Original Article
Yonsei Med J 2022 Aug;63(8):783-789
https://doi.org/10.3349/ymj.2022.63.8.783
Yonsei Medical Journal
YMJ
pISSN: 0513-5796 · eISSN: 1976-2437

The Impact of Masticatory Function on Cognitive Impairment in Older Patients: A Population-Based Matched Case-Control Study

Kyung-A Ko[1,2*], Jin-Young Park[1,2*], Jung-Seok Lee[1,2], Byoung Seok Ye[3], Ui-Won Jung[1], Seong-Ho Choi[1,2], and Jae-Kook Cha[1,2]

[1]Department of Periodontology, Research Institute of Periodontal Regeneration, Yonsei University College of Dentistry, Seoul;
[2]Innovation Research and Support Center for Dental Science, Yonsei University Dental Hospital, Seoul;
[3]Department of Neurology, Yonsei University College of Medicine, Seoul, Korea.

Purpose: The aim of this study was to investigate the association between the changes in masticatory function and cognitive impairment by analyzing longitudinal data of older Korean patients.

Materials and Methods: Patients aged over 60 years with dental records between 2005 to 2010 (baseline; T1) and 2014 to 2020 (follow-up; T2) were selected in a single medical center. Based on the dementia diagnosis after T2, the cohort was classified into two groups, the dementia group (n=122) and the control group (n=366). Changes in masticatory function were calculated using the total functional tooth unit (T-FTU) in both groups. The incidence of tooth extraction (%) and the subsequent rehabilitation during the observation period were also evaluated.

Results: In the dementia group, T-FTU significantly decreased from T1 to T2 (9.81±2.78 to 9.11±3.16, respectively, p=0.008), while no significant change was observed in the control group. During the mean observation period of 9 years, significantly more teeth were extracted and neglected to be prosthetically restored in the dementia group than in the control group. Regression analysis revealed that the number of missing teeth neglected [odds ratio (OR)=1.195, 95% confidence interval (CI)=1.025–1.393, p=0.023] and previous alcohol consumption (OR=4.445, 95% CI=1.831–1.795, p=0.001) were the most significant risk factors of dementia.

Conclusion: There might be a causative relationship between the neglected missing dentition and the onset of dementia.

Key Words: Masticatory function, tooth loss, oral health, cognitive impairment, dementia

INTRODUCTION

Dementia is a complex clinical syndrome encompassing a wide range of neuropsychiatric medical conditions that cause gradual impairment of brain functions and cognitive impairment in older people.[1,2] Large number of studies have reported potential risk factors of dementia, such as less education, hypertension, hearing impairment, smoking, obesity, depression, physical inactivity, diabetes, and low social contact.[3,4]

Recently, increased research attention has been devoted to the relationship between tooth loss and cognitive impairment,[5] and tooth loss has been regarded as a possible risk factor of dementia. It has also been described that the reduction of masticatory function due to tooth loss might negatively influence learning and memory.[6,7] Another prospective study showed that fewer the remaining natural teeth, higher the incidence of dementia.[8,9] A retrospective study on an elderly population has shown that those with greater number of extracted teeth exhibited a significantly higher risk of dementia,[10] and that complete edentulism might be one of the contributing sources to the onset and progression of dementia.

Received: April 27, 2022 **Revised:** May 24, 2022
Accepted: May 26, 2022
Corresponding author: Jae-Kook Cha, DDS, PhD, Department of Periodontology, Research Institute for Periodontal Regeneration, Yonsei University College of Dentistry, 50-1 Yonsei-ro, Seodaemun-gu, Seoul 03722, Korea.
Tel: 82-2-2228-3191, Fax: 82-2-392-0398, E-mail: chajaekook@yuhs.ac

*Kyung-A Ko and Jin-Young Park contributed equally to this work.
•The authors have no potential conflicts of interest to disclose.

Several potential mechanisms have been proposed to explain the relationship between tooth loss and cognitive impairment.[11] A preceding review suggested three mechanisms of concern: 1) impaired chewing ability due to tooth loss leads to reduced nutritional status; 2) "incremental tooth loss" causes progressively fewer "interocclusal contact" and reduces somatosensory feedback; and 3) chronic periodontitis during the active inflammatory stage propagates a systemic effect. These mechanisms allegedly compromise the central nervous system and lead to a progressive cognitive decline.[12] However, none of the proposed mechanisms clearly explain the relationship between the rehabilitation of edentulism and dementia.

