Research, Society and Development, v. 10, n. 5, e42410514911, 2021
(CC BY 4.0) | ISSN 2525-3409 | DOI: http://dx.doi.org/10.33448/rsd-v10i5.14911

Is there any association between cognitive decline with the oral health condition?

Existe associação entre o declínio cognitivo e a saúde oral?

¿Existe Asociación entre la declinación cognitiva y la condición de salud oral?

Recebido: 10/04/2021 | Revisado: 18/04/2021 | Aceito: 27/04/2021 | Publicado: 12/05/2021

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Abstract
Objective: This study aimed to evaluate the cognitive decline and its association with the oral health condition through the number of remaining teeth (NRT) and related oral maintenance and rehabilitation (OMR). Material and Methods: This study was classified as observational,cross-sectional and prospective. The oral examination included the NRT and OMR. The mental health status was obtained through the Mini-Mental State Examination (MMSE). Other parameters included the American Society of Anesthesiologists Classification (ASA) modified for Dentistry, a handheld electrocardiogram (ECG) and blood tests. Results: The sample was composed with 63 patients. It was found correlation between NRT and MMSE scores (p= 0.01). Healthy patients (ASA I) have more teeth when compared to unhealthy (p=0.004). When better was the OMR, better was the scores of MMSE (p< 0.001) and better was the health status (p=0.004). Conclusion: The findings showed several associations between oral condition, systemic health and cognitive decline. Decreased NTR and compromised oral maintenance and/orrehabilitation was more frequently observed in patients classified as systemically unhealthy and with reduced MMSE scores.
Keywords: Oral health; Tooth loss; Cardiovascular disease; Cognitive symptom; Mini-mental state examination.

Resumo
Objetivo: Este estudo teve como objetivo avaliar o declínio cognitivo e sua associação com a condição de saúde bucal por meio do número de dentes remanescentes (NDR) e da manutenção e reabilitação bucal relacionadas (MRO). Metodologia: Este estudo foi classificado em observacional, transversal e prospectivo. O exame bucal incluiu o NDR e MRO. O estado de saúde mental foi obtido por meio do Mini Exame do Estado Mental (MEEM). Outros parâmetros incluíram a classificação da Sociedade Americana de Anestesiologistas (ASA) modificada para Odontologia, um eletrocardiograma de mão (ECG) e exames de sangue. Resultados: A amostra foi composta por 63 pacientes. Foi encontrada correlação entre os escores do NDR e do MEEM (p = 0,01). Pacientes saudáveis (ASA I) apresentam mais dentes quando comparados aos não saudáveis (p = 0,004). Quanto melhor o MRO, melhores os escores do MEEM (p <0,001) e melhor o estado de saúde (p = 0,004). Conclusão: Os achados mostraram várias associações entre condição bucal, saúde sistêmica e declínio cognitivo. NDR diminuída e manutenção e / ou reabilitação oral comprometidas

foram mais frequentemente observadas em pacientes classificados como sistemicamente não saudáveis e com escores MEEM reduzidos.
Palavras-chave: Saúde bucal; Perda de dente; Doença cardiovascular; Sintoma cognitivo; Mini exame do estado mental.

Resumen
Objetivo: Este estudio tuvo como objetivo evaluar el deterioro cognitivo y su asociación con el estado de salud bucal a través del número de dientes remanentes (NDR) y el mantenimeitno y rehabilitación bucal relacionadas (MRB). Metodología: Este estudio se clasificó en observacional,transversal y prospectivo. El examen oral incluyó el NDR y MRB. El estado de salud mental se obtuvo a través del Mini Examen del Estado Mental (MEEM). Otros parámetros incluyeron la Clasificación de la Sociedad Estadounidense de Anestesiólogos (SAA) modificada para Odontología, un electrocardiograma de mano (ECG) yexámenes hematológicos. Resultados: La muestra estuvo conformada por 63 pacientes. Se encontró correlación entre las puntuaciones NDR y MMSE (p = 0,01). Los pacientes sanos (ASA I) tienen más dientes en comparación con los enfermos (p = 0,004). Cuanto mejor sea el MRB, mejores serán las puntuaciones del MMSE (p <0,001) y mejor será el estado de salud (p = 0,004). Conclusión: Los resultados mostraron varias asociaciones entre la condición bucal, la salud sistémica y el deterioro cognitivo. La disminución de la NDR y el deterioro de el mantenimiento y / o la rehabilitación oral se observaron con mayor frecuencia en pacientes clasificados como sistémicamente no saludable y con puntuaciones MEEM reducidas.
Palabras clave: Salud Bucal; Pérdida de diente; Enfermedades Cardiovasculares; Disfunción Cognitiva; Mini Examen de Estado Mental.

