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Periodontitis, tooth loss and cognitive functions among older adults

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Abstract

Objectives: This study aims to evaluate the potential association between periodontitis, the number of teeth and cognitive functions in a cohort of older adults in Sweden.

Material and methods: In total, 775 individuals from 60 to 99 years of age were selected for the study. A clinical and radiographic examination was performed. The number of teeth and prevalence of periodontal pockets and bone loss was calculated and categorised. Cognitive functions were assessed using The Mini-Mental State Examination, (MMSE) and Clock-test. The education level was obtained from a questionnaire.

Data were analysed using Chi-square tests and multivariate logistic regression.

Results: Age and gender were associated with the prevalence of bone loss. Age and education were associated with lower number of teeth. Gender was also associated with the presence of pockets. The multivariate logistic regression analysis demonstrated a statistically significant association between prevalence of bone loss, the number of teeth and the outcome on MMSE test. This association remained even after adjustment for age, education and gender. Tooth loss was also associated with lower outcome on Clock test. Presence of periodontal pockets ≥ 5 mm was not associated with cognitive test outcome.

Conclusions: A history of periodontitis and tooth loss may be of importance for cognitive functions among older adults.

Clinical relevance: Diseases with and inflammatory profile may have an impact on cognitive decline

Introduction

As a consequence of the demographic transitions, leading to an increasing proportion of elderly, the prevalence of cognitive impairment and dementia tend to increase [1]. Mild cognitive impairment (MCI) is defined as cognitive decline, greater than expected for age and education level but which does not interfere notably with the activities of daily life [2].

Individuals with mild cognitive impairment have an increased risk of later in life developing dementia [2]. Various forms of tests have been used to screen for cognitive impairment and dementia. It has been demonstrated that Mini-Mental-State Examination (MMSE) and Clock-

test may predict development of Alzheimer's disease (AD) as accurate as cerebrospinal fluid biomarkers [3].

Impaired cognitive functions and dementia have been associated with oral health parameters in cross-sectional studies [4-6]. Epidemiological studies have reported that individuals with serum markers of peripheral systemic inflammation are at higher risk of developing dementia [7, 8].

Periodontitis is an inflammatory driven disease, initiated by a bacterial biofilm, resulting in pocket formation, loss of alveolar bone and eventually tooth loss. The severe form is the sixth-most prevalent disease in the world with a prevalence of 11,2% [9]. Periodontitis may contribute to a low-grade systemic inflammation and has in numerous studies been associated with systemic diseases with an inflammatory profile such as diabetes, cardiovascular diseases and recently also to cognitive impairment and dementia [6, 10-12].

Regarding the association between mild cognitive impairment (MCI) and clinically diagnosed periodontal disease, Linden et al. (2013) stated that the evidence from currently published studies for an association between periodontitis and MCI is weak [13]. Also in a more recent systematic overview, Wu and coworkers (2016) concluded that it is still unclear how and whether oral health and cognitive status are related since many studies are underpowered or based on self-reported registrations [14]. Acknowledging the continued lack of knowledge within this field our objective of the present study was to further investigate the potential association between cognitive functions and periodontal parameters and tooth loss in a cohort of older adults.

Material and methods

This cross-sectional study was conducted in Karlskrona community, Blekinge, Sweden. The participants were enrolled in a population-based longitudinal multicenter cohort study, Swedish National Study on Ageing and Care (SNAC). Aiming to represent the elderly population in Sweden a random selection was made in 2001-2003 from the Swedish civil registration database in the age cohorts, 60,66,72,78. Among the oldest, in the age cohorts of 81,84,87 (and older) all individuals in the community were invited.

A more detailed description of the study design and structure has been outlined by Lagergren et al. [15]. The individuals included in the present study were all examined during 2007-2009. This cohort consisted of 840 individuals from the baseline study group (2001-2003) invited for a 6-year follow-up. Of the total baseline sample (1402) 452 individuals had died. Of the remaining 950, 110 (11,6%) refused further participation. According to the study design, new cohorts of 60 and 81-year-olds were invited in the same geographic area and according to the same randomization principles as the baseline group. In total 278 accepted with an acceptance rate of 70%.