To add to this scientific evidence, we hypothesized that the incidence of cognitive impairment, including dementia, would decrease when masticatory function has been recovered using prosthetic restoration, such as fixed bridge or dental implants. Therefore, this study aimed to investigate the relationship between the changes in masticatory function and cognitive impairment by analyzing the retrospective longitudinal data from older Korean patients.

MATERIALS AND METHODS

Data source and study population

This retrospective study was performed using the Clinical Data Warehouse of the Severance Clinical Research Analysis Portal at Yonsei University Medical Center, Seoul, Korea. The participants selected for the present study were over 60 years of age, and had detailed dental records and panoramic radiographs taken at Yonsei University Dental Hospital between 2005 to 2010 (baseline; T1) and 2014 to 2020 (follow up; T2). Based on whether the participant was diagnosed with dementia after T2, the participants were allocated into two groups: the dementia group (n=132) and the control group (n=5775). Participants who had removable partial or complete dentures were excluded (n=10), since masticatory function could not be assessed using the dental panoramic radiography in denture wearers. Propensity score matching (PSM) was performed to provide a matching control group, adjusted for age and sex. As a result, there were 122 and 366 (ratio of 1:3) participants from the dementia and control groups, respectively, providing a total of 488 participants (Fig. 1). This study protocol was approved by the Institutional Review Board of Yonsei University Dental Hospital (2-2020-0066) and the study was reported in accordance with the STROBE (strengthening the reporting of observational studies in epidemiology) guidelines.

Data collection

Demographic data, including age, sex, smoking and alcohol consumption, were collected. Physician-diagnosed systemic illnesses, including hypertension, diabetes, heart diseases (coronary heart disease and arrhythmia), and cerebrovascular disease were recorded for each patient. Dental panoramic radiograph, periodontal diagnosis, and subsequent treatment received for each patient were collected from the electronic dental records. Periodontal diagnoses had been made by periodontal specialists at the Department of Periodontology according to the 1999 periodontal disease classification system presented by the American Academy of Periodontology.[13]

Dementia diagnosis

The participants in the dementia group had never been diagnosed with dementia before T2. The dementia group had been screened and clinically diagnosed by the respective physicians who were either psychiatrists or neurologists with the aid of either the Korean version of Mini-Mental State Examination (MMSE-K) or the Korean MMSE (K-MMSE) questionnaires after T2. The maximal threshold scores indicating dementia were 22 and 18 out of 30 for MMSE-K and K-MMSE, respectively.[14] Classification of cognitive impairment included in this study was in accordance with the International Classification of Diseases, 10th Revision, Clinical Modification codes F00, F01, F02, F03, and G30, which corresponds with dementia in Alzheimer disease, vascular dementia, dementia in other diseases classified elsewhere, unspecified dementia and Alzheim-

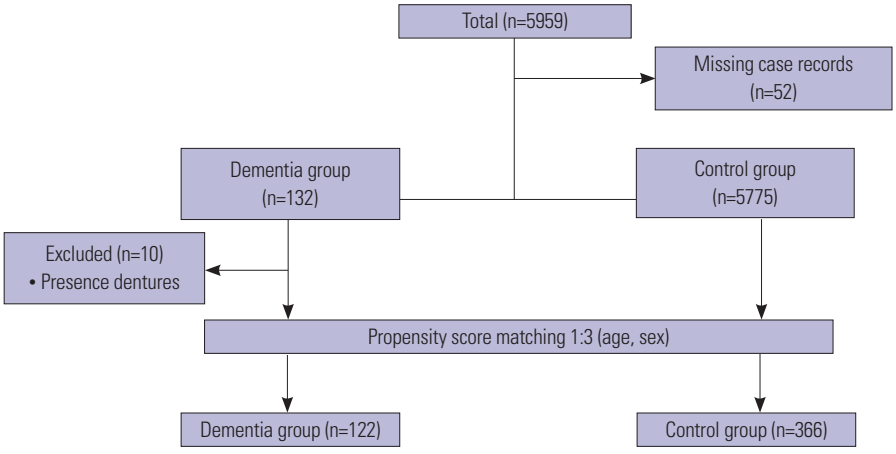

Fig. 1. Flow chart of this study.

https://doi.org/10.3349/ymj.2022.63.8.783

er's disease, respectively.[15]

Evaluation of masticatory function

Masticatory function was evaluated by analyzing the dental chart and panoramic radiograph of each patient at two time points (T1 and T2) by one experienced researcher (K.K.A). The following parameters were considered:

1) Total functional tooth unit (T-FTU): Pairs of opposing sound natural, restored, or replaced premolars and molars, such that a total of 12 units represents a fully intact posterior occlusion (molars=2 units; premolars=1 unit per quadrant).[16]

2) Total number of teeth: The total number of crowns in each patient including natural (sound and compromised) and replaced teeth apart from the third molars.