1. Introduction

There is cumulative evidence that common oral diseases such as periodontitis, caries, apical periodontitis and tooth loss, as consequence of those conditions, may promote or is, somehow, associated with some systemic diseases, mainly cardiovascular and cerebrovascular (Hansen, Egeberg, Holmstrup, & Hansen, 2016; Gomes et al., 2016; Cotič et al., 2017; Virtanen et al., 2017; Yang et al., 2017; Aoyama et al., 2017; Daly et al 2018; Dintica et al., 2018). Other authors have also observed associations between oral health with conditions such as; denture wearing during sleep and pneumonia development (Iinuma et a., 2015), periodontal disease and obstructive lung disease (Peter et al., 2013; Parashar et al., 2018), tooth loss and the increased risk of cancer (Yang et al., 2017; Maisonneuve, Amar & Lowenfels, 2017) and mortality (Holmlund, Holmm & Lindm, 2010; Koka & Gupta 2018; Peng et al., 2019). Masticatory dysfunction, periodontitis and tooth loss has also been associated with cognitive decline and dementia (Daly et al., 2018; Li, Xu, Pan, & Wu, 2017; Lin, 2018; Nilsson, Berglund & Renvert, 2018). A study has linking patients with complete or partial tooth loss with significantly lower total brain volume (Dintica et al., 2018), as well as, it was observed, in mice, that tooth extraction may have induced a significantly reduction of regional volumes of cortical brain regions involved in processing somatosensory, motor, cognitive and emotional functions (Avivi-Arber et al., 2017). Fukushima-Nakayama et al. (2017) reported that the reduced mastication in mice during the growth period, resulted in impaired spatial memory and learning function. While, the opposite, or good oral condition, seems to bring beneficial associations and, according to Janket et al. (2013) keeping many teeth, both natural and artificial, while simultaneously reducing oral inflammatory foci appear to impact positively on cardiovascular survival, however, this matter is also subject of controversy (Peng et al., 2019; Liu et al., 2019).

The pathophysiology by which oral diseases can influence the development of some systemic diseases is still unknown and it is also under discussion due to discrepant findings among studies which may be due to differences in methods and designs, or due to differences in assessment of oral and systemic conditions or, even, insufficient adjustment for potential confounders (Daly et al., 2018; Dintica et al., 2018; Peng et al., 2019). The most frequently proposed mechanism presume that the chronic oral diseases may create a life-long accumulation of increased levels of systemic inflammation and produce frequent and transient bacteremia, which in turn, increases endothelial dysfunction, and these both conditions are supposed to increase the chances of development of cardiovascular and cerebrovascular diseases (Holmlund, Holmm & Lindm, 2010; Peng et al., 2019), meanwhile, in a large cohort study, Dintica et al. (2018) proposed that the association between tooth loss and cognitive decline is not fully

accounted for cardiovascular disease or higher inflammation. The mechanism or the cause-and-effect relationship for poor oral condition and cardiovascular and cerebrovascular diseases are not understood (Li, Xu, Pan, & Wu, 2017; Lin, 2018). Nevertheless, the hypothesis of cognitive decline associated to oral condition may due to "antimicrobial protection hypothesis" which is related to the formation of extracellular amyloid-beta (Aβ) plaques and hyper-phosphorylation of tau protein, implicated in neuroinflammation and neurodegeneration, which may be resultant of host responses from central nervous system (CNS) invasion by pathogens. The formation of the Aβ in brain tissue, which is highly implicated in Alzheimer's disease (AD) and cognitive decline, is itself, a result of the immune response to CNS infection and represents an immediate and continued physiological response to invading microorganisms, stimulating chronic neuroinflammation and subsequent compromise of blood–brain-barrier function (Schere & Scherer, 2020; Da Silva et al., 2021).

There is a currently estimate that there are around 50 million persons currently living with dementia worldwide with several studies showing association between poor oral status and cognitive decline and also pointing to the importance of keeping good oral health for maintain good cognitive health (Kiuchi et al., 2021; Scherer & Scherer, 2020; Da Silva et al., 2021; Dibello et al., 2021). The aim of this observational and prospective study was to evaluate the oral health condition for tooth loss and related oral rehabilitation and the cognitive decline, as well as, to investigate other systemic health parameters in order to search for possible associations between both oral and systemic conditions.

