DR. MÁRCIO DINIZ-FREITAS (Orcid ID : 0000-0001-5349-1091)

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Authors: Cardoso M[1], Diniz M[2], Vázquez P[2], Cerqueiro S[3], Diz P[2], Limeres J[2],

1. Department of Dental Sciences, CESPU, Institute of Research and Advanced Training in Health Sciences and Technologies, Portugal.

2. Medical-Surgical Dentistry Research Group (OMEQUI), Health Research Institute of Santiago de Compostela (IDIS), University of Santiago de Compostela (USC), Santiago de Compostela, Spain.

3. Assisted Living for the Elderly of Oleiros, Government of Galicia (*Residencia Asistida de Mayores de Oleiros, Xunta of Galicia*), Oleiros, Spain.

Author for correspondence:

Márcio Diniz Freitas

Department of Surgery and Medical-Surgical Specialties

Faculty of Medicine and Odontology, University of Santiago de Compostela

c/ Entrerríos sn, 15782 Santiago de Compostela, Spain.

Tel: +34 881812344, Fax: +34 981562226, E-mail: marcio.diniz@usc.es

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ABSTRACT

Background

Studies on the elderly have reported that the risk of cognitive impairment is affected by chewing difficulty.

Objective

To determine whether there is a relationship between the number of pairs of antagonist teeth that come into contact when the mouth is closed (functional masticatory units [FMUs]) and the level of cognitive impairment.

Methods

We conducted a cross-sectional observational study with 502 institutionalized white individuals older than 65 years, living in the northwest of Spain and Portugal. Through a direct visual inspection, we recorded the number of FMUs. Cognitive impairment was assessed by applying the Mini-Cognitive Examination (MCE), a test derived from the Mini-Mental State Examination. To describe the statistical relationship between the FMUs and the MCE values, a generalized linear model (GLM) was applied. We assessed the GLM predictive capacity for detecting cognitive impairment (MCE ≤23) in a new study group consisting of 156 elderly individuals.

Results

A large number of FMUs was significantly associated with a lower probability of cognitive impairment, regardless of the nature of the contact and its location (explained deviance, 30.1%). The model's discriminatory capacity for cognitive impairment based on the FMUs was "good" (0.820). The model's predictive capacity for cognitive impairment was "acceptable" (sensitivity, 0.786; positive predictive value, 0.900; accuracy, 0.729).

Conclusion

In white, elderly institutionalized individuals, the absolute number of FMUs is significantly related to their MCE scores.

Keywords: Dental occlusion, Cognitive impairment, Dementia, Mini-Mental State Examination, Elderly.

INTRODUCTION

Studies conducted in countries with highly disparate sociocultural characteristics, such as South Korea, Japan, Brazil and Sweden, have reported a significant relationship between a considerable loss of teeth and poor cognitive function,[1-6] a finding confirmed in several longitudinal studies.[7-9] One of the most popular of these studies is known as the “Nun Study”, which started in 1993 and included 114 nuns between the ages of 75 and 98 years from the Notre Dame congregation (Milwaukee, WI).[7] The nuns underwent an annual cognitive examination during a 10-year follow-up period and had the shared characteristics of living in very similar conditions and being examined by the same dentist. Subsequent studies within the epidemiological framework and with larger numbers of participants, such as the Action in Diabetes and Vascular Disease: PreterAx and Diamicron MR Controlled Evaluation (ADVANCE) trial[8] and the Hispanic Established Populations for the Epidemiologic Study of the Elderly (HEPESE) study,[9] confirmed that the number of remaining teeth was an indicator of the risk for the onset of cognitive impairment and dementia.

Most of these studies assumed that the absence of teeth entails greater chewing difficulty (Table 1). Paradoxically, however, a number of authors have indicated that if the results are adjusted to the patient’s original intelligence level, the loss of teeth loses its relationship with cognitive capacity.[10] Using models adjusted by age, sex and educational level, Lexomboon et al.[2] also showed that the risk of cognitive impairment was determined by chewing difficulty and not by the loss of multiple teeth.