The participants were invited by mail to take part in a medical, psychological and dental examination performed in a research clinic by professionals specially trained for the purpose. All participants gave their signed informed consent. The Research Ethics Committee at Lund University approved the study (LU 604-00, LU 744-00).

In the present study, grouping according to age was performed. Individuals in age groups 60 and 66 years were allocated to the young age cohort and individuals in age groups 72 and 78 years to the old age cohort and individuals 81 years and older to the old-old age cohort.

Dental examination

All individuals were subjected to a comprehensive clinical and radiographic examination by an experienced dental hygienist. The clinical examination included registration of number of teeth, including erupted third molars and dental implants. Probing pocket depth (PD) was assessed from the gingival margin to the base of the pocket at four sites at all existing teeth using a periodontal probe (CP-12 probes, HU Friedy Inc.Chicago, IL, USA). The deepest PD at each tooth was used to calculate the proportion of teeth with pockets ≥ 5 mm for each individual. Panoramic radiographs were taken using an orthopantomograph (Instrumentarium Dental, OP 100; Tuusula, Finland) with a standard exposure of 75kV/10 mA. The extent of alveolar bone loss was evaluated at the mesial and distal aspect of each tooth using a millimeter graded transparent ruler, and 2x magnification viewer and a light box. The number of readable interproximal sites was used to calculate the proportion of sites with distance from

the cement-enamel junction (CEJ) to the alveolar bone level exceeding 4 and 5 mm respectively. An experienced independent examiner masked to age, gender, dental and medical information performed all the radiographic measurements. Reliability analyses were done for the double readings of the X-rays during the baseline examinations. The ICC correlation coefficient for the distance between the apex and CEJ was 0.93 (95% CI= 0.91-0.96, $p < 0.01$), based on a total of 91 observations, with a mean difference of 0.94 mm (SD $\pm$ 1.3). Intra-class correlation (ICC) analysis result between randomly selected cases for double assessments regarding the reproducibility of bone level ≥ 5 mm between the first and second reading of 110 randomly selected panoramic radiographs and analysed by one and the same examiner was 0.87 (95 % CI 0.81, 0.91; $p < 0.001$). According to the purpose of this study only dentate individuals were included in the present study.

Education

The level of education was captured from questionnaires and categorised according to final school grade, elementary (≤ 9 years) or higher education (>9 years).

Cognitive tests

Mini-mental State Examination (MMSE) and Clock-test were used to evaluate cognitive functions.

MMSE

MMSE, consists of 20 items and the total sum of the test scores are maximum 30 (worst to best) [16]. In this study a cut-off level < 25 were adopted, and a sub-analysis were done between individuals in the group having 25-27 points compared to the group having 28-30 points.

Clock-test

The participants were asked to draw an analogue clock-face in a pre-drawn circle and put the numbers in the correct position and the arms indicating "ten past eleven" [17]. The sum can result in a total score of 10, and in this study, a cut-off value of <8 was set for lower cognitive test outcome [18].

Statistical methods

A statistical software program (IBM SPSS version 22.0, IBM Statistics, Amarak, NY) was used for the analysis. Descriptive statistics were used to present the population. A Chi-square test for independence was performed to evaluate potential associations between the candidate explanatory covariables; age, education, gender and the periodontal variables (degree of bone loss and presence of periodontal pockets) and number of teeth. In the statistical analysis bone-loss was defined as having ≥ 4 mm distance from CEJ to marginal bone level on $\geq 30\%$ of readable site. Periodontal pockets were categorised into having $\geq 30\%$ of teeth with pockets ≥ 5 mm and number of teeth present were divided into 1-19 versus ≥ 20 . The impact of the covariables on the likelihood of having lower cognitive test outcome was analysed first by univariate logistic regression and after that with adjustment for the covariables with multivariate logistic regression. Odds ratio (OR), 95% confidence interval (CI) and p-values were calculated; p-values <0.05 were regarded as statistically significant.