1.1 Oral Examination

The clinical oral exam was performed by trained and calibrated examiners composed by fourth year dental students, and performed in dental clinical setting using dental lighting. The exam underwent under direct orientation of three experienced professors of oral medicine.

(a) Tooth loss (TL) or the number of remaining teeth (NRT); was obtained by counting the remaining teeth including third molars. Residual roots whenever present and without crown were not included in the count for TL. Additionally, it was also collected the number of teeth with endodontic involvement and indicated dental extraction, such as residual roots. Bone examination was made basically by radiographs and clinical searching for expansions, pain, dental residual roots and fistulas.

(b) Oral maintenance and rehabilitation (OMR) was classified accordingly to the preserved number of teeth and rehabilitation of the maxilla and mandible, individually, as follows: 0, toothless without any prosthesis; 1, toothless with denture; 2, partially dentate without any prosthesis; 3, partially dentate with removable prosthesis; 4, partially dentate with dental implants or fixed prosthesis; 5, preserved oral condition due to the presence of most teeth and dental implants or fixed prosthesis; 6, preserved oral condition due to the presence of all teeth (not necessary to include third molars). In order to create an index for preserved oral condition, the above scores for maxilla and mandible were added, forming an index of Oral maintenance and rehabilitation (OMR) which range from 0 to 12, with high scores pointing to the best-preserved oral condition and rehabilitation.

1.2 Systemic Evaluation

1.2.1 Mini-Mental State Examination (MMSE)

A Brazilian version of the MMSE was applied and the results confirmed trough online calculator (https://aps.bvs.br/apps/calculadoras/?page=11). The scores of the tests range from 0 to 30, and lower scores indicate poorer performance and may be indicative of cognitive impairment. As indication of cognitive impairment was taken into account the patients' schooling, being the cutoff lower than 17 (≤16) points for patients with elementary school (≤ 8 years of study) and lower than 24 (≤23) points for patients with high school (≥ 9 years of study) or more, in accordance with the accepted guideline for Brazilian population (Diniz, Volpe & Tavares, 2007).

1.2.2 American Society of Anesthesiologists Classification (ASA)

A modified ASA physical classification system for dentistry was obtained through the questionnaire European Medical Risk Related History (EMRRH). The changes in the system occurred to assess the risk to patients of dental treatment carried out under local anesthesia. The ASA V category is not included in the EMRRH, as a patient in this condition would be too ill to visit a dentist. It was designed to register medical pathology that can interfere with dental treatment, to indicate the degree of medical risk involved and to recommend measures to be taken (Abraham-Inpijn, 2008). According to the questionnaire the patient was then classified as ASA I or healthy patient, ASA II or patient with mild to moderate systemic disease not interfering with daily life, ASA III or patient with severe systemic disease that limits activity but is not incapacitating and ASA IV or patient with severe systemic disease that limits activity and is a constant threat to life (Abraham-Inpijn, 2008).

1.2.3 Handheld Electrocardiogram (ECG)

Studies using a single-lead handheld ECG machines have reported that those devices are feasible to identify some cardiac diseases especially atrial fibrillation, with minimal training (Grubb et al., 2019; Proietti et al., 2019). As a screening method a handheld portable ECG PC-80-B was used (Food and Drug Administration approved: PC80B Easy ECG Monitor, Shangai Lishen Scientific Equipment Co., LTD, China). Each patient was submitted to, at least, two tests to confirm the suspected alteration. The device automatically analyses the ECG and suggest 16 cardiac waveforms anomalies through an automated ECG interpretation algorithm. ECG tracings were collected through the device with a 30 seconds long recording. The data of the patients with suspected anomaly was then stored and verified according to the accompanying software, the ECG Viewer Manager. All patients with ECG suspected anomaly were referred to medical evaluation.

1.2.4 Body Mass Index (BMI)

Body Mass Index was obtained through patient information (height and weight) and the index obtained through calculator and classified according to World Health Organization (WHO) as follows; underweight BMI <18.5, normal range BMI 18.5-24.9; overweight 25.0-29.0; obese ≥ 30 (also classified as class I, II and III).

1.2.5 Blood Tests (BLOT)

For the patients were asked, as clinic routine, for blood tests, including; complete blood count, C-reactive protein (CRP) and glycated hemoglobin (HbA1c) test. All blood tests were performed in the same university-school laboratory.