Studies to date have not definitively established whether the behavior of natural teeth differs from that of artificial teeth, because rehabilitation with dental prostheses also provides an increase in cerebral blood flow and prefrontal cortex activation.[11-14]

The aim of the present study was to determine whether the elderly have a significant relationship between the total number of functional masticatory units (FMUs), regardless of the location and nature of these units (natural or prosthetic teeth), and the level of cognitive impairment.

MATERIALS AND METHODS

We conducted a cross-sectional observational study with a convenience sample consisting of 542 white individuals older than 65 years, institutionalized in geriatric residences in Portugal and the northwest of Spain. The field work was performed between September 2013 and December 2015 at the following geriatric residences: “Residencia de Maiores de Santiago de Compostela”, “Residencia de Maiores del Meixoeiro” (Vigo, Spain), “Residencia O Abrigo” (Santa Maria da Feira, Portugal), “Centros de Dia da Obra Diocesana de Promoção Social” (Oporto, Portugal) and “Lar São João Deus da Santa Casa da Misericórdia” (Famalicão, Portugal). The exclusion criterion was a degree of impairment that precluded conducting an oral examination or completing a cognitive assessment test, even with the help of the responsible caregiver. We also excluded those users with a history of congenital or acquired disease that could significantly hinder the implementation of the cognitive assessment test. Applying these criteria, the definitive study group consisted of 502 white participants (389 women and 113 men) between the ages of 65 and 102 years (mean, 83.7±7.2 years).

All participants or, if necessary, their legal guardians gave their consent to participate in the study. Ethical approval for the study was provided by the Ministry of Work and Well-being of the Government of Galicia (*Consellería de Traballo e Benestar de la Xunta de Galicia*) (reference no. 2014/CP07).

We recorded the sex, age and medical history of all participants. A team of 2 dentists and an assistant performed the oral examinations with the participants seated in a conventional chair, except for those who used wheelchairs or were bedridden. The team performed the examinations through direct visual inspection (naked eye), using a portable artificial spotlight, a single-use oral examination kit (napkin, tongue depressors, gauze) and disposable nitrile gloves. For each patient, we recorded the number of pairs of antagonist teeth that came into contact when the mouth was closed, which were referred to as functional masticatory units (FMUs). In terms of the location of the FMUs, the occlusal patterns were classified as follows: unilateral, when there was contact exclusively between teeth of the first/fourth or second/third quadrants; bilateral, when there was at least 1 contact between teeth of the first/fourth and second/third quadrants; anterior, when there was contact between the incisors and/or canines but not between the teeth distal to the canine; and total, when there were 14 FMUs (as occurs in carriers of complete prostheses). We differentiated the following types of FMUs: natural/natural, as the contact between 2 natural teeth; natural/artificial, as the contact between a natural tooth and an artificial tooth, whether a fixed or removable prosthesis; and artificial/artificial, as contact between 2 teeth from 2 prostheses, fixed or removable.

The degree of cognitive impairment was assessed by previously trained staff, applying the Mini-Cognitive Examination (MCE), which was derived from the Mini-Mental State Examination (MMSE)[15] and adapted to and validated for Spain.[16] This adaptation entailed a number of changes to the original test, adding 2 new items (repetition of sentences and similarities) and increasing the total score from 30 to 35 points (MCE-35). The MCE-35 was subsequently revalidated and standardized according to age and educational level. Setting the cutoff at 22/23 has shown a sensitivity of 85.7% and a specificity of 88.9%.[17]

We performed the statistical analysis on the Biostatech company platform, using the R software environment, version 2.12.0 (R Development Core Team, Vienna, Austria). To describe the statistical relationship between the FMUs and the continuous response variable (MCE values), we applied a generalized linear model (GLM), an analysis of variance procedure in which the calculations are performed using a least squares regression approach. As a measure of discrepancy (observed data vs. fitted data), we determined the percentage of explained deviance, a generalization of the analysis of variance for the GLM obtained for a sequence of nested models.

To model the probability of cognitive impairment depending on the number of FMUs, we only included participants between the ages of 70 and 95 years to balance the number of women and men, and we applied the following logistical GLM:

$$Logit\ \{P(Dependence/Explanatory\ Variable)\} = \alpha + \beta_1\ Explanatory\ Variable + \beta_2\ Age$$

The results are expressed using the odds ratio (OR) and confidence intervals obtained from the β coefficients of the logistical model.