Results

The total sample consisted of 1118 individuals (56% women). Data on dental status lacked in 170 individuals, and 102 were edentulous. Additionally, 39 participants had not completed MMSE, and 32 lacked information about education level. Thus the final results are based on 775 individuals (55% women). Age distribution in the different cohorts were; 43% in the young old cohort (60,66), 32% in the old cohort (72,78 years) and 25% in the oldold cohort (≥ 81 years). Level of education were equally distributed in the study population (51% lower, ≤ 9 years and 49% higher (>9 years)). Descriptive characteristics are presented in Table 1.. In 585 individuals panoramic radiographs were available for analysis of alveolar bone loss in which 115 had findings of bone loss ≥ 4 mm at $\geq 30\%$ of readable sites. In eight individuals only

radiographs were available and no clinical examination. High age and male gender were significantly associated to bone-loss ($p<0.01$) and ($p<0.001$) respectively. Having between 1-19 teeth ($n=249$) was associated with high age and lower education ($p<0.001$). Individuals with many teeth also had many teeth with periodontal pockets $\geq 5\text{mm}$ (Pearson 0.167, $p=0.01$). When periodontal disease was defined as having presence of periodontal pockets $\geq 5\text{mm}$ at $\geq 30\%$ of the teeth, 6.4% of the individuals fulfilled this criteria and this was more common among males, ($p=0.01$).

A MMSE-score below 25 was evident in 64 individuals and additionally 167 had MMSE-score 25-27. Regarding Clock-test, 136 individuals scored < 8 .

Results from the multivariate logistic regression analysis when age, gender and education are entered into the model are presented in Table 2-3. The results demonstrate that bone loss, $\geq 4\text{mm}$ at $\geq 30\%$ of readable sites, was associated with cognitive test outcome (MMSE < 25) after adjustments, (OR 2.7; $p = 0.013$) (Table 2). The association persisted after exclusion of individuals with the lowest cognitive test outcomes < 25 , comparing the group with an MMSE score of 25-27 to those with an MMSE ≥ 28 , (OR; 1.7 $p=0.05$) (Table 3). The corresponding results for having between 1 and 19 teeth were OR 2.0 ($p=0.03$) for MMSE < 25 (Table 2) and OR 1.9 ($p=0.002$) for MMSE 25-27 compared to individuals with MMSE-score ≥ 28 (Table 3). Having between 1 and 19 teeth also influenced the risk for lower cognitive test-outcome using the Clock-test, although this was not significant in the final model.

None of the periodontal variables were significantly associated with the outcome of the Clock test. Dental implants were uncommon and therefore no subanalysis was done.

Discussion

This study evaluated the association between tooth loss, periodontal bone loss or presence of periodontal pockets and MMSE and Clock-test in a cohort of older adults living in Sweden. Our main finding was that individuals with a bone loss of $\geq 4\text{mm}$ at $\geq 30\%$ of the readable sites had a higher OR for lower test outcome on MMSE. This association remained if periodontal disease was defined as individuals with a bone loss of $\geq 5\text{mm}$ at $\geq 30\%$ of readable sites, OR 2.8 (p-value 0.06) and OR 1.9 (p-value 0.1) respectively. With a higher threshold for

periodontal bone loss the number of individuals fulfilling the criteria declined. This may have affected the statistical model, leading to non-significant results.

The results of the present study are mainly in agreement with a recent case-control study where attachment level loss (AL) was significantly associated with cognitive impairment after adjusting for confounders such as age, gender, educational attainment and hyperlipidemia [6]. In that study, similar periodontal conditions were observed in both early (mild cognitive impairment) and late (severe dementia) stages of the disease. The authors, therefore, suggest that the cause may precede the effect. This observation is in line with our results as the prevalence of bone loss also impacts an assumptive early decline in cognitive function. However, no conclusions regarding causality can be drawn with this study design.

Clinical attachment loss and loss of alveolar bone evidenced on radiographs reflect a history of periodontitis. It is unlikely that a change in oral health behaviour in a later phase of dementia is the primary cause of bone level changes that often takes years to develop.

Among elderly, periodontal disease is one of the major risk factors for tooth loss. In a previous publication, we found that number of teeth was associated with cognitive functions [4]. An interesting finding in this study is that the associations between lower number of teeth and cognitive outcome persisted also after exclusion of the edentulous group.