3) Number of sound teeth: The number of teeth in each patient i) having periodontal alveolar bone loss limited to the coronal third of the root, and ii) without any significant local pathology, such as advanced dental caries, that may interfere with mastication.

4) Number of compromised teeth: The number of teeth having i) root fracture, ii) extensive coronal destruction caused by dental caries or crown fracture, or iii) periodontal bone loss extending to the middle third of the root and beyond, and iv) presence of any symptoms or discomfort (e.g. pain) as recorded in medical charts.

5) Number of artificial teeth: The number of pontics within multi-unit fixed dental or implant prostheses.

6) Number of dental implants: The number of installed implant fixtures.

T-FTU was chosen as the primary outcome to represent masticatory function. The changes in T-FTU between T1 and T2 were calculated. The incidence rate of extraction (%), the number of natural teeth lost, and the subsequent rehabilitation were also evaluated. The number of replaced teeth and missing teeth neglected between T1 and T2 were also counted.

Risk factors for incidence of dementia

Based on a previous study, potential risk factors for dementia with significant differences between groups were selected,[17] and the strength of their association with incidence of dementia were compared using multiple logistic regression. The result of the correlation analysis of masticatory factors showed that the number of natural teeth lost might potentially confound several factors, and the number of replaced teeth was selected instead of the number of natural teeth lost, based on the hypothesis of this study. The selected risk factors for comparison were cerebrovascular disease, alcohol consumption, number of replaced teeth, number of missing teeth neglected, and the change in T-FTU between T1 and T2.

Statistical analysis

All analyses were performed using a dedicated statistical software (SPSS version 23; IBM Corp., Armonk, NY, USA) apart from PSM, which was performed on another software (R version 3.4.3; The R Foundation for Statistical Computing, Vienna, Austria). PSM was conducted to select a comparable cohort from the control group that matched the dementia group with respect to age and sex. The ratio of population size was set to 1:3 for dementia and control groups, respectively. Normal distribution of data was evaluated using the Shapiro-Wilk test. The chi-squared test was used to compare the demographic characteristics between the two groups. Changes in masticatory function parameters between T1 and T2 were analyzed using Wilcoxon signed rank test, and the comparison between the two groups was performed using Mann Whitney test. The multiple logistic regression was used to estimate the relationship between the change in dental status and later onset of dementia. Statistical significance was considered when the p-value from two-tailed test was lower than 0.05. The data in this study has been presented as mean±standard deviation.

RESULTS

Demographics information

Baseline demographic information has been presented in Table 1. There were no significant differences in the baseline characteristics, including sex, age, and geographical region, between the two groups (p>0.05). The dementia group showed significantly higher prevalence of cerebrovascular disease (p=0.023). Hypertension, diabetes mellitus, and heart diseases were also higher in the dementia group than in the control group; however, the difference was not statistically significant. Alcohol and cigarette consumption were higher in the dementia group; however, only alcohol consumption showed statistical significance (p<0.001). There was no significant difference in the prevalence of periodontal disease at baseline between the groups, and all patients diagnosed with periodontal disease had undergone active periodontal therapy since then on. The mean follow-up period between T1 and T2 was approximately 9 years, which was similar in both groups.

Evaluation of masticatory function

At T1, there was no difference between the dementia and control groups in terms of all parameters, including the T-FTU and the number of teeth (p=0.098 and 0.110, respectively) (Table 2). However, at T2, the dementia group exhibited a significant reduction in the mean±standard deviation T-FTU compared to T1 (9.81±2.78 to 9.11±3.16, respectively; p=0.008), which was accompanied by a significant reduction in the number of functional teeth (26.61±1.99 to 25.55±3.43, p<0.001). For the control group, there was also a significant reduction in the number of functional teeth (26.95±1.57 to 26.58±2.31, p=0.002); however, the T-FTU was maintained. Moreover, greater number of total functional teeth (p=0.019), specifically, sound teeth (p=0.006), were lost in the dementia group compared to

the control group (Table 3). Therefore, at T2, the T-FTU was significantly smaller for the dementia group compared to the control group (9.11±3.16 and 10.05±2.59, respectively; p=0.003).