To assess the discriminatory capacity of the FMUs with regard to cognitive impairment (cognitive impairment vs. cognitive nonimpairment), we employed receiver operating characteristic (ROC) curves (specifically, ROC-GLM). The discriminatory capacity was established by determining the area under the curve (AUC); values greater than 0.80 were indicative of a good discriminator.

We analyzed the predictive capacity of GLM for detecting cognitive impairment (MCE ≤23) between January and May 2016 in a new study group consisting of 216 users of the Assisted Living for the Elderly of Oleiros (*Residencia Asistida de Maiores de Oleiros*). Applying the exclusion criteria described earlier, we selected 156 white participants (135 women and 21 men) between the ages of 68 and 101 years (mean age, 85.3±6.1 years). The results are expressed in terms of sensitivity, specificity, positive predictive value, negative predictive value and accuracy.

RESULTS

In the study group, 52.7% were completely edentulous, and 44.2% wore dental prostheses. The mean number of natural remaining teeth, teeth with caries, teeth with fillings and root fragments was 6.4±8.1, 1.0±2.0, 0.7±3.4 and 1.0±2.4, respectively. The mean number of FMUs in the study group was 6.3±5.9 (6.0±5.9 in the women and 7.2±5.6 in the men). Based on the location of the FMUs, the most common occlusal pattern was anterior (53.5%), followed by bilateral (39.1%) (Table 2). The most common type of FMU corresponded to artificial/artificial contact (mean, 3.1±5.3), followed by natural/natural (mean, 1.9±3.4) and natural/artificial (mean, 0.9±2.1).

The study group's mean MCE score was 19.1±10.4 points (median, 22.0). The men had significantly higher MCE scores than the women ($p<0.001$) (Table 3). Age had a significant effect on the MCE scores for both sexes but only above the age of 85 years for the women ($p<0.005$).

After including the FMU locations (occlusal patterns) and contact types in the multivariate model and adjusting for age and sex, we determined that all analyzed variables were significant, except for unilateral occlusion (the p-value for the number of natural-artificial contacts was 0.048). The percentage of explained deviance with this model was 30.2% (Table 4). After analyzing the model just for the women, the explained deviance was 32%, and the variables that lost their significance were unilateral occlusion and the number of natural-artificial contacts. For the men, the explained deviance was 29.7%, but the only significant variable was total occlusion.

A large FMU number (adjusted for age and sex) was significantly associated with high MCE scores, regardless of the nature of the contact and its location (explained deviance, 30.1%; $p<0.005$).

The MCE scores for 271 (52.5%) participants did not exceed 23 points; these patients were therefore diagnosed with cognitive impairment and had a mean of 3.7±5.3 FMUs. Among the 231 participants with MCE scores >23 points, the mean number of FMUs was 9.4±5.5. In the logistic model corresponding to the FMUs variable and after adjusting for age, the percentage of explained deviance was 26% ($p<0.001$; OR, 0.833; 97.5% CI 0.793-0.892). The OR corresponding to the explanatory variable was less than 1, which means that the greater the number of FMUs, the lower the occurrence of the event (cognitive impairment) and can therefore be considered a protection factor. The probability of cognitive impairment (MCE score ≤23 points), estimated based on an age-adjusted logistical model, was 25% for patients with 10 FMUs, 50% for those with 5 FMUs and 75% for those with 2 FMUs.

After analyzing the ROC-GLM curves obtained with the logistic model described earlier, "good" AUC values (0.820) were achieved for the study group. The model's predictive capacity based on the number of FMUs for the diagnosis of cognitive impairment can be considered highly appropriate, because the sensitivity was 0.735, the positive predictive value was 0.894, and the accuracy was 0.729 (CI 0.612-0.823).

DISCUSSION

In this study, we showed that individuals older than 65 years had a positive association between the number of FMUs and the MCE scores. The number of FMUs represents a protective factor (the more the occlusal contacts, the higher the MCE scores) and has a predictive capacity for identifying individuals with cognitive impairment. This study's most outstanding characteristics are that it is one of the few studies of this type to date performed with white participants, and it is the first to quantitatively assess all FMUs regardless of their location (anterior or posterior) and nature (natural or prosthetic). In addition, the study assessed cognitive impairment by applying a version of the MMSE culturally adapted to the countries in which the study was conducted (Spain and Portugal).