1.3 Statistical Procedures

A statistical program (IBM® SPSS® 15.0) was used to explore the data through descriptive and inferential analysis. A two-tailed probability $P \leq 0.05$ was regarded as statistically significant. The values were explored through the characteristics of the variable as continuous, ordinal or nominal with the statistical tests applied as recommended for those criteria. Some scalar or ordinal variables were dichotomized as for example, the scores of MMSE were analyzed as scalar continuous for searching associations of oral conditions in which the values were also continuous and, MMSE was also analyzed as dichotomous, when schooling was taken into account and the indications of those scores where within the normal values or indicative of cognitive impairment (dichotomous). As well as, ordinal values such ASA classification could be analyzed as ordinal (nonparametric) for correlations tests, as well as, dichotomous as systemically healthy or non-healthy patient. All variations in the analysis were fully described in the main results, according to the used analyze.

2. Methodology

This study was classified as observational, cross-sectional and prospective and it was submitted to the State University of Ponta Grossa Committee for Human Ethics Research and accepted under the number 2.364.242. Informed consent was obtained from all study participants. The inclusion criteria were patients older than 30 years who sought care in the university oral medicine clinic. The exclusion criteria were patients who present an advanced mental disease or mental limitation in which the patient may not understand the terms of the research and questionnaires; patients with oral malignant neoplasia, due to urgent diagnosis and referral to treatment and; patients who don't agree with the research participation. The socio-demographic characteristics of the patients were obtained through an interview questionnaire.

3. Results

3.1 Sample Characteristics

The sample was composed with 63 patients with age ranging from 32 to 77 years old (Mean 55) obtained consecutively by a convenience. Female patients composed the main group (43/68.3%) and thirty patients (52.4%) have only the elementary schooling. Related to smoking, 30 patients (47.6%) never smoked, 17 are ex-smokers (27%) and 16 are currently smokers (25.4%). According to World Health Organization (WHO) body mass index (BMI) classification, only 16 patients were within the normal range, while one patient was classified as underweight. Table 1 (Table 1) summarizes the bivariate analysis of the socio-demographic characteristics with NRT and OMR.

Table 1. Bivariate analysis of socio-demographic variables with the number of remaining teeth (NRT) and oral maintenance and rehabilitation (OMR).

Socio-demographic Variables	NRT	OMR
Gender	NS* (T1*)	NS* (T1*)
Age	P< .001 r_s= -.47 (T2*)	P< .001 r_s= -.51 (T2*)
BMI	NS* (T2*)	NS* (T2*)
Schooling (years of study)	P= .001 r_s= -.42 (T2*)	P< .001 r_s= -.49 (T2*)
Smoking	NS* (T2*)	NS* (T2*)

NS: Statistically non significant differences between groups or association between variables.
T1: Mann-Whitney Test.
T2: Spearman Correlation Test (Two-way).
Source: Authors.

The ASA questionnaire (EMRRH) classified as systemically healthy 17 patients (27%). The ECG analysis showed 8 patients with abnormalities in repeated measurements and in 6 of then the ASA classification was II or superior (unhealthy). CPR positive was observed in 12 (19%) patients. None abnormality was found in hemoglobin results and, for white blood cells, leukopenia (<4,000cells per mm^3) was observed in 3 patients and leukocytosis (>11,000 cells per mm^3) in 2 patients. Table 2 (Table 2) summarizes the bivariate analysis of systemic health conditions with the number of remaining teeth (NRT) and oral maintenance and rehabilitation (OMR).

Table 2. Bivariate analysis of systemic health conditions with the number of remaining teeth (NRT) and oral maintenance and rehabilitation (OMR).

Systemic Health Condition Variables	NRT	OMR
Handheld Electrocardiogram	NS* (T1*)	NS* (T1*)
ASA Classification	P= .009 r_s= -.32 (T2*)	P= .005 r_s= -.35 (T2*)
Mini-Mental State Examination	P= .01 r_s= .31 (T2*)	P< .001 r_s= .42 (T2*)
C-reactive protein (CRP)	NS* (T1*)	NS* (T1*)
Glycated hemoglobin (HbA1c)	NS* (T3*)	NS* (T3*)
White blood cells	NS* (T2*)	NS* (T2*)

NS: Statistically non significant differences between groups or association between variables.
T1: Mann-Whitney Test.
T2: Spearman Correlation Test (Two-way).
T3: Kruskal-Wallis Test
Source: Authors.