There was no difference in the incidence of extraction in both groups (73% and 72.1% for the control and dementia groups, respectively) (Table 3). The number of dental implants had increased significantly between T1 and T2 in both groups (p< 0.001), however, they were placed in greater numbers in the control group than the dementia group (1.71±2.46 and 1.46± 2.74, respectively; p=0.002). The findings showed that the number of natural teeth lost was greater in the dementia group than in the control group (2.97±3.28 and 2.14±2.39, respectively; p=0.045); however, these missing teeth were more often neglected in the dementia group (1.26±2.27 and 0.64±1.29, respectively; p=0.004).

Risk factors for the incidence of dementia

Regression analysis revealed that the number of missing teeth neglected was a significant risk factor for dementia [odds ratio (OR)=1.195, 95% confidence interval (CI)=1.025–1.393, p= 0.023]. The number of replaced teeth and change in T-FTU were not significant risk factors of dementia. Cerebrovascular disease presented a higher risk of dementia despite the lack of statistical significance (OR=1.793, 95% CI=0.709–4.535). Past

Table 1. Demographic Characteristics in Propensity Score-Matched Patients

Characteristics	Control group (n=366)	Dementia group (n=122)	p value*
Age (yr)	77.90±7.88	77.95±7.89	-
Sex			-
Male	150 (40.9)	50 (40.9)	
Female	216 (59.1)	72 (59.1)	
Systemic disease			
None	65 (17.7)	15 (12.3)	0.158
Hypertension	245 (66.9)	92 (75.4)	0.080
Diabetes mellitus	109 (29.8)	40 (32.8)	0.532
Heart disease	127 (34.7)	48 (39.3)	0.354
Cerebrovascular	12 (3.3)	10 (8.2)	0.023
Alcohol history			<0.001
None	329 (89.9)	95 (77.9)	
Past experienced	9 (2.5)	14 (11.5)	
Current	28 (7.6)	13 (10.6)	
Smoking history			0.086
None	337 (92.1)	104 (85.2)	
Former smoker	24 (6.5)	15 (12.3)	
Current smoker	5 (1.4)	3 (2.5)	
Periodontal disease severity			0.198
Healthy	96 (26.2)	30 (24.6)	
Incipient	117 (32.0)	48 (39.4)	
Moderate	119 (32.5)	39 (31.9)	
Advanced	34 (9.3)	5 (4.1)	
Mean F/U period between T1 and T 2 (year. month)			
	9.2	9.2	

Data are presented as mean±standard deviation or n (%).
*p-value for chi-square test.

Table 2. Evaluation of Masticatory Function

	T1	T2	p value†
Total FTU			
Control group	10.27±2.45	10.05±2.59	0.131
Dementia group	9.81±2.78	9.11±3.16	0.008
p-value*	0.098	0.003	
Number of total teeth			
Control group	26.95±1.57	26.58±2.31	0.002
Dementia group	26.61±1.99	25.55±3.43	<0.001
p-value*	0.110	<0.001	
Number of sound teeth			
Control group	24.92±3.58	22.97±4.72	<0.001
Dementia group	24.39±3.71	21.59±5.42	<0.001
p-value*	0.062	0.007	
Number of compromised teeth			
Control group	0.42±0.97	0.20±0.78	<0.001
Dementia group	0.42±0.92	0.25±0.66	0.113
p-value*	0.830	0.170	
Number of artificial teeth			
Control group	1.15±1.70	1.21±1.59	0.344
Dementia group	1.24±1.81	1.72±2.07	0.002
p-value*	0.790	0.013	
Number of dental implants			
Control group	0.38±1.43	2.10±2.95	<0.001
Dementia group	0.52±2.17	1.99±3.40	<0.001
p-value*	0.783	0.195	

Data are presented as mean±standard deviation.
*Compared between groups; p-value for Mann-Whitney test; †Compared within group; p-value for Wilcoxon signed-rank test.