However, the present study is not exempt from a number of methodological limitations. The clear predominance of women in our study is consistent with other previous studies.[18,19] Oral examination by direct viewing is a slightly crude procedure, but it is a fast, noninvasive and easy method, even for less cooperative patients for whom other systems for measuring chewing capacity are not applicable (such as intermaxillary recording, digital intraoral scanning and even chewing gum).[20] The reliability of MCE is debatable for individuals with moderate to severe levels of disability or with difficulties reading and writing.[21] Lastly, we did not record a number of factors that could play a relevant role in cognitive impairment, such as socio-economic level[22] and malnutrition.[23]

Assuming that the preservation of a greater number of teeth entails greater chewing efficacy[24] and that this condition represents a protective factor for cognitive impairment,[9] we can expect that the number of FMUs is as important (or more so) than the number of teeth. Although specific references regarding this issue are scare, a recently published systematic review concluded that elderly individuals have a positive association between chewing and cognitive function, including dementia.[25] Moriya et al.[26] conducted a study with a group of 208 individuals between the ages of 70 to 74 years, applying a series of neuropsychological tests and classifying the patients into 3 categories based on their chewing ability: able to chew all types of food, able to chew only up to semi-hard food and only able to chew soft food. The authors' most relevant result was that chewing ability was significantly associated with better brain function. Recently, Kim et al.[27] published a study in which they determined, among other variables, the patients' chewing efficacy (using chewing gum that changed color with active chewing) and cognitive impairment (using the MMSE). The study was conducted with a group of 295 South Koreans between the ages of 70 and 102 years who lived in rural settings. The authors concluded that a poor chewing ability was significantly associated with cognitive impairment and dementia. The design of the present study partially reproduces that of a study published by Takeuchi et al. in 2015,[23] who studied the relationship between the number of FMUs and cognitive function (measured with the MMSE) in 279 residents of a geriatric center in the Japanese city of Aso. The most substantial methodological differences between this study and our study were that the participants were of Asian origin and that only posterior FMUs were quantified (corresponding to premolars and molars). After adjusting for various covariates, the authors concluded that the participants with a greater number of FMUs achieved higher MMSE scores (results similar to ours), suggesting that loss of occlusion in the posterior sectors constitutes an independent factor of cognitive impairment.

In terms of biological plausibility, a possible relationship has been suggested in murine models between chewing restriction and loss of hippocampal neurons, which could represent a risk factor for the senile deterioration of spatial memory[28,29] and the ability to recognize new objects.[30] By applying sophisticated imaging techniques to healthy volunteers, studies have shown that chewing increases blood flow in the oral region of the sensorimotor cortex, the supplemental motor areas, insula, corpus striatum and cerebellum.[31,32] The activation of these brain areas implies that chewing could speed or recover the working memory process and improve the level of attention.[33] A study recently indicated that a number of chronic inflammatory diseases such as periodontitis could participate in the etiopathogenesis of edentulism and cognitive impairment and could even affect an individual's longevity.[34] A study with murine models also showed that the consequences at the brain level of losing molars is accentuated as this condition continues over time and that, conversely, the consequences significantly attenuate when restoring the lost molars with artificial crowns.[35] This finding could justify the results of various studies that concluded that cognitive impairment in the elderly increases when they are edentulous and do not use dental prostheses.[35,36] We therefore decided for our study to quantify the FMUs in absolute numbers, regardless of whether they consisted of natural or artificial teeth.

In terms of the model's predictive capacity to detect individuals with cognitive impairment (MCE scores ≤23) based on the number of FMUs, the explained deviance was greater in the men than in the women. Along these lines, Paganini-Hill et al.[36] analyzed data extracted from the Leisure World Cohort Study, conducted with a retirement community established in California at the start of the 1980s. Most of the study participants were middle-class white retirees, with a good educational level. The authors concluded that the men who had inadequate chewing function (<10 natural maxillary teeth or <6 mandibular teeth) and who did not wear dental prostheses had a 91% greater probability of dementia than those who preserved adequate oral functionality. Among the women with poor chewing activity, this risk was also greater but did not achieve statistical significance.