3.2 Number of Remaining Teeth (NRT)

The mean of remaining teeth was 12 (0 to 28 teeth, ±10), while 13 patients (20.6%) had none remaining teeth. It was found a positive correlation concerning the NRT and the scores of MMSE (r_s 0.31; p= 0.012; Spearman Correlation Test). A linear regression test indicates that NRT (p=0.006; Linear Regression) is responsible for near 11% of the MMSE variability. The NRT was negatively associated with age (r_s -0.48; p< 0.001; Spearman Correlation Test) and positively correlated with schooling (r_s 0.43; p= 0.001; Spearman Correlation Test). A partial correlation of NRT and MMSE controlled by age and schooling, showed that schooling is a more relevant factor to explain the lower scores of MMSE.

ASA was analyzed as normal or healthy (ASA I) and not normal or diseased (ASA II to IV) and, it showed a significant difference, meaning that more teeth is present in healthy patients (mean 17 teeth) when compared to unhealthy (mean 10 teeth) (p=0.004; Mann-Whitney Test).

Among the patients, 9 of them have at least one tooth requiring endodontic treatment or requiring dental extraction. None statistical association was found between these patients and the systemic conditions evaluated.

3.3 Oral maintenance and rehabilitation (OMR)

The index of oral rehabilitation, as described above, range from 0 to 12 points, with high values indicating a better oral maintenance or rehabilitation, based on the presence of teeth and oral rehabilitation. It was found a positive correlation concerning the OMR and the scores of MMSE (r_s 0.43; p< 0.001; Spearman Correlation Test). A partial correlation with OMR and MMSE controlled by age and schooling still preserved the association implicating that not only teeth but the preserved condition and/or rehabilitation is important for a better score in the mental examination (r 0.25; p= 0.048; Partial Correlation Test, controlled by age & schooling) and both, schooling (r_s 0.49; p< 0.001; Spearman Correlation Test) and age (r_s 0.52; p< 0.001; Spearman Correlation Test) were associated with OMR.

It was also observed that a greater ASA classification the lower were the OMR scores (r_s -0.35; p= 0.005; Spearman Correlation Test). Healthy patients (ASA I) showed better scores OMR with ~7 points, while unhealthy (ASA II-IV) showed ~4 points (p=0.004; Mann-Whitney Test).

3.4 Multivariate analysis

In order to understand the interactions between the clinical variables and having 10 or less teeth, a model of logistic regression was created and can be visualized in table 3 (Table 3). This analysis showed that patients with 10 or less teeth are linked with patients older than 50 years, with cognitive decline, altered handheld EEG and with ASA different than I.

Table 3. A multivariate model of Logistical Regression showing the associated variables with having 10 teeth or less and more than 10 teeth (Negelkeke R square = .55).

Variables included in the model	P value	Exp(B)	95% C.I.for EXP(B)	
			Lower	Upper
Gender	,34	,4	,06	2,5
Age (more than 50 years)	**,004***	21,4	2,7	168,2
HbA1C (Normal/Changed)	,10	,2	,03	1,3
Smoker (Yes/No)	,43	2,0	,33	12,6
BMI (Normal/Changed)	,27	,3	,06	2,2
MMSE/Schooling (Normal/Cognitive Decline)	**,03***	,07	,006	,8
ECG (Normal/Changed)	**,01***	,04	,004	,6
PCR (Normal/Changed)	,12	5,9	,6	57,0
ASA (Healthy/ Disease)	**,01***	15,0	1,6	141,4

* Statistical Significant.
Source: Authors.

4. Discussion

In the past few years, there has been accumulating evidence which suggests that chronic oral infections and related inflammatory foci may significantly enhance the risk for certain systemic diseases and/or alter the natural course of such conditions (Hansen, Egeberg, Holmstrup, & Hansen, 2016; Lin, 2018,) however, the pathophysiology of those interactions has not been proved yet. This study sought to explore associations between the oral health condition and the systemic condition in a prospective study, giving a glace of when the diseases (oral and systemic) coexist. At this point, is necessary to remember that the method of this study, as many others used as reference for this work, does not allow any inference of cause-and-effect relationship but only give a glimpse of what is going on in oral health which may be a marker for development of systemic diseases.