Table 3. Changes in Masticatory Function between T1 and T2

	Control group (n=366)	Dementia group (n=122)	p value*
Changes in masticatory function			
Number of total teeth	-0.04±2.08	-1.05±3.04	0.019
Number of sound teeth	-1.94±2.98	-2.80±3.04	0.006
Number of compromised teeth	-0.21±1.18	-0.17±1.16	0.404
Number of artificial teeth	0.06±1.18	0.47±1.78	0.060
Number of dental implants	1.71±2.46	1.46±2.74	0.002
Total FTU	-0.22±2.59	-0.70±2.98	0.151
History of extraction and restoration			
Extraction incidence†	267 (73.0)†	88 (72.1)†	-
Number of natural teeth lost	2.14±2.39	2.97±3.28	0.045
Number of replaced teeth	1.45±2.06	1.71±2.45	0.811
Number of missing teeth neglected	0.64±1.29	1.26±2.27	0.004

Data are presented as mean±standard deviation.
*Compared between groups; p-value for Mann-Whitney test; †Calculated percentage total number of control group, dementia group.

https://doi.org/10.3349/ymj.2022.63.8.783

Table 4. Multiple Lgistic Regression for Incidence of Dementia

Predictor	Regression coefficient (B)	SE	*p* value	Exp (B) (95% CI)
Cerebrovascular (ref: none)	0.584	0.474	0.218	1.793 (0.709–4.535)
Alcohol (ref: none)				
Past experienced	1.492	0.453	0.001*	4.445 (1.831–10.795)
Current	0.318	0.368	0.387	1.374 (0.669–2.826)
Number of replaced teeth	0.042	0.049	0.392	1.043 (0.947–1.148)
Number of missing teeth neglected	0.178	0.078	0.023*	1.195 (1.025–1.393)
Change in T-FTU	0.001	0.048	0.987	1.001 (0.911–1.099)

CI, confidence interval; T-FTU, total functional tooth unit.
*$p<0.05$.

alcohol drinkers who have abstained from drinking, as well as the current drinkers, were both presented with higher risk of dementia compared to the non-drinkers (OR=4.445, 95% CI=1.831–10.795 and OR=1.374, 95% CI=0.669–2.826, respectively); however, only the abstainers showed statistical significance (p=0.001) (Table 4).

DISCUSSION

In the present study, we investigated the relationship between the loss of oral masticatory function and the risk of dementia using a 9-year longitudinal data of an older Korean population. The main findings of this study were as follows: 1) the number of neglected missing teeth and past alcohol consumption were significant risk factors for dementia and 2) T-FTU, which is an index for masticatory function, was significantly reduced in the dementia group at T2, whereas no change was shown in the control group.

T-FTU was primarily used in this study as an indicator of the masticatory function in the study population. A critical consideration would be whether T-FTU can accurately represent one's chewing ability. According to the literature, the number of teeth needed to maintain adequate oral function remained controversial; nonetheless, it is widely accepted that the number and distribution of remaining teeth are closely related to the chewing ability.[18] A recent study suggested that at least 10 FTUs were required for satisfactory chewing if the posterior compartment consisted of both natural and fixed prosthesis.[16] In the current study, the mean T-FTU of the control group was maintained above 10, whereas that of the dementia group was below 10 even at baseline and was significantly reduced after 9 years. Since the diagnosis of cognitive impairment was made after the study period, the data from this study might reveal a possible causative relationship between diminishing masticatory function and cognitive decline. This result was in line with several epidemiological studies, in which the loss of posterior occluding pairs was associated with cognitive impairment.[19,20]

The regression analysis in this study revealed that the number of neglected missing teeth and previous alcohol consumption were significant risk factors of cognitive impairment. Similar association between tooth loss and cognitive impairment has also been demonstrated by several other epidemiological studies.[10,21] In addition, a recently published retrospective study based on two USA national health surveys reported that edentulism was highly associated with cognitive decline, and that there was a gradient effect between a decreasing number of teeth and an increasing risk of cognitive impairment.[22] Another recent study of national database from Japan reported that older people with fewer teeth were more likely to develop Alzheimer's disease.[23]

In addition, it is well-known that excessive alcohol consumption over a prolonged period can lead to detrimental brain damage and increase the risk of dementia.[24] In this study, only the cross-sectional data was available on whether the participant was an ongoing drinker, an abstainer, or a non-drinker. The results revealed that abstainers were 4.5 times as likely to develop dementia compared to the non-drinkers, whereas the ongoing drinkers were not significantly different from the non-drinkers. Neither the exact timing of abstinence nor the amount and frequency of alcohol consumption had been recorded for analysis in this study. A prospective cohort study of 9087 participants over 23 years has shown a comparable outcome to the current study, as the risk of dementia increased in people who abstained from alcohol in midlife.[25] The same study also demonstrated that the increased risk of dementia in abstainers can be attributed to the greater risk of cardiometabolic disease in those people. Therefore, it can be interpreted that the reason for modification of drinking habits in those subjects was other debilitating health-related problems, which are also known to have positive associations with dementia.[26]