One of the most common criticisms of this type of study is the unidirectional causality, because if we reverse the order of the explanatory variables, it could be speculated that the individuals with an established diagnosis of cognitive impairment would have a greater likelihood of losing teeth and consequently a lower number of FMUs. Chalmers et al.[37] conducted a longitudinal study in Australia with 116 elderly patients with dementia and 116 patients without dementia (based on MMSE scores) and found that the number of teeth lost in a year was similar in the 2 groups. However, the group with dementia had more root fragments, which presumably indicated fewer FMUs. Miura et al.[38] analyzed the relationship between cognitive function and chewing in a group of 88 Japanese women older than 65 years, 44 with dementia and 44 without dementia. The authors concluded that the maximum bite strength, the occlusal contact area and the chewing scale values were significantly greater in those who had no cognitive impairment. In the present study, the explained deviance decreased significantly when inverting the order of the dependent and independent variables, which seems to indicate that the FMUs represent the explanatory variable, while MCE is the explained variable. However, this statement is not definitive and can only be confirmed with a prospective study.

In conclusion, this study shows that for white elderly institutionalized individuals, the absolute number of FMUs, regardless of their nature and location, is significantly related to the MCE scores.

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Table 1. Most relevant studies that related the number of natural remaining teeth to cognitive impairment in elderly individuals

First author Country (reference)	**Sample (age in years)**	**Study design**	**Dental variable**	**Measurement of cognitive impairment**	**Primary endpoint**
Kim JM et al. South Korea[1]	686 (≥65)	Prospective (2.4±0.3 years)	Number of natural teeth	MMSE CSID CDR HAS-DDS	Having fewer teeth could be a marker for the risk of dementia
Lexomboon D et al. Sweden[2]	557 (≥77)	Cross-sectional	Self-assessment of the dental state and difficulty chewing	MMSE	There is an association between the ability to chew and cognitive impairment
Miranda LP et al. Brazil[3]	218 (≥60)	Cross-sectional	Clinical dental examination	MMSE	There is an association between MMSE scores and edentulism and the use of prosthesis
Okamoto N et al. Japan[4]	4031 (≥65)	Cross-sectional	Number of natural teeth and duration of the edentulous period	MMSE	There is a significant association between tooth loss and cognitive function
Park H et al. South Korea[5]	438 (>50)	Cross-sectional	Number of natural teeth	MMSE	The number of teeth lost is correlated with cognitive impairment
Saito Y et al. Japan[6]	462 (≥60)	Cross-sectional	Number of natural teeth	MMSE	There is a relationship between tooth loss and cognitive function
Stein PS et al. USA[7]	144 nuns (75-98)	Prospective (10 years)	Clinical dental examination	MMSE	Tooth loss is associated with an increased risk of dementia
Batty GD et al. 20 countries[8]	11,140 diabetics (55-88)	Prospective (5 years)	Self-assessment of the number of teeth and gingival bleeding	MMSE	Tooth loss is associated with an increased risk of dementia and cognitive impairment
Reyes-Ortiz CA et al. USA[9]	3032 Mexican-Americans (≥65)	Prospective (5 years)	Number of natural teeth	MMSE DWRT BNT Others	Having fewer teeth over time is associated with greater cognitive impairment

MMSE, Mini-Mental State Examination; CSID, Community Screening Interview for Dementia; CDR, Clinical Dementia Rating; HAS-DDS, History and Aetiology Schedule - Dementia Diagnosis and Subtype; DWRT, Delayed Word Recall Test; BNT, Boston Naming Test; Others, the verbal fluency test and constructional praxis test.