Probabilistically or simply following the principle of entropy in thermodynamics, it is reasonable that at some period of the life of an individual, as he gets old, he gets chronic systemic and oral diseases accumulated together and then, they get diagnosed. That should be the simple answer about the associations between oral diseases and systemic diseases, since the severity and prevalence of those chronic conditions increases with age. However, the answer may not be that simple, and to complicate it, there are some intriguing manuscripts, mainly in animal model such the described by Avivi-Arber et al. (2017), which report a series of brain modification, or compensatory mechanisms, occurring after removing teeth. Interestingly, our results showed that tooth loss and oral maintanace and/or rehabilitation were associated with MMSE test, indicating that these factors may be of relevance for mental health.

Several studies have investigated the relationship between oral function and cognitive function. Tooth loss effects spatial memory and increases the risk of diminished cognitive function suggesting that reduced masticatory function may be a risk factor for dementia (Kiuchi et al., 2021; Schere & Scherer, 2020; Da Silva et al., 2021). The findings of the present study showed that when greater is the number of remaining teeth, better were the scores for the mini-mental state examination (MMSE). Kuroki et al. (2018) also showed similar association between the NRT and MMSE scores using different statistical approaches and with greater number of subjects. This study also showed that patients classified as ASA I (healthy subjects) by the questionnaire European Medical Risk Related History (EMRRH) (Abraham-Inpijn et al., 2008) had statistically more teeth than those classified as unhealthy, as well as, the healthy patients had a better blood pressure control. ASA classification has not been traditionally used to explore the associations between the oral condition and general conditions, nevertheless, our findings indicate that ASA classification through the EMRRH questionnaire could be valuable. No similar studies have been found in recent literature

concerning this subject, however, Katsoulis et al. (2012) did not found associations between ASA and NRT, besides those authors used an ASA six grade scale, based on medical records and in institutionalized group of patients with starting age at 60 (mean of 83 years old), (Katsoulis, Schimmel, Avrampou, Stuck, & Mericske-Stern, 2012) which clearly imposes the differences between both studies.

The analysis of the OMR, which in this study clinically indicates the situation of the maxilla and mandible, based on tooth loss and rehabilitation showed that the preservation of the oral condition was associated with a better general health. When more preserved the oral condition better was the scores of the MMSE, whenever when it was analyzed isolated or controlled by age and schooling and when more preserved are the oral conditions healthier were the subjects (ASA I). The findings about the OMR may follow the same viewpoints of teeth loss; besides, the effect of rehabilitation may be beneficial due to the stimulatory effect of chewing and other mechanisms not well understood (Daly et al., 2018; Li, Xu, Pan & Wu, 2017; Lin, 2018; Nilsson, Berglund & Renvert, 2018; Kuroki et al., 2018; Hosadurga et al., 2020).

This research is an cross-sectional, prospective and observational study that may raise more questions at the end than answers to the many doubts that the dentistry science is proposing as real associations between oral health, general health and cognitive decline. The weak points of this study are mainly concerning the observational aspect of it, which may preclude any affirmative cause-effect relation between those variables, and for these, different approaches of experimental studies are necessary. Nevertheless, our findings made explicit the associations that were also found by others authors in large studies, highlighting the necessity to understand the pathophysiology of such interactions or associations. It is also important to note that the diagnoses for systemic diseases are based in single test results or questionnaires and, for this reason, this does not mean with absolute certainty that the disease is present and the association between diseases must be viewed with caution. The MMSE employed here, it is a screening tool and not a diagnose method, besides it has been showing a fair sensitivity to indicate dementia and cognitive decline. Based on the results, our objective for future is to fairly increase the sample size and improve our statistical methods to observe how different variables interact and modulate each other effects.

5. Conclusion

In conclusion, the findings of this study showed associations between oral condition, the systemic health and cognitive decline. The continuous loss of teeth showed association with poor scores in the MMSE and with patients being classified as unhealthy (ASA classification). The oral maintenance and/or rehabilitation, based on the condition of the maxilla and mandible, showed that a weak index was associated with negative impacts on MMSE scores and with unhealthy patients (ASA classification). The multivariate analysis showed that patients with 10 or less teeth are linked with patients older than 50 years, with cognitive decline, altered handheld EEG and with ASA different than I (ASA II to IV). Further experimental or cohort and prospective studies are needed to confirm these findings.

Ethical approval

This study was submitted and approved by the University's Ethical Committee for Human Research (https://www3.uepg.br/propesp-cep/) under the number 2.364.242 and informed consent was obtained from all study participants.