It has been indicated in the literature that the recovery of masticatory function using prosthetic dentures would be an important factor for reducing the risk of cognitive impairment.[27,28] Previous studies have shown that the improvement of masticatory ability by prosthetic restoration stimulates the masticatory muscles and enhances the cognitive function.[29,30] Another systematic review on the influence of dental prostheses on cognitive health reported that denture played an important role in preventing cognitive impairment. However, most of those studies had a cross-sectional design of oral rehabilitation with partial or removable denture and cognitive impairment decline.[15,31,32] A

clear mechanism through longitudinal studies is yet to be revealed.

Based on the previously reported findings, we speculated that the restoration using fixed substitutes for missing teeth would be an important factor in preventing cognitive impairment. In the present study, both groups exhibited similar incidence of extraction during the study period, but the number of natural teeth lost in the dementia group was greater than that of the control group (2.97±3.28 and 2.14±2.39, respectively). In addition, the number of replaced teeth was similar, but the number of missing teeth neglected was twice of larger values in the dementia group than in the control group (1.26±2.27 and 0.64±1.29, respectively, p=0.004). Therefore, this finding suggests that rehabilitation of edentulism is inversely associated with cognitive decline.

Chewing has been reported to be the most common daily activity affected by impaired dental status.[33] Since substantial food products require considerable amount of chewing, it has been argued that reduced chewing ability due to fewer teeth and occluding posterior pairs may lead to compromised nutrition.[34] In the context of cognitive impairment, various nutritional deficiencies have been indicated as a potential contributing factor. For example, the lack of serum vitamin D levels has been shown to be positively associated with dementia and Alzheimer's disease,[35] as well as folate, cobalamin, and dietary fatty acids.[36] Furthermore, it has been suggested that mastication stimulates specific areas of the brain, which produces a preventive effect on cognitive health.[37]

Nevertheless, these mechanisms have yet to receive widespread scientific support. There are other confounding variables, such as socioeconomic status, access to quality dental and medical care, and the level of education, which can also contribute to tooth loss and dementia in the later years of life. Additionally, it is also possible that the causative relationship has been reversed. Subjects with cognitive decline have reduced ability to maintain oral hygiene, which will inevitably lead to increased tooth loss.[38]

Our study had some limitations. First, the FTU index used in this study was based only on the dental records and radiographic data for the dentition status of each subject, and this could not indicate the clinical diagnosis of the presence or absence of direct occlusal contact and occlusal force. Second, there was a paucity of data to confirm the correlation between masticatory function and dementia risk. Therefore, the results of this study should be interpreted with caution.

Within the limitations of this study, there might be a causative relationship between the neglected missing posterior dentitions and the onset of dementia. In addition, the history of alcohol consumption was a significant risk factor for dementia.

ACKNOWLEDGEMENTS

This research was supported by the National Research Foundation of Korea (NRF) grant funded by the Korean government (MSIT) (No. NRF-2019R1C1C1006622).

This research was supported by a grant of the Medical data-driven hospital support project through the Korea Health Information Service (KHIS), funded by the Ministry of Health & Welfare, Republic of Korea.

AUTHOR CONTRIBUTIONS

Conceptualization: Jae-Kook Cha. Data curation: Kyung-A Ko. Formal analysis: Kyung-A Ko. Funding acquisition: Jae-Kook Cha. Investigation: Kyung-A Ko and Jin-Young Park. Methodology: Jae-Kook Cha and Byoung Seok Ye. Project administration: Jae-Kook Cha. Resources: Jae-Kook Cha. Software: Kyung-A Ko. Supervision: Jung-Seok Lee, Byoung Seok Ye, Ui-Won Jung, Seong-Ho Choi, and Jae-Kook Cha. Validation: Jae-Kook Cha. Visualization: Jae-Kook Cha. Writing—original draft: Kyung-A Ko and Jin-Young Park. Writing—review & editing: Kyung-A Ko, Jin-Young Park, Byoung Seok Ye, Jung-Seok Lee, and Jae-Kook Cha. Approval of final manuscript: all authors.