Table 2. Study group distribution (n=542) according to dental status (presence of natural teeth, edentulism and prosthesis carriers) and occlusal patterns, as well as the corresponding number of functional masticatory units

Variable	**Both sexes** (n= 542)	**Female** (n= 412)	**Male** (n= 130)	**FMUs** **Both sexes** (m ± sd)
Patients with natural teeth	256 (47.2%)	219 (53.1%)	37 (28.4%)	6.7 ± 5.1
Patients with natural teeth without prostheses	179 (33.0%)	157 (38.1%)	22 (16.9%)	4.0 ± 2.9
Patients with natural teeth carriers of prostheses	77 (14.2%)	62 (15.0%)	15 (11.5%)	12.9 ± 2.7
Totally edentulous patients	286 (52.7%)	193 (46.8%)	93 (71.5%)	7.9 ± 6.4
Totally edentulous patients without prostheses	123 (22.6%)	73 (17.7%)	50 (38.4%)	0 ± 0
Totally edentulous patients carriers of prostheses	163 (30.0%)	120 (29.1%)	43 (33.0%)	14 ± 0
Carriers of prostheses*	240 (44.2%)	182 (44.1%)	58 (44.6%)	9.9 ± 5.0
Carriers of fixed prostheses	41 (6.4%)	21 (5.0%)	14 (10.7%)	9.0 ± 4.7
Carriers of removable prostheses	204 (36.9%)	157 (38.1%)	43 (33.0%)	10.2 ± 5.0
Anterior occlusion	290 (53.5%)	206 (50.0%)	84 (64.6%)	10.4 ± 3.9
Unilateral occlusion	59 (10.8%)	39 (9.4%)	20 (15.3%)	5.4 ± 3.1
Bilateral occlusion	212 (39.1%)	151 (36.6%)	61 (46.9%)	12.2 ± 2.4
Total occlusion	163 (30.0%)	120 (29.1%)	43 (33.0%)	13.4 ± 1.0

FMUs, functional masticatory units; (m ± sd), (mean ± standard deviation); * 5 patients were carriers of fixed and removable prostheses; Anterior, Unilateral, Bilateral and Total occlusion are explained in the Materials and Methods section.

Table 3. Mini-Cognitive Examination scores in the study group (n= 542) according to sex, age, number and nature of the functional masticatory units and occlusal patterns

	Mean	Standard deviation	Median	Range
Sex				
Female	17.9	10.4	18.0	35
Male	23.0	9.7	26.0	35
Age, years				
65-74	24.3	8.8	26.5	35
75-84	20.5	10.0	24.0	35
85-94	15.9	11.0	17.0	35
95-102	9.9	8.4	11.0	34
Number of FMUs				
FMUs= 0	12.8	9.6	12.2	35
FMUs≥ 1	21.8	8.8	24.3	35
Natural/natural contact				
FMUs= 0	16.8	9.9	18.0	35
FMUs≥ 1	21.5	9.8	25.0	35
Natural/artificial contact				
FMUs= 0	16.7	10.0	18.0	35
FMUs≥ 1	23.7	8.3	26.0	35
Artificial/artificial contact				
FMUs= 0	16.2	10.4	17.0	35
FMUs≥ 1	22.9	7.7	25.0	35
Anterior occlusion	22.0	8.8	25.0	35
Unilateral occlusion	19.4	9.0	20.0	33
Bilateral occlusion	23.6	8.0	26.0	35
Total occlusion	15.8	10.2	17.0	35

FMUs, functional masticatory units; Anterior, Unilateral, Bilateral and Total occlusion are explained in the Materials and Methods section; Natural, remaining natural tooth; Artificial; prosthesis tooth.

Table 4. Generalized linear model adjusted for age and sex, which relates the locations (occlusal patterns) of the functional masticatory units and their types to the Mini-Cognitive Examination scores

	Estimate	Standard error	T value	p-value
(Intercept)	12.830	0.752	17.040	<0.001
Unilateral occlusion	2.259	1.528	1.478	0.140
Bilateral occlusion	4.199	1.262	3.325	<0.005
Total occlusion	3.201	1.142	2.801	<0.001
Natural/natural contact	0.444	0.148	2.988	<0.005
Natural/artificial contact	0.435	0.220	1.975	<0.050
Artificial/artificial contact	0.605	0.080	7.505	<0.001
Sex (male)	3.318	0.995	3.334	<0.001

Unilateral, Bilateral and Total occlusion, are explained in the Materials and Methods section; Natural, remaining natural tooth; Artificial, prosthesis tooth