References

Abraham-Inpijn, L., Russell, G., Abraham, D. A., Bäckman, N., Baum, E., Bullón-Fernández, P. et al. (2008). A patient-administered Medical Risk Related History questionnaire (EMRRH) for use in 10 European countries (multicenter trial). *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*, 105(5), 597-605

Aoyama, N., Suzuki, J. I., Kobayashi, N., Hanatani, T., Ashigaki, N., Yoshida, A., et al. (2017). Periodontitis deteriorates peripheral arterial disease in Japanese population via enhanced systemic inflammation. *Heart Vessels*, 32(11), 1314-1319

Avivi_Arber, L., Seltzer, Z., Friedel, M., Lerch, J. P., Moayedi, M., Davis, K. D., et al. (2017). Widespread Volumetric Brain Changes following Tooth Loss in Female Mice. *Front Neuroanat*, 10, 121

Cotič, J., Ferran, M., Karišik, J., Jerin, A., Pussinen, P. J., Nemec, A., et al. (2017). Oral health and systemic inflammatory, cardiac and nitroxid biomarkers in hemodialysis patients. *Med Oral Patol Oral Cir Bucal*, 22(4), e432-e439

Daly, B., Thompsell, A., Sharpling, J., Rooney, Y. M., Hillman, L., Wanyonyi, K. L., et al. (2018). Evidence summary: the relationship between oral health and dementia. *Br Dent J*, 223(11), 846-853

Dibello, V., Lozupone, M., Manfredini, D., Dibello, A., Zupo, R., Sardone, R., Daniele, A., Lobbezoo, F., & Panza, F. (2021). Oral frailty and neurodegeneration in Alzheimer's disease. *Neural Regen Res*. 2021 Nov;16(11), :2149-2153. 10.4103/1673-5374.310672. PMID: 33818486.

Diniz, B. S. O., Volpe, F. M., & Tavares, A. R. (2007). Nível educacional e idade no desempenho no Miniexame do Estado Mental em idosos residentes na comunidade/ Educational level and age and the performance on the Mini-Mental State Examination in community-dwelling elderly. [Portuguese] *Rev Psiquiatr Clín*, 34(1), 13-17

Dintica, C. S., Rizzuto, D., Marseglia, A., Kalpouzos, G., Welmer, A. K., Wårdh, I., et al. (2018). Tooth loss is associated with accelerated cognitive decline and volumetric brain differences: a population-based study. *Neurobiol Aging*, 67,23-30

Fukushima-Nakayama, Y., Ono, T., Hayashi, M., Inoue, M., Wake, H., Ono, T., et al. (2017) Reduced Mastication Impairs Memory Function. *J Dent Res.*, 96(9), 1058-1066.

Gomes, M. S., Hugo. F. N., Hilgert, J. B., Sant'Ana Filho, M., Padilha, D. M., Simonsick, E. M., et al. (2016). Apical periodontitis and incident cardiovascular events in the Baltimore Longitudinal Study of Ageing. *Int Endod J*, 49(4), 334-42

Grubb, N. R., Elder, D., Broadhurst, P., Reoch, A., Tassie, E., & Neilson, A. (2019). Atrial fibrillation case finding in over 65 s with cardiovascular risk factors - Results of initial Scottish clinical experience. *Int J Cardiol.* 288, 94-99

Hansen, G. M., Egeberg, A., Holmstrup, P., & Hansen, P. R. (2016). Relation of Periodontitis to Risk of Cardiovascular and All-Cause Mortality (from a Danish Nationwide Cohort Study). *Am J Cardiol*, 118(4), 489-93

Holmlund, A., Holmm G, Lindm L. (2010). Number of teeth as a predictor of cardiovascular mortality in a cohort of 7,674 subjects followed for 12 years. J *Periodontol*, 81(6), 870-6

Hosadurga R., Htoo, K. S. H., Tan., P. L. A., Abdul., A., & Melvin., M. (2020). Association between tooth loss and hypertension: A cross-sectional study. *J Family Med Prim Care*, 9:925-32

Iinuma, T., Arai, Y., Abe, Y., Takayama, M., Fukumoto, M., Fukui, Y., et al. (2015). Denture wearing during sleep doubles the risk of pneumonia in the very elderly. *J Dent Res*, 94(3 Suppl), 28S-36S

Janket, S. J., Surakka, M., Jones, J. A., Lam, A., Schnell, R. A., Rose, L. M. et al. (2013). Removable dental prostheses and cardiovascular survival: a 15-year follow-up study. *J Dent*, 41(8), 740-6

Katsoulis, J., Schimmel, M., Avrampou, M., Stuck, A. E., & Mericske-Stern, R. (2012). Oral and general health status in patients treated in a dental consultation clinic of a geriatric ward in Bern, Switzerland. *Gerodontology*, 29(2), e602-10

Kiuchi, S., Kusama, T., Sugiyama, K., Yamamoto, T., Cooray, U., Yamamoto, T., Kondo, K., Osaka, K., & Aida, J. (2021). Longitudinal association between oral status and cognitive decline by fixed-effects analysis. *J Epidemiol*,. 2021 Jan 30. 10.2188/jea.JE20200476.

