga** por ter iniciado este lindo trabalho, e ser minha grande amiga sempre. A **Bruna A M Sarafim da Silva**, por me auxiliar em absolutamente tudo em todos os trabalhos que desenvolvi e na minha pós-graduação. Por estar sempre pronta a me ajudar, mesmo que isso lhe custe parar suas coisas. Por me ouvir, aconselhar e orientar. Sem vocês nada disso seria possível, obrigada!

Aos membros do **Núcleo de Pesquisa em Psicossomática e Educação** e do **Laboratório de Psiconeuroimunologia**, por cada aprendizado compartilhado.

Aos amigos da pós-graduação, principalmente da área de concentração em estomatologia, em especial **Ingrid Silva, Daniela Bastos, Jessica Figueira, Giseli Kayahara, Tamara Teixeira e Felipe Yuddi** pelos momentos e aprendizado compartilhado. Ao querido **Winícius Araujo** por se tornar essencial dentro e fora dos muros da faculdade. As amigas de PG e de vida **Daniella Cantieri, Maria Clara Botelho e Gabriela Lopes**, por cada vitória, medo, angústia, risada, lágrima, café da tarde e tantos outros momentos compartilhados, por todo acolhimento e cada palavra de incentivo, otimismo e apoio, mesmo estando longe uma das outras, juntas somos mais fortes.

A todos os profissionais pelos quais passei de outubro até hoje, em especial a equipe da **Santa Casa de Misericórdia de Araçatuba** que cuidou de mim com tanto carinho, humanidade, atenção, profissionalismo e competência. Sem a dedicação de vocês eu não estaria aqui e esse momento não seria possível. Estendo os

agradecimentos a todos profissionais que lutam bravamente contra a pandemia instaurada pelo Covid-19 em todo mundo.

As minhas famílias do coração: meus amigos de infância e adolescência, de Presidente Prudente e das graduações que passei. A **Daniela Batista, Bruna Cicerelli, Maysa Ramos, Laura Domingos, Rodrigo Copalbo, Jessica Paiva, Paula Bazani, Barbara Curi, Maryelisa Vicente, Ana Maria Galdino, Cesar Augusto Galdino** (*In memorian*) e **Karina B. Barros** (*In memorian*). A Família **Bezerra** e a família **Teodoro**. A **Karen Rawen Tonini** e sua família maravilhosa. A minha família consanguínea, em especial **Rosemary Spínola, Marilsa dos Santos, Juliana Corassa, Dinamar Spínola, Larissa Spínola**. Aos meus irmãos **André Spínola** e **Priscila de Paula Silva**. Aos meus sobrinhos **David** e **Melissa**. A minha esposa incrível, compreensiva e cuidadosa **Claudia Rodrigues Antunes Spínola**. Minha sogra **Marilena M R Antunes** e cunhada **Rita de Cássia Rodrigues Antunes**. Ao meus “pequenos” **Danilo Spínola** e **Maria Julia Spínola Fernandes**. As minhas eternas e amadas mãe **Elzimar Ferreira Spínola** e madrinha **Idamar Ferreira Spínola**. Para todos vocês, minha gratidão, obrigada principalmente por nunca me deixarem desistir, mesmo nos momentos de medo e desanimo. Não há como traduzir em palavras meu amor e gratidão, mesmo assim, obrigado por tudo, obrigado por tanto... Obrigado por serem minha âncora com esse mundo e minha luz mesmo nos momentos mais sombrios.

As minhas famílias espirituais na figura das 3 casas de oração que me acolhem: **CEOC André Luiz e pai Oxalá** (Araçatuba), **TU Estrela Guia** (São Caetano do Sul) e **TEU Luzes de Olorum** (São Paulo). A **Priscila Mariano** e **Rodrigo Di Castro**. A minha amada mentora, e os demais espíritos de luz que me guiam e fortificam. E acima de tudo a Deus, que com Sua onisciência trilha meus caminhos, com Sua onipresença sempre me acompanha e ampara por meio de seus seres de luz e centelhas de amor, e com onipotência me permitiu continuar viva e em pé após cada obstáculo. Obrigada por serem meu ponto de equilíbrio, e sempre restaurarem minha força, paz e fé.

“... A felicidade pode ser encontrada mesmo nas horas mais difíceis, se você lembrar de acender a luz.” (Alvo Dumbledore – J. K. Rolling)

"O vício não é uma escolha que se faça, é uma resposta à dor emocional.

E ninguém escolhe sentir dor."

Gabor Maté

ANTUNES, A. D. S. S. **Influência dos fatores clinicopatológicos e psicológicos na manutenção do tabagismo em pacientes com câncer de cabeça e pescoço.** 2021. 41 f. Dissertação (Mestrado) – Faculdade de Odontologia, Universidade Estadual Paulista, Araçatuba, 2021.