Periodontal disease can result in a systemic pro-inflammatory burden and elevation of pro-inflammatory markers [12]. Neurodegenerative diseases have in various ways been associated with systemic inflammation although the mechanisms are not entirely clarified [19, 20].

Increased risk for AD has also been associated with polymorphisms in pro-inflammatory genes [21, 22]. Another association to systemic inflammation is the reduced risk of dementia in individuals treated with nonsteroidal anti-inflammatory drugs (NSAID) seen in several epidemiological studies [23]. Infections with various forms of bacteria can also influence cognitive functions, and in a recent case-cohort study an association between serological markers of periodontal disease and incident AD were identified [24].

In clinical practice, MMSE and Clock-test are used as screening tools for cognitive functions, but the cognitive abilities they intend to measure are probably different in some perspectives [25]. Memory deficits, in particular, loss of memory events (episodic memory) are affected

early in Alzheimer disease and therefore considered a hallmark [26]. Verbal abilities, semantic memory are also affected [27]. The MMSE, includes parts were memory capacity are evaluated, and that may be a reason explaining the differences in results between the tests in this population.

In the present study both clinical and radiographic outcomes were obtained and evaluated in a substantial sample of elderly individuals. Having periodontitis defined by presence of periodontal pockets $\geq 5\text{mm}$ at $\geq 30\%$ of the teeth was not significant associated to any of the cognitive tests used. Deep probing depth at teeth as a definition for periodontitis may in an elderly population underestimate the prevalence of periodontitis [28] and in this sample, only a small percentage of the individuals was categorised as periodontitis patients based solely on probing depths which has an impact in the statistical analysis. Comparable studies regarding periodontitis defined by proportion of teeth with pockets among older adults are scarce. The prevalence is most likely influenced by a number of factors such as tooth loss and gingival recessions [29]. In this study participants with many teeth also had many teeth with pockets. Loss of alveolar bone as a result of longstanding inflammation in the periodontal tissues may therefore in a better way describe the periodontal disease in the elderly population.

A methodological shortcoming in the present study could be that bone loss was evaluated on panoramic x-rays. A risk with this type of x-ray is that distortion, especially in certain areas makes it difficult to define the bone level. This could be the case in the front area where periodontal bone-loss is rather common, resulting in an underestimation of the prevalence of bone-loss [30, 31]. As the association between cognitive tests and periodontal bone loss persisted when the 5 mm cut-off point was used it is unlikely that the use of panoramic radiographs influenced the main results of the study. It should also be noticed that individuals without dental examination (170) were older. This group also demonstrated lower values on the cognitive tests. Accordingly, it may be anticipated that individuals with more severe cognitive and physical disabilities were not included in the final analysis. Since systemic inflammation is considered a risk factor for the development of dementia, a longitudinal study to further explore whether periodontitis is a risk indicator for the development of cognitive impairment and dementia is warranted.

Conclusions

Adjusted for age, gender and level of education, a statistically significant association between loss of alveolar bone, the number of teeth and the outcome of the MMSE test was confirmed. Oral health parameters may be of importance for decline in cognitive functions among older adults.

Compliance with ethical standards

Conflict of interest: Helena Nilsson declares that she has no conflict of interest. Johan Sanmartin Berglund declares that he has no conflict of interest. Stefan Renvert declares that he has no conflict of interest.

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Ethical approval: all procedures performed in the study were in accordance with the ethical standards of the regional research ethics committee and with the 1964 Helsinki declaration and its later amendments.

Informed consent was obtained from all individual participants included in the study.

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Table 1.
Descriptive characteristics of the study population (n=775)

Age cohort	
Young old 60,66 years n (%)	330 (43)
Old 72,78 years n (%)	247 (32)
Oldold ≥81 years n (%)	198 (25)
Gender	
Male n (%)	351 (45)
Education	
Higher > 9 years n (%)	382 (49)
MMSE <25 n (%)	64 (8)
MMSE 25-27 (n=711)	
n (%)	167 (23)
Clock-test (n=770)	
<8 n (%)	136 (18)
Bone-level category (n=585)	
≥4mm ≥ 30 %	
of sites, n (%)	115 (20)

Bone-level category (n=585)	
≥5mm ≥ 30 % of sites, n (%)	37(6)
Number of teeth (n=767)	
Mean ± SD	21.3 ± 7
Median	23
Category	
20-32 n (%)	518 (67.5)
1-19 n (%)	249 (32.5)
Prevalence of pockets (n=751)	
≥5mm on ≥ 30% of teeth n (%)	50 (6.7)

MMSE=Mini-Mental State Examination.