ORCID iDs

Kyung-A Ko https://orcid.org/0000-0002-4835-8509
Jin-Young Park https://orcid.org/0000-0002-6408-1618
Jung-Seok Lee https://orcid.org/0000-0003-1276-5978
Byoung Seok Ye https://orcid.org/0000-0003-0187-8440
Ui-Won Jung https://orcid.org/0000-0001-6371-4172
Seong-Ho Choi https://orcid.org/0000-0001-6704-6124
Jae-Kook Cha https://orcid.org/0000-0002-6906-7209

REFERENCES

1. Scott KR, Barrett AM. Dementia syndromes: evaluation and treatment. Expert Rev Neurother 2007;7:407-22.
2. Hane FT, Lee BY, Leonenko Z. Recent progress in Alzheimer's disease research, part 1: pathology. J Alzheimers Dis 2017;57:1-28.
3. Livingston G, Sommerlad A, Orgeta V, Costafreda SG, Huntley J, Ames D, et al. Dementia prevention, intervention, and care. Lancet 2017;390:2673-734.
4. Wu YT, Beiser AS, Breteler MMB, Fratiglioni L, Helmer C, Hendrie HC, et al. The changing prevalence and incidence of dementia over time - current evidence. Nat Rev Neurol 2017;13:327-39.
5. Tonsekar PP, Jiang SS, Yue G. Periodontal disease, tooth loss and dementia: is there a link? A systematic review. Gerodontology 2017;34:151-63.
6. Weijenberg RA, Scherder EJ, Lobbezoo F. Mastication for the mind--the relationship between mastication and cognition in ageing and dementia. Neurosci Biobehav Rev 2011;35:483-97.
7. Lexomboon D, Trulsson M, Wårdh I, Parker MG. Chewing ability and tooth loss: association with cognitive impairment in an elderly population study. J Am Geriatr Soc 2012;60:1951-6.
8. Ueno M, Yanagisawa T, Shinada K, Ohara S, Kawaguchi Y. Masticatory ability and functional tooth units in Japanese adults. J Oral Rehabil 2008;35:337-44.
9. Zaitsu T, Ohnuki M, Ando Y, Kawaguchi Y. Evaluation of occlusal status of Japanese adults based on functional tooth units. Int Dent J 2022;72:100-5.