RESUMO

O tabagismo é fator de risco para vários tipos de câncer, dentre eles o câncer de cabeça e pescoço (CCP). Apesar do consumo de tabaco também estar relacionado com a ocorrência de segundo tumor primário e menor expectativa de vida, uma taxa considerável dos pacientes com CCP não consegue abandonar o hábito de fumar após o diagnóstico da doença. O objetivo deste estudo foi investigar a influência de fatores sociodemográficos, biocomportamentais, clinicopatológicos e psicológicos na manutenção ou cessação do tabagismo em pacientes com CCP após o tratamento da doença. O estudo foi composto por 71 pacientes com CCP que terminaram o tratamento oncológico há no mínimo 12 meses. As características demográficas, clinicopatológicas e biocomportamentais foram coletadas dos prontuários clínicos e o histórico de tabagismo ao longo do tratamento do câncer foi avaliado por meio de entrevista semi-estruturada. Sintomas de ansiedade e depressão foram avaliados no período pré-tratamento por meio do Inventário de Ansiedade de Beck (BAI) e Inventário de Depressão de Beck (BDI), respectivamente. Vinte e oito pacientes (39,4%) com CCP ainda fumavam imediatamente após o término do tratamento oncológico. Esta taxa aumentou para 43,7% quando o status do consumo de tabaco foi avaliado após 12 meses do final do tratamento. Na análise univariada foi encontrada associação entre variáveis sociodemográficas, clinicopatológicas e psicológicas e a alteração do hábito do tabagismo em pacientes após tratamento de CCP. Análise de regressão logística mostrou que ter o tumor primário localizado em boca e a ocorrência do sintoma de tristeza mensurado pelo BDI antes do tratamento foram preditivos para a manutenção do tabagismo 12 meses após o final do tratamento oncológico. Sentimento de fracasso antes do tratamento oncológico foi fator de risco para maior dificuldade em parar de fumar, tanto logo depois do término do tratamento, quanto 12 meses depois. Os sintomas de ansiedade mensurados pelo BAI no período pré-

tratamento não foram associados na análise multivariada à manutenção do tabagismo após o tratamento oncológico. Os resultados do presente estudo mostram que uma importante parcela de pacientes com CCP continuam fumando mesmo decorrido um ano do final do tratamento da doença, e que ter o tumor primário localizado em boca e a ocorrência de sintomas depressivos são preditivos para a manutenção do vício. Portanto, fatores clinicopatológicos e psicológicos devem ser considerados no planejamento do tratamento antitabagismo de pacientes com CCP.

Palavras-chave: Neoplasias de cabeça e pescoço. Tabagismo. Ansiedade. Depressão.

ANTUNES, A. D. S. S. **Influence of the clinicopathological and psychological factors on the smoking maintenance in head and neck cancer patients.** 2021. 41 f. Dissertação (Mestrado) – Faculdade de Odontologia, Universidade Estadual Paulista, Araçatuba, 2021.

ABSTRACT

Smoking is a risk factor for several types of cancer, including head and neck cancer (HNC). Although tobacco consumption is also related to the occurrence of second primary tumor and shorter life expectancy, a considerable rate of HNC patients is unable to quit smoking after the diagnosis of cancer. The aim of this study was to investigate the influence of sociodemographic, biobehavioral, clinicopathological and psychological factors on the smoking maintenance after HNC treatment. The study was composed of 71 HNC patients who had completed cancer treatment for at least 12 months. Demographic, clinicopathological and biobehavioral characteristics were collected from clinical records and smoking history throughout cancer treatment was assessed by a semi-structured interview. Anxiety and depression symptoms were assessed in the pre-treatment period using the Beck Anxiety Inventory (BAI) and Beck Depression Inventory (BDI), respectively. Twenty-eight patients (39.4%) with HNC were still smoking immediately after the end of the oncological treatment. This rate increased to 43.7% when cigarette smoking status was assessed 12 months after the end of treatment. In the univariate analysis, an association was found between sociodemographic, clinicopathological and psychological variables and changes in the habit of smoking in patients after HNC treatment. Logistic regression analysis showed that having the primary tumor located in the oral cavity and the symptom of sadness measured by the BDI before treatment were predictive for the smoking maintenance 12 months after the end of cancer treatment. Feeling of failure before cancer treatment was a risk factor for higher difficulty in quitting smoking both immediately after the end of treatment and 12 months later. In the multivariate analysis anxiety symptoms in the pretreatment period were not associated with maintenance smoking after cancer treatment. The results of the current study show that a significant number of HNC patients continue to smoke even one year after the end of treatment, and that having the primary tumor located in the oral cavity and specific depressive symptoms are predictive for the maintenance of tobacco dependence. Therefore, clinicopathological and

psychological factors should be considered in anti-smoking treatment of HNC patients.

Keywords: Head and neck neoplasm. Smoking. Anxiety. Depression.