Table 2

Uni- and multivariate logistic regression for the cognitive test outcome MMSE < 25 and number of teeth and prevalence of bone loss respectively, adjustments for age, gender and education.

	Without adjustments OR(95%CI) n= 767	p-value	With adjustments OR(95%CI) n= 767	p-value		Without adjustments OR(95%CI) n=585	p-value	With adjustments OR(95%CI) n=585	p-value
<i>Age</i>									
60,66	Ref.		Ref.			Ref.		Ref.	
72,78	2.1(0.8-5.1)	0.1	1.5(0.6-3.9)	0.4		1.4(0.4-4.3)	0.6	1.2 (0.4-4.0)	0.7

≥81	11.5 (5.3-25.1)	<0.001	7.5 (3.2-17.4)	<0.001	9.0 (3.5-23.2)	<0.001	7.2 (2.9-20.2)	<0.001
Gender								
Female	Ref.		Ref.		Ref.		Ref.	
Male	0.9(0.6-1.6)	0.8	0.9(0.5-1.7)	0.9	2.1(1-4.4)	0.06	1.8(0.8-4.1)	0.14
Education								
Higher	Ref.		Ref.		Ref.		Ref.	
Elementary	2.1(1.2-3.6)	0.07	1.5(0.8-2.7)	0.2	1.7(0.8-3.6)	0.15	1.6(0.7-3.4)	0.3
Number of teeth					Bonelevel category			
20-32	Ref.		Ref.		Category* 0	Ref.	Ref.	
1-19	4.2(2.5-7.2)	<0.001	2.0(1.1-3.6)	0.03	Category* 1	3.7(1.8-7.7)	0.001	2.7(1.2-5.9) 0.013

* Category 0=not fulfilling category 1

Category 1= $\geq$ 4mm distance from cementoenamel junction (CEJ) to marginal bone level on $\geq$ 30% of readable sites

Table 3

Uni- and multivariate logistic regression for the cognitive test outcome MMSE 25-27 compared to 28-30 and number of teeth and prevalence of bone loss respectively, adjustments for age, gender and education.

	Without adjustments OR(95%CI) n=703	p-value	With adjustments OR(95%CI) n=703	p-value		Without adjustments OR(95%CI) n=554	p-value	With adjustments OR(95%CI) n=554	p-value
Age									
60,66	Ref.		Ref.			Ref.		Ref.	

72,78	2.3(1.5-3.7)	<0.001	1.8(1.1-2.9)	0.01	2.1(1.3-3.5)	<0.01	1.9(1.1-3.2)	0.01
≥81	5.8(3.6-9.2)	<0.001	4.0(2.4-6.6)	<0.001	5.4(3.1-9.4)	<0.001	5(2.9-8.7)	<0.001
Gender								
Female	Ref.		Ref.		Ref.		Ref.	
Male	1(0.7-1.4)	0.9	1.0(0.7-1.5)	0.8	0.9(0.6-1.3)	0.6	0.9(0.5-1.3)	0.5
Education								
Higher	Ref.		Ref.		Ref.		Ref.	
Elementary	2(1.4-2.8)	<0.001	1.5(1.0-2.2)	0.03	1.6(1.1-2.4)	0.02	1.3(0.8-2.1)	0.2
Number of teeth					Bonelevel category			
20-32	Ref.		Ref.		Category* 0	Ref.	Ref.	
1-19	3.3(2.3-4.7)	<0.001	1.9(1.3-2.9)	0.002	Category*1	1.8(1.1-3.0)	0.015	1.7(1.0-2.8) 0.05

* Category 0=not fulfilling category 1

Category 1= $\geq$ 4mm distance from cementoenamel junction (CEJ) to marginal bone level on $\geq$ 30% of readable sites