https://doi.org/10.3349/ymj.2022.63.8.783

10. Tsai YC, Wang HJ, Wang LY, Shaw CK, Lee YP, Lin MC, et al. Retrospective analysis of the association between tooth loss and dementia: a population-based matched case-control study. Community Dent Health 2020;37:59-64.
11. Weijenberg RAF, Delwel S, Ho BV, van der Maarel-Wierink CD, Lobbezoo F. Mind your teeth-the relationship between mastication and cognition. Gerodontology 2019;36:2-7.
12. Thomson WM, Barak Y. Tooth loss and dementia: a critical examination. J Dent Res 2021;100:226-31.
13. Armitage GC. Development of a classification system for periodontal diseases and conditions. Ann Periodontol 1999;4:1-6.
14. Kim JM, Shin IS, Yoon JS, Lee HY. Comparison of diagnostic validities between MMSE-K and K-MMSE for screening of dementia. J Korean Neuropsychiatr Assoc 2003;42:124-30.
15. Kim YT, Choi JK, Kim DH, Jeong SN, Lee JH. Association between health status and tooth loss in Korean adults: longitudinal results from the National Health Insurance Service-Health Examinee Cohort, 2002-2015. J Periodontal Implant Sci 2019;49:158-70.
16. Hsu KJ, Yen YY, Lan SJ, Wu YM, Chen CM, Lee HE. Relationship between remaining teeth and self-rated chewing ability among population aged 45 years or older in Kaohsiung City, Taiwan. Kaohsiung J Med Sci 2011;27:457-65.
17. Takeuchi K, Ohara T, Furuta M, Takeshita T, Shibata Y, Hata J, et al. Tooth loss and risk of dementia in the community: the Hisayama study. J Am Geriatr Soc 2017;65:e95-100.
18. Naka O, Anastassiadou V, Pissiotis A. Association between functional tooth units and chewing ability in older adults: a systematic review. Gerodontology 2014;31:166-77.
19. Han JH, Lee HJ, Han JW, Suh SW, Lee JR, Byun S, et al. Loss of functional dentition is associated with cognitive impairment. J Alzheimers Dis 2020;73:1313-20.
20. Saito S, Ohi T, Murakami T, Komiyama T, Miyoshi Y, Endo K, et al. Association between tooth loss and cognitive impairment in community-dwelling older Japanese adults: a 4-year prospective cohort study from the Ohasama study. BMC Oral Health 2018;18:142.
21. Xu S, Huang X, Gong Y, Sun J. Association between tooth loss rate and risk of mild cognitive impairment in older adults: a population-based longitudinal study. Aging (Albany NY) 2021;13:21599-609.
22. Galindo-Moreno P, Lopez-Chaichio L, Padial-Molina M, Avila-Ortiz G, O'Valle F, Ravida A, et al. The impact of tooth loss on cognitive function. Clin Oral Investig 2022;26:3493-500.
23. Tsuneishi M, Yamamoto T, Yamaguchi T, Kodama T, Sato T. Association between number of teeth and Alzheimer's disease using the National Database of Health Insurance Claims and Specific Health Checkups of Japan. PLoS One 2021;16:e0251056.
24. Xu W, Wang H, Wan Y, Tan C, Li J, Tan L, et al. Alcohol consumption and dementia risk: a dose-response meta-analysis of prospective studies. Eur J Epidemiol 2017;32:31-42.
25. Sabia S, Fayosse A, Dumurgier J, Dugravot A, Akbaraly T, Britton A, et al. Alcohol consumption and risk of dementia: 23 year follow-up of Whitehall II cohort study. BMJ 2018;362:k2927.
26. Ricci C, Wood A, Muller D, Gunter MJ, Agudo A, Boeing H, et al. Alcohol intake in relation to non-fatal and fatal coronary heart disease and stroke: EPIC-CVD case-cohort study. BMJ 2018;361:k934.
27. Kim MS, Oh B, Yoo JW, Han DH. The association between mastication and mild cognitive impairment in Korean adults. Medicine (Baltimore) 2020;99:e20653.
28. Ming Y, Hsu SW, Yen YY, Lan SJ. Association of oral health-related quality of life and Alzheimer disease: a systematic review. J Prosthet Dent 2020;124:168-75.
29. Narita N, Kamiya K, Yamamura K, Kawasaki S, Matsumoto T, Tanaka N. Chewing-related prefrontal cortex activation while wearing partial denture prosthesis: pilot study. J Prosthodont Res 2009;53:126-35.
30. Shoi K, Fueki K, Usui N, Taira M, Wakabayashi N. Influence of posterior dental arch length on brain activity during chewing in patients with mandibular distal extension removable partial dentures. J Oral Rehabil 2014;41:486-95.
31. Ahmed SE, Mohan J, Kalaignan P, Kandasamy S, Raju R, Champakesan B. Influence of dental prostheses on cognitive functioning in elderly population: a systematic review. J Pharm Bioallied Sci 2021;13(Suppl 1):S788-94.
32. Hosoi T, Morokuma M, Shibuya N, Yoneyama Y. Influence of denture treatment on brain function activity. Jpn Dent Sci Rev 2011;47:56-66.
33. Sheiham A, Steele J. Does the condition of the mouth and teeth affect the ability to eat certain foods, nutrient and dietary intake and nutritional status amongst older people? Public Health Nutr 2001;4:797-803.
34. Joshipura KJ, Willett WC, Douglass CW. The impact of edentulousness on food and nutrient intake. J Am Dent Assoc 1996;127:459-67.
35. Jayedi A, Rashidy-Pour A, Shab-Bidar S. Vitamin D status and risk of dementia and Alzheimer's disease: a meta-analysis of dose-response. Nutr Neurosci 2019;22:750-9.
36. Del Parigi A, Panza F, Capurso C, Solfrizzi V. Nutritional factors, cognitive decline, and dementia. Brain Res Bull 2006;69:1-19.
37. Kubo KY, Ichihashi Y, Kurata C, Iinuma M, Mori D, Katayama T, et al. Masticatory function and cognitive function. Okajimas Folia Anat Jpn 2010;87:135-40.
38. Naorungroj S, Slade GD, Beck JD, Mosley TH, Gottesman RF, Alonso A, et al. Cognitive decline and oral health in middle-aged adults in the ARIC study. J Dent Res 2013;92:795-801.