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LISTA DE ABREVIATURAS E SIGLAS

BAI	Beck Anxiety Inventory
BDI	Beck Depression Inventory
CCP	Câncer de cabeça e pescoço
Chemo	Chemotherapy
CI	Confidence interval
HNC	Head and Neck Cancer
Radio	Radiotherapy
UICC	Union for International Cancer Control
UNESP	São Paulo State University

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1 INTRODUCTION*

Head and neck cancer (HNC) is a type of cancer with a great increase all over the world [1,2], and chronic tobacco use is highly known as the main etiological factor [1-7]. A better prognosis for HNC depends mainly on the initial clinical stage, as patients with early-stage disease are subjected to less aggressive treatments [3]. However, other factors, such as the maintenance of smoking can also affect the outcomes of HNC treatment [3-7]. Smoking cessation is highly related to a better response to cancer treatment [4-7]. It is known that tobacco consumption, especially at high intensity, can reducing the effects of radiotherapy [6] and chemotherapy [8], increasing the side effects of oncological treatments [5], as well as the length of stay [4]. Maintaining tobacco consumption after the cancer treatment also increases the recurrence and second primary tumor rates [9], in addition to decreasing the survival time [4,7,10].

Despite that, evidence show that the impact of the HNC diagnosis is not sufficient for smoking cessation, since a significant number of smokers patients maintain their addiction throughout cancer treatment and follow-up period [7,11-13]. The maintenance of tobacco addiction may be associated with sociodemographic, clinicopathological and biobehavioral factors [12-19]. The difficulty in quitting smoking in non-oncological patients has been associated with being over 40 years old [13], living with smokers [13], having a low level of education [13,16,18], the absence of comorbidities [13,16], and not be married [18]. The high intensity and prolonged time of tobacco use [13,16] and not having a negative perception of smoking [13] have also been linked to the maintenance of addiction in non-oncological patients. The intensity of the tobacco withdrawal syndrome also is strongly associated with the smoker's difficulty in quitting smoking, even after cancer diagnosis [5]. For the HNC patients, being single [12,15], being over 40 years old [17], having low education [17], and consuming alcohol and cannabis [17] are factors seen as influencing to maintain smoking after diagnosis and treatment of the disease. The clinical staging of cancer [12,15], the location of the tumor [12] and the type of cancer treatment received [12,15,19] are clinicopathological predictors that also affect the tobacco addiction after HNC treatment.

* Normalizado de acordo com as normas da Oral Oncology (Anexo B)

Psychological disorders such as anxiety and depression are also predictors for maintenance of tobacco dependence [15,19,20-31]. In addition to the high levels of anxiety and depression throughout oncological treatment, the fear of recurrence and social support are also predictors associated with changes in the intensity of tobacco consumption in cancer patients [15,19,20-29]. Higher levels of depression also have been associated with continued smoking [32]. Tobacco can be used as “self-medication” to alleviate anxiety symptoms, thus suggesting that anxiety leads to continued smoking [33]. Therefore, the relationship between smoking and psychological disorders such as depression and anxiety can be bidirectional [33-36].

To help cancer patients quit their addiction, it is necessary to recognize how changing the smoking habit is multifactorial and complex, as well as knowing the main factors that may be related to tobacco addiction [19,29]. Although the link between psychological factors and smoking in cancer patients is known [15,19,20-31], no study has explored the influence of specific symptoms of anxiety and depression before starting the oncological treatment on the smoking addiction in HNC patients. Thus, the aim of this study was to investigate the influence of sociodemographic, clinicopathological, biobehavioral and psychological factors on the smoking cessation after HNC treatment.

2 PATIENTS AND METHODS

2.1. Patients

This is a retrospective cross-sectional study, approved by the Research Ethics Committee of São Paulo State University (Unesp), School of Dentistry Araçatuba (Number: 4.425.141). This study included patients with definitive diagnosis of head and neck squamous cell carcinoma, who were treated in the Oral Oncology Center, São Paulo State University (Unesp), School of Dentistry Araçatuba, SP, Brazil. The patients should be smokers when they noticed the first sign or symptom of tumor and have data available from anxiety and depression symptoms measured in the cancer pre-treatment period. Patients who did not have the primary tumor located in the oral cavity, pharynx (hipopharynx or oropharynx) and larynx, those who refused to participate or those who had any cognitive deficit that made he/she impossible to understand the questions asked were excluded from the study.

2.2 Study Variables

2.2.1 Sociodemographic, clinicopathological and Biobehavioral Variables

Sociodemographic (gender, age, marital status, living alone, religion, color skin, education and family income), clinicopathological (occurrence or not of comorbidities, anatomical location of the primary tumor, clinical staging and type of oncological treatment) and biobehavioral (alcohol and tobacco consumption at the time of diagnosis) data were obtained from the clinical records of patients. The tumor location was classified into three anatomical regions: oral cavity, pharynx and larynx. The clinical staging of HNC was defined according to the Union for International Cancer Control (UICC) [37]. A structured interview was conducted with each patient to explore the smoking habit throughout cancer treatment and the period after treatment. The patients answered about age at smoking initiation and if they lived with smokers in their childhood. The type of cigarette and the intensity of smoking at the time of diagnosis were also asked. Smoking intensity was evaluated according to the number of cigarettes smoked per day, graded into light (1 to 10 cigarettes), moderate (11 to 20 cigarettes) and severe addiction (more than 20 cigarettes) [38].

Smoking status of each patient immediately and 12 months after the end of cancer treatment was also recorded.