Koka, S., Gupta, A. (2018). Association between missing tooth count and mortality: A systematic review. *J Prosthodont Res*, 62(2), 134-151

Kuroki, A., Sugita, N., Komatsu, S., Wakasugi, M., Yokoseki, A., Yoshihara, A. et al. (2018). The number of remaining teeth as a risk indicator of cognitive impairment: A cross-sectional clinical study in Sado Island. *Clin Exp Dent Res*, 4(6), 291-296

Li, J., Xu, H., Pan, W., & Wu, B. (2017). Association between tooth loss and cognitive decline: A 13-year longitudinal study of Chinese older adults. *PLoS One*, 12(2), e0171404

Lin, C.S. (2018). Revisiting the link between cognitive decline and masticatory dysfunction. *BMC Geriatr*, 18(1), 5

Liu, W., Cao, Y., Dong, L., Zhu, Y., Wu, Y., Lv, Z. et al. (2019). Periodontal therapy for primary or secondary prevention of cardiovascular disease in people with periodontitis. *Cochrane Database Syst Rev*, 12, CD009197

Maisonneuve, P., Amar, S., & Lowenfels, A.B. (2017). Periodontal disease, edentulism, and pancreatic cancer: a meta-analysis. *Ann Oncol*, 28(5), 985-995

Nilsson, H., Berglund, J. S., & Renvert, S. (2018). Periodontitis, tooth loss and cognitive functions among older adults. *Clin Oral Investig*, 22(5), 2103-2109

Parashar, P., Parashar, A., Saraswat, N., Pani, P., Pani, N., & Joshi, S. (2018). Relationship between Respiratory and Periodontal Health in Adults: A Case-Control Study. *J Int Soc Prev Community Dent*, 8(6), 560-564

Peng, J., Song, J., Han, J., Chen, Z., Yin, X., Zhu, J., et al. (2019). The relationship between tooth loss and mortality from all causes, cardiovascular diseases, and coronary heart disease in the general population: systematic review and dose-response meta-analysis of prospective cohort studies. *Biosci Rep*, 39(1)

Peter, K. P., Mute, B. R., Doiphode, S. S., Bardapurkar, S. J., Borkar, M. S., & Raje, D. V. (2013). Association between periodontal disease and chronic obstructive pulmonary disease: a reality or just a dogma? *J Periodontol*, 84(12), 1717-23

Proietti, M., Farcomeni, A., Goethals, P., Scavee, C., Vijgen, J., Blankoff, I. et al. (2019). Cost-effectiveness and screening performance of ECG handheld machine in a population screening programme: The Belgian Heart Rhythm Week screening programme. *Eur J Prev Cardiol*, 26(9), 964-972

Scherer, R. X., & Scherer, W. J. (2020). U.S. state correlations between oral health metrics and Alzheimer's disease mortality, prevalence and subjective cognitive decline prevalence. *Sci Rep.*, 10(1), 20962. 10.1038/s41598-020-77937-8.

Silva, J. D., Ni, S. C., Lee, C., Elani, H., Ho, K., Thomas, C., Kuwajima, Y., Ishida, Y., Kobayashi, T., & Ishikawa-Nagai, S. (2021). Association between cognitive health and masticatory conditions: a descriptive study of the national database of the universal healthcare system in Japan. A*ging* (Albany NY), 19;13(6), :7943-7952. 10.18632/aging.202843. Epub 2021 Mar 19. PMID: 33739304;

Virtanen, E., Nurmi, T., Söder, P.Ö., Airila-Månsson, S., Söder, B., & Meurman, J. H., (2017). Apical periodontitis associates with cardiovascular diseases: a cross-sectional study from Sweden. *BMC Oral Health*, 17(1), 107

Yang, B., Petrick, J. L., Abnet, C. C., Graubard, B. I., Murphy, G., Weinstein, S. J., et al. (2017). Tooth loss and liver cancer incidence in a Finnish cohort. *Cancer Causes Control*, 28(8), 899-904. 10.1007/s10552-017-0906-y.