2.2.2 Psychological Variables

The information regarding anxiety and depression symptoms were extracted from the database of the Psychosomatic and Education Research Center, Oral Oncology Center, São Paulo State University (Unesp), School of Dentistry Araçatuba, SP, Brazil. These data were collected through the Beck Anxiety Inventory (BAI) [39] and Beck Depression Inventory (BDI) [40] after the diagnosis of cancer before starting the treatment.

The BAI is a self-report scale that measures the occurrence and intensity of anxiety symptoms [39]. Symptom severity levels are graded by four scores: 1 (absolutely not), 2 (slightly: it didn't bother me too much), 3 (moderately: it was very unpleasant, but I could bear it) and 4 (severely: I could hardly bear it). The BDI [40] was created to measure the intensity of depressive episodes in the week prior to its application. It is a questionnaire consisting of 21 questions. The scale contains four possibilities of answers that vary in severity of depressive symptoms ranging from 0 to 3.

2.3 Statistical Analysis

The collected data were stored in the Microsoft Office Excel 2010 program. The simple frequency, univariate and multivariate analyzes were performed with SPSS program (IBM® SPSS® Statistics version 21, Inc., Chicago, IL). The chi-square and Fisher's exact tests were used to investigate the association between the study variables and the outcomes of smoking status (immediately and 12 months after the end of cancer treatment). The tumor location was also categorized into tumors located or not in the oral cavity. The marital status was divided into being married and not being married. The psychological data were used considering the presence or absence of BAI and BDI symptoms the levels of these symptoms classified as minimal, mild, moderate or severe. Based on the total score of BAI and BDI, the measures of lower or higher occurrence of anxious and depressive symptoms also were used, respectively. For the multivariate analysis, logistic regression was performed using the all sociodemographic, clinicopathological, biobehavioral and

psychological variables as independent variables, while the two smoking outcomes (smoking maintenance/cessation immediately and 12 months after treatment completion) were used as response variables. In the multivariate analysis, each symptom of anxiety and depression was evaluated by a binary measure (yes or no). The P values $< .05$ were considered significant for all analyses.

3 RESULTS

3.1 Sociodemographic, clinicopathological, and biobehavioral characteristics in HNC Treated Patients

Of the 71 patients included in the study, most were male (90.1%), with middle-aged (69% between 45 and 65 years old) (Table 1). The mean age of the patients was 61.7 years, with the youngest participant 44 and the oldest 89 years. Regarding the marital status, 46 patients (64.8%) were married and 60 (84.5%) did not live alone (Table 1). Forty seven patients (66.3%) were catholic and 46 (64.8%) self-declared white skin color (Table 1). Eighteen patients (25.4%) have completed middle school, while 16 (22.5%) stopped before finishing (Table 1). The monthly income of most patients was between R\$1,000 and R\$5,000 (52.1%) or was below R\$1,000 (45.1%) (Table 1).

Forty-six (64.8%) HNC patients had no comorbidities, had the tumor in the oral cavity, had the disease in an initial clinical stage (I or II) (Table 1). Regarding the modality of cancer treatment, most patients (50.8%) underwent only surgery (Table 1).

Table 1 Sociodemographic and Clinicopathological Data of HNC Treated Patients

Variable	N (%)
Sex	
Male	64 (90.1)
Female	7 (9.9)
Age	
0-45 y	1 (1.4)
45-65 y	49 (69.0)
>65 y	21 (29.6)
Marital Status	
Married	46 (64.8)
Divorced	12 (16.9)
Single	8 (11.3)
Widowed	5 (6.0)
Living alone	
No	60 (84.5)
Yes	11 (15.5)

Table 1 Sociodemographic and Clinicopathological Data of HNC Treated Patients

Variable	N (%)
Religion	
Catholic	47 (66.3)
Protestant	12 (16.9)
Deist	5 (7.0)
Spiritist	5 (7.0)
Candomble	1 (1.4)
No religion	1 (1.4)
Skin Color	
White	46 (64.8)
Non-white	25 (35.2)
Education	
Elementary School	12 (16.8)
Incomplete Elementary School	9 (12.7)
Middle School	18 (25.4)
Incomplete Middle School	16 (22.5)
High School	6 (8.5)
Incomplete High School	7 (9.9)
University	1 (1.4)
Postgraduate	2 (2.8)
Income	
< R\$ 1.000	32 (45.1)
R\$1.000 a R\$ 5.000	37 (52.1)
> R\$5.000	2 (2.8)
Comorbidity	
No	46 (64.8)
Yes	25 (35.2)
Tumor location	
Oral cavity	46 (64.8)
Pharynx	14 (19.7)
Larynx	11 (15.5)
Clinical stage	
Early stage (I/II)	46 (64.8)
Advanced stage (III/IV)	25 (35.2)
Treatment	
Surgery	36 (50.8)
Surgery + Radio	15 (21.1)
Radio	10 (14.1)
Radio + Chemo	5 (7.0)
Surgery + Radio + Chemo	5 (7.0)

Thirty-eight patients (53.3%) were current drinker at the time of diagnosis (Table 2). All patients were smokers when they noticed the first sign or symptom of the disease, 35 (49.3%) were severe smokers and paper cigarettes was the main type of cigarette consumed by most patients (69%) (Table 2). Thirty-eight patients (53.5%) started smoking in adolescence (between 12 and 18 years old) (Table 2) and 61 patients (85.9%) reported that when they were children they lived with a relative who was a smoker (Table 2). The mean time of smoking among patients in this study was 43.1 years. With most patients (40.8%) smoked for 40 to 50 years (Table 2). Forty-three patients (60.6%) no longer smoked after the end of cancer treatment, while 28 patients (39.4%) maintained tobacco use. After 12 months of the end of cancer treatment, the rate of smokers increased to 43.7% (Table 2).

Table 2 Biobehavioral Data of HNC Treated Patients

Variable	N (%)
Alcohol consumption at the time of diagnosis	
None	8 (11.3)
Current drinker	38 (53.5)
Ex drinker	25 (35.2)
Tobacco intensity at the time of diagnosis	
Light	8 (11.3)
Moderate	28 (39.4)
Severe	35 (49.3)
Type of cigarette smoked at diagnosis	
Straw cigarette	2 (2.8)
Paper cigarette	49 (69.0)
Straw and paper cigarette	20 (28.2)
Age of first cigarette use	
Childhood (0 -12 years)	15 (21.1)
Adolescence (12 – 18 years)	38 (53.5)
Adult (>18 years)	18 (25.4)
Living with a smoker in childhood	
No	10 (14.1)
Yes	61 (85.9)
Time of smoking	
< 20 year	1 (1.4)
20-30 years	7 (9.9)
30-40 years	18 (25.4)
40-50 years	29 (40.8)
> 50 years	16 (22.5)

Table 2 Biobehavioral Data of Smokers Patients of Treated HNC

Variable	N (%)
Tobacco consumption immediately after the end of cancer treatment	
No	43 (60.6)
Yes	28 (39.4)
Tobacco consumption 12 months after the end of treatment	
No	40 (56.3)
Yes	31 (43.7)

3.2 Anxiety and Depression Symptoms in HNC Treated Patients

Table 3 show that anxiety symptoms were present in 63 (88.7%). When the anxiety symptoms were graded by intensity, 49 (69%) patients had minimum symptoms, 18 (25.4%) had mild symptoms, 2 patients (2.8%) had moderate symptoms and 1 (4.2%) had symptoms severe (Table 3). Depression symptoms were reported by 54 patients (76.1%) (Table 3). Fifty-one patients (71.9%) had depression symptoms graded as minimum, 11 (15.5%) mild symptoms, 5 patients (7%) had moderate symptoms of depression while 1 (1.4%) had severe symptoms (Table 3).

Table 3 Anxiety and Depression Symptoms in Smokers Patients of Treated HNC at diagnosis

Variables	N (%)
Anxiety symptoms (BAI)	
Present	63 (88.7)
Absent	7 (9.9)
Missing	1 (1.4)
Anxiety symptoms – level	
Minimum	49 (69.0)
Mild	18 (25.4)
Moderate	2 (2.8)
Severe	1 (1.4)
Missing	1 (1.4)

Table 3 Anxiety and Depression Symptoms in Smokers Patients of Treated HNC at diagnosis

Depression symptoms (BDI)	
Present	54 (76.1)
Absent	14 (19.7)
Missing	3 (4.2)
Depression symptoms - Level	
Minimum	51 (71.9)
Mild	11 (15.5)
Moderate	5 (7.0)
Severe	1 (1.4)
Missing	3 (4.2)

3.3 Associations between marital status, tumor location and time of smoking with smoking outcomes

The univariate analysis showed that divorced patients with HNC had greater difficulty in quitting smoking compared to single, married and widowed patients immediately ($P= 0.015$) and 12 months ($P = 0.031$) after the end of cancer treatment (Table 4). The same difficulty was observed in both outcome in patients with tumor located in the oral cavity compared to those with tumor in the pharynx and larynx ($P=0.047$; $P=0.012$, respectively) (Table 4). Patients who smoked for 40 to 50 years had greater difficulty in quitting when compared to patients who smoked for less than 40 years and for more than 50 years, both soon after ending oncological treatment ($P=0.005$) and 12 months after the end of treatment ($P=0.005$) (Table 4).

Table 4 Associations between sociodemographic, clinicopathological and biobehavioral variables and smoking outcomes

Variables	Immediately after the end of treatment	12 months after the end of treatment
Marital Status	.015 ^{a,b}	.031 ^{a,b}
Tumor location	.047 ^{a,c}	.012 ^{a,c}
Time of smoking	.005 ^{a,d}	.014 ^{a,d}

^a Values were considered statistically significant at $P < .05$ (chi-square test or Fisher's exact test).

^b Values were measured with the categories (married, divorced, single or widowed).

^c Values were measured with the categories (oral cavity, pharynx and larynx).

^d Values were measured with the categories (< 20 year, 20-30 years, 30-40 years, 40-50 years, > 50 years).

3.4 Association between symptoms of anxiety and depression and smoking outcomes

Having low levels of anxiety symptoms was associated with quitting smoking immediately after ($P=0.022$) and 12 months ($P=0.004$) after the end of treatment (Table 5). Patients who claimed to feel tremors in the legs ($P=0.044$; $P=0.079$) and difficult to relax ($P=0.044$; $P=0.017$) were associated with not quitting smoking in HNC patients immediately after and 12 months after the end of treatment, respectively (Table 5). Patients who reported feeling imbalance ($P=0.035$) and to be very nervous ($P=0.020$) before starting cancer treatment had more chances to maintain the smoking addiction immediately after the end of oncological treatment (Table 5). HNC patients who had no depressive symptoms ($P=0.005$) or had minimal symptoms ($P=0.020$) were more likely to quit smoking immediately after ending the treatment (Table 5). Patients with lower occurrence of depressive symptoms measured by the BDI were more likely to quit smoking, when compared to patients with more intense symptoms, immediately after ($P=0.022$) and 12 months after the end of treatment ($P=0.043$) (Table 5). Patients who reported feeling sadness ($P=0.002$; $P=0.011$ respectively), failure ($P=0.002$; $P=0.023$, respectively) or guilty ($P=0.008$; $P=0.008$, respectively) before starting cancer treatment had more chances to keep tobacco consumption immediately and 12 months after the end of cancer treatment, respectively (Table 5). According to the univariate analysis, depressive symptoms such as feeling a worse than others ($P=0.036$), having the idea of killing yourself ($P=0.029$), having difficulty making decisions ($P=0.034$), having

difficulty sleeping ($P=0.022$) and concern for health ($P=0.035$) were associated with continuing to smoke immediately after the end of cancer treatment (Table 5).

Table 5 Associations between psychological variables and smoking outcomes

Variables	Immediately after the end of cancer treatment	12 months after the end of treatment
Anxiety symptoms – Class	.022 ^{a,b}	.004 ^{a,b}
Tremors in the legs	.044 ^{a,b}	.079 ^b
Unable to relax	.044 ^{a,b}	.017 ^{a,b}
Imbalance	.025 ^{a,b}	.068 ^b
Nervous	.020 ^{a,b}	.064 ^b
Depression symptoms (BAI)	.005 ^{a,c}	.477 ^c
Depression symptoms – Class	.020 ^{a,b}	.149 ^b
Depression symptoms	.022 ^{a,d}	.043 ^{a,d}
Sad	.002 ^{a,b}	.011 ^{a,b}
Failure	.002 ^{a,b}	.023 ^{a,b}
Guilty	.008 ^{a,b}	.008 ^{a,b}
Worse than others	.036 ^{a,b}	.347 ^b
Ideas to kill yourself	.029 ^{a,b}	.046 ^{a,b}
Decisions	.034 ^{a,b}	.350 ^b
To sleep	.022 ^{a,b}	.091 ^b
Health concern	.035 ^{a,b}	.077 ^b

^a Values were considered statistically significant at $P < .05$ (chi-square test or Fisher's exact test).

^b Values were measured with the severity categories (minimum, mild, moderate, or severe).

^c Values were measured with the binary measure (yes or no).

^d Values were measured with the intensity measure (Lower or Higher).

3.5 Depression symptoms and tumors located as predictors of smoking maintenance after HNC treatment

In the multivariate analysis, HNC patients with tumors located in the oral cavity were more likely to continue smoking after 12 months of the end of oncological treatment when compared to patients who did not have tumors located in the oral cavity ($\beta = 6.891$, 95% confidence interval [CI] = 1.661-28.580, $P = .008$; Table 6). Patients who reported prior to cancer treatment having failed in life had greater difficulty in quitting smoking soon ($\beta = 13.455$, 95% CI = 3.210-56.395, $P < 0.001$; Table 6) and 12 months after the end of cancer treatment ($\beta = 4.537$, 95% CI = 1.049-19.628, $P = 0.043$; Table 6). Those HNC patients who reported feeling sad in the pre-treatment period were 5.2 times more likely to continue smoking 12 months after the end of treatment when compared to patients who did not feel sad ($\beta = 5.279$, 95% CI = 1.254-22.235, $P = 0.023$; Table 6).

Table 6 Predictors of smoking maintenance after head and neck cancer treatment

Dependent Variables	Response Variables					
	Immediately after the end of cancer treatment			12 months after the end of treatment		
	β	95% IC	P	B	95% IC	P
Tumor location ^{a,b}	—	—	—	6.891	1.661-28.580	0.008
Failure ^{a,c}	13.455	3.210-56.395	<0.001	4.537	1.049-19.628	0.043
Sadness ^{a,c}	—	—	—	5.279	1.254-22.235	0.023

^a These variables remained in the final regression model.

^b Values were measured with the categories (tumor located in the oral cavity or tumor not located in the oral cavity).

^c Values were measured with the binary measure (yes or no).

4 DISCUSSION AND CONCLUSION

The results of the current study reveal that 39.4% of patients with HNC were still smoking right after treatment ended. The maintenance of smoking after diagnosis and treatment in HNC patients has been proven [12,13]. Ostroff et al. showed that one-third of the patients with cancer in the upper aerodigestive tract, who smoked before the cancer diagnosis, continued to smoke even after ending the cancer treatment [12]. The current study observed an increase in the proportion of smokers patients 12 months after the end of HNC cancer treatment. This finding is possibly due to the belief of patients that, if they do not reduce the use of tobacco, they may have less chance of cure or greater chance of occurrence of a second cancer. According to Gritz et al., although the relevance of smoking cessation by cancer patients is known, the stage of the cancer diagnosis has not been so well explored by health professionals, who underestimate this moment as an opportunity to stimulate the smoker patient learning to quit smoking [41]. Most health professionals who address the issue of combating smoking in cancer patients, do so only in the first consultations, not discussing treatment or support options for quitting addiction [41-44]. This support throughout cancer treatment is essential for success in quitting smoking [43-46].

Our results also indicated that having the primary tumor located in the oral cavity positively influenced continuing smoking soon after the end of treatment in HNC patients. Patients with tumors in the oral cavity were 6.8 times more likely to continue smoking than those with tumors in the pharynx or larynx. This same finding has been reported in other studies [12,19]. Ostroff et al. conducted a study with 74 HNC patients and found that those with tumors in the oral cavity were 3.2 times more likely to continue smoking than those with tumors located in the larynx or pharynx [12]. Normally HNC patients with primary lesion located in the oral cavity are subjected to less extensive surgeries, with a reduction in the occurrence of aesthetic and functional sequels compared to patients with tumors in other sites [19,47]. One hypothesis is that the fact of having fewer sequels may lead the patient to minimize the severity of the cancer and its etiological factor, which could negatively influence the patient's decision to quit smoking [19].

We also found that HNC patients who felt sad before starting treatment had greater difficulty in quitting smoking compared to those who did not have this

depressive symptom. Another depressive symptom reported by HNC patients before treatment that was associated with smoking both soon and after 12 months after the end of treatment it was the feeling of having failed in life. A study from our center explored the main motivations for smoking according to the smoker's own perception, and found negative emotions and feelings as factors highly related to smoking and its intensity [31]. Sarafim-Silva et al. observed that the majority of the smokers (83.7%) believed that they consumed cigarettes due to stress, anxiety and nervousness [31]. Khodadadi et al. in a study with HNC patients found that stress relief was often reported as a benefit to continuing to smoke [42]. The relationship between the occurrence of anxiety and depression symptoms in HNC patients and the maintenance of the smoking habit has already been proven [15,19,23,24-29].

Humphris et al. evaluated smokers with oral and oropharyngeal cancer and observed that 15 months after the end of treatment, the levels of anxiety were higher among those who continued smoking cigarettes, when compared to those who stopped smoking [29]. Chang et al. when analyzing factors that influenced to keep smoking after oral cancer treatment, it found that depression was significantly associated with this continuing [15]. Guimond et al observed that those cancer patients who had a higher occurrence of depressive symptoms after cancer treatment were also more likely to continue to smoke [22]. They also showed that patients who stopped smoking had a decrease in depressive symptoms [22]. Bloom et al. found the same evidence when evaluating 134 patients with HNC and lung cancer. In this study, patients who stopped smoking had fewer depressive symptoms when compared to those who continued to smoke after 12 months of cancer surgery [24]. Duffy et al. observed that HNC patients who controlled the symptoms of depression were more successful in quitting tobacco [26].

Although other studies have found an association between difficulty in quitting smoking and depressive symptoms in patients with HNC [15,19,26-29] to our knowledge this is the first study that has assessed the association of each symptom measured by a depression assessment instrument in the HNC population. Dorison et al. in a study with non-cancer patients, found that sadness had a stronger association with smoking than the other negative emotions evaluated, in addition to being a factor linked to relapse into addiction even after 20 years of abstinence [48]. A study evaluated smokers who participated in an anti-smoking cognitive-behavioral treatment program and found that for those patients who were able to quit and

relapsed in less than 3 months, the frustration feeling was an important predictor [49]. We believe that this relationship between feeling sad or feeling of having failed in life and maintenance of smoking found in our study can be explained by the fact that negative emotions can influence decisions making [50,51] and increase the craving for cigarettes [52].

To continue smoking is harmful to cancer patients [4-11]. A study evaluated 202 patients with HNC and observed that the rate of toxicity of radiotherapy was 49% for those who continued smoking during treatment, while this adverse effect was observed only in 31% of patients who had stopped smoking before starting treatment [11]. When analyzing the overall survival over five years, they found that those patients who stopped smoking had a survival rate of 55%, while in patients who were still smokers the survival rate was 23% [11]. Tabuchi et al. evaluated the correlation of smoking with mortality in 30.658 patients with various types of cancer in the city of Osaka-Japan. They found that the risk of death in 10 years was 11% higher for patients who continued smoking, when compared to patients who stopped smoking [7]. The lack of psychological data of patients with HNC after tumor treatment can be considered a limitation of this study. As well as the fact that data collected in the interview depend only on the patient's self-report, which can be harmed by the lack of memories or insecurity of the patient. The absence of biochemical laboratory analyzes in bodily fluids that confirm the absence of tobacco use can also be considered a limitation of this study.

In general, our results show that symptoms of depression in the pre-treatment period and location of the primary tumor are associated with maintaining tobacco consumption after treatment in HNC patients. Those patients who felt they had already failed at some point in their life or who felt sad before starting cancer treatment has greater difficulty in quitting smoking. The same difficulty is observed in HNC patients with the tumor located in the oral cavity. This study is of great importance for a better understanding of the different factors that make it difficult for HNC patients to abstain from smoking, which can provide them with a better quality of life and prognosis. In view of our results specific depressive symptoms should be considered in the development of anti-smoking strategies for HNC patients.

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ANEXO A- Comitê de Ética em Pesquisa

UNESP - FACULDADE DE
ODONTOLOGIA-CAMPUS DE
ARAÇATUBA/ UNIVERSIDADE
ESTADUAL PAULISTA "JÚLIO
DE MESQUITA FILHO"



PARECER CONSUBSTANCIADO DO CEP

DADOS DO PROJETO DE PESQUISA

Título da Pesquisa: Avaliação da influência dos fatores clínico-patológicos e psicológicos na manutenção ou cessação do consumo de tabaco em pacientes com Câncer de Cabeça e Pescoço.

Pesquisador: Ana Daniela Spinola

Área Temática:

Versão: 3

CAAE: 17214119.4.0000.5420

Instituição Proponente: Faculdade de Odontologia do Campus de Araçatuba - UNESP

Patrocinador Principal: Financiamento Próprio

DADOS DO PARECER

Número do Parecer: 4.425.141

Apresentação do Projeto:

O estudo será uma análise observacional analítica longitudinal retrospectiva. Os procedimentos de coleta de dados serão executados por meio de pesquisa em prontuários clínicos e por meio de entrevista com o paciente.

Objetivo da Pesquisa:

Objetivo Primário:

Analisar a influência de fatores clínico-patológicos e psicológicos sobre a manutenção ou cessação do consumo de tabaco em pacientes com câncer de cabeça e pescoço (CCP).

Objetivo Secundário:

Avaliar a associação das variáveis sociodemográficas e clínico-patológicas com a manutenção ou cessação do tabagismo em pacientes com CCP. • Avaliar a associação dos níveis de ansiedade e depressão pré-tratamento com a manutenção ou cessação do tabagismo em pacientes com CCP

Avaliação dos Riscos e Benefícios:

Riscos:

O estudo oferece risco mínimo aos participantes da pesquisa.

Benefícios:

Esperamos que os resultados da presente pesquisa gere maior entendimento sobre os influenciadores do consumo de tabaco durante e após o tratamento do câncer, e este conhecimento estimule o desenvolvimento de estratégias de suporte mais efetivas por parte da equipe oncológica.

Comentários e Considerações sobre a Pesquisa:

Objetivos são claros e bem definidos.

A metodologia proposta é capaz de atender os objetivos do estudo.

Considerações sobre os Termos de apresentação obrigatória:

Os termos obrigatórios foram apresentados.

Recomendações:

Não há.

Conclusões ou Pendências e Lista de Inadequações:

Não havendo pendências, recomenda-se a aprovação do projeto.

Considerações Finais a critério do CEP:

Não havendo pendências, o CEP propõe a aprovação do projeto de pesquisa salientando que, de acordo com a Resolução 466 CNS de 12/12/2012 (título X, seção X.1., art. 3, item b, e, título XI, seção XI.2., item d), há necessidade de apresentação de relatórios semestrais, devendo o primeiro relatório ser enviado até 17/04/2020. O CEP reitera a necessidade de entrega de uma via (não cópia) do TCLE ao sujeito participante da pesquisa e solicita ao pesquisador responsável leitura da carta circular 003/2011 CONEP/CNS antes do início do projeto.

Este parecer foi elaborado baseado nos documentos abaixo relacionados:

Tipo Documento	Arquivo	Postagem	Autor	Situação
Informações Básicas do Projeto	PB_INFORMAÇÕES_BÁSICAS_DO_PROJETO_1395576.pdf	13/09/2019 22:23:26		Aceito
Cronograma	Cronograma.docx	13/09/2019 22:22:07	Ana Daniela Spinola	Aceito
TCLE / Termos de Assentimento / Justificativa de Ausência	TCLE.doc	19/08/2019 16:48:20	Ana Daniela Spinola	Aceito
Folha de Rosto	folhaderosto.pdf	10/07/2019 18:43:32	Ana Daniela Spinola	Aceito
Projeto Detalhado / Brochura Investigador	Projeto.pdf	10/07/2019 18:19:36	Ana Daniela Spinola	Aceito

Situação do Parecer:

Aprovado

Necessita Apreciação da CONEP:

Não

ARACATUBA, 18 de Outubro de 2019

Assinado por:

**Aldiéris Alves Pesqueira
(Coordenador(a))**

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Município: ARACATUBA

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ANEXO B– Guide for Authors da Oral Oncology

ORAL ONCOLOGY

A Journal Related to Head & Neck Oncology

ISSN: 1368-8375

[Guide for Authors - https://www.elsevier.com/journals/oral-oncology/1368-8375/guide-for-authors](https://www.elsevier.com/journals/oral-oncology/1368-8375/guide-for-authors)