Observational Study

Medicine®

OPEN

Does reduced chewing ability efficiency influence cognitive function? Results of a 10-year national cohort study

Mi-Sun Kim, RDH[a], Dong-Hun Han, DDS, PhD[b,c,*]

Abstract

A growing body of literature suggests that oral health can influence cognitive function during aging. However, it is currently unclear whether reduced masticatory efficiency influences cognitive impairment in longitudinal studies.

This study sought to investigate the effects of reduced chewing ability on the incidence of cognitive impairment using national representative data from 10 years of follow-up in Korea. Among the 10,254 people recruited in 2006 (1st wave), 7568 with normal cognitive function were selected. The participants were followed up every 2 years. The number of participants followed up until the 6th wave was 5020 in 2016. Chewing ability and scores on the Mini-Mental State Examination were recorded using self-reported questionnaires. Risk factors for dementia taken from systematic literature reviews were used as covariates. We performed logistic regression and created general estimating equation models after controlling for all covariates to assess the relationship between chewing ability and cognitive decline. Decreased chewing function was associated with mild cognitive impairment after controlling for confounding variables.

The odds ratio for cognitive impairment was about 1.28 times higher than in people with poor chewing function as in those with good chewing function. We identified changes in chewing function from the 1st wave to the 6th wave; the odds ratios were 2.21 (95% confidence interval = 1.90–2.58) in the good-poor group and 2.11 (95% confidence interval = 1.74–2.55) in the poor-poor group.

We identified an impairment in cognitive function in the poor (poor-poor and good-poor) chewing ability group. Therefore, we have confirmed that reduced mastication efficiency may contribute to a deterioration in cognitive function. People with deteriorated chewing ability must be given additional attention to aid in the prevention of cognitive decline.

Abbreviations: KLoSA = Korean Longitudinal Study of Aging, MMSE = Mini Mental State Examination, OR = odds ratio.

Keywords: cognitive impairment, mastication, oral health

1. Introduction

The United Nations defines aging and super-aged societies as those in which ≥7% and ≥15% of the population are age 65 or older, respectively.[1] South Korea reached aging society status by 2000 and is approaching super-aged status, with adults age 65 and older accounting for 14.4% of the total population in 2018.[2] The US Census Bureau predicted that the percentage of the population aged 65 and over in South Korea will reach 35.9% by 2050, making South Korea the second most super-aged society next to Japan.[3] Moreover, the personal and national burdens associated with geriatric diseases will continue to increase as the percentage of older adults gradually increases worldwide.[4,5] Dementia, 1 of the most widely recognized geriatric diseases, is characterized by diminished brain function due to the deformation and degeneration of brain tissues. Cognitive impairment is a main clinical feature of dementia and individuals with cognitive impairment have an approximately 10% to 15% greater risk of transitioning to dementia than healthy people (1%–2%).[6–7] Previous studies involving patients with cognitive impairment have reported that approximately 30% and 80% transition to Alzheimer disease within 3 and after 6 years, respectively.[7,8] The World Health Organization reported that the prevalence of dementia in high-income countries in the Asia-Pacific region, including South Korea, was approximately 7% in 2015. This rate is predicted to increase by

The authors have no funding and conflicts of interest to disclose.

The datasets generated during and/or analyzed during the current study are publicly available.

[a] Department of Dental Hygiene, Kyungdong University, Gangwon-do, South Korea, [b] Department of Preventive and Social Dentistry, Seoul National University School of Dentistry, Seoul, South Korea, [c] Dental Research Institute, Seoul National University, Seoul, South Korea.

[*] Correspondence: Dong-Hun Han, Department of Preventive and Social Dentistry, Seoul National University, 1, Gwanak-ro, Guanak-gu, Seoul, 08826, South Korea (e-mail: dhhan73@snu.ac.kr).

How to cite this article: Kim MS, Han DH. Does reduced chewing ability efficiency influence cognitive function? Results of a 10-year national cohort study. Medicine 2022;101:25(e29270).

Received: 10 October 2020 / Received in final form: 22 March 2022 / Accepted: 29 April 2022

http://dx.doi.org/10.1097/MD.0000000000029270

approximately 56% by 2030 and 115% by 2050. New cases of dementia are occurring at a rate of 1 every 3 seconds worldwide and 1 every 12 minutes in South Korea.[9,10] As of 2017, the prevalence of dementia among adults age 65 and over was estimated to be 9.94%, equivalent to approximately 700,000 patients, and this figure is expected to increase to 15% by 2050. As of 2013, the social cost associated with dementia in South Korea was approximately 1% of the gross domestic product (11.7 trillion won), although this cost is expected to increase to approximately 1.5% of the gross domestic product (43.2 trillion won) by 2050.[11] Based on a systematic literature review, Norton has reported that obesity, hypertension, diabetes, lack of exercise, smoking, low education level, and depression are major risk factors for dementia.[12] Several recent studies have also suggested that oral diseases represent another risk factor for cognitive impairment. Such studies have indicated that reduced chewing ability may be a major risk factor for cognitive impairment.[13] In many cross-sectional studies, chewing ability was associated with cognitive states, while some longitudinal studies have reported that reduced chewing ability can cause cognitive impairment.[14–16] However, most of these studies also included older adults from specific regions and included only those patients who already exhibited poor cognitive function and chewing ability. Thus, they may not have been able to accurately assess the effects of chewing function on the incidence of cognitive impairment. We also confirmed in previous studies that mastication is associated with cognitive decline.[17] However, there was a limitation of cross-sectional research that could not explain the causal relationship between mastication and cognitive impairment.

Accordingly, the present study aimed to investigate the effects of reduced chewing ability on the incidence of cognitive impairment using national data from 11 years of follow-up on patients who were aged ≥45 years of age with normal cognitive function.

2. Methods

2.1. Study population

The present study used long-term follow-up data from the Korean Longitudinal Study of Aging (KLoSA).[18] The data were collected by the Korea Employment Information Service and represented middle-aged Korean adults age 45 years and older. Participants were selected via stratified cluster sampling based on 90% of all census data from 2005 census. While the first wave of the KLoSA began in 2006, the study remains ongoing, and the same patients are followed up every 2 years. In the present study, the total duration of follow-up was 11 years: 2006 (first wave) to 2016 (recently released sixth wave). Among the 10,254 people included in the first wave, 2473 who already exhibited reduced cognitive function and 213 people with missing answers for major variables were excluded. As a result, 7568 people were selected for secondary follow-up. In subsequent years, the numbers of people followed up were 6301, 5712, 5505, 5246, and 5020 in 2008, 2010, 2012, 2014, and 2016, respectively, after excluding the deceased and drop outs (Fig. 1). Prior to the interview, written informed consent was given by all participants of the KLoSA survey. The data were anonymized and de-identifiable with no personal information, with careful protection on confidentiality. The Institutional Review Boards approval of this study was replaced by a research ethics review because KLoSA was nationally approved statistics and publicly available data (http://survey.keis.or.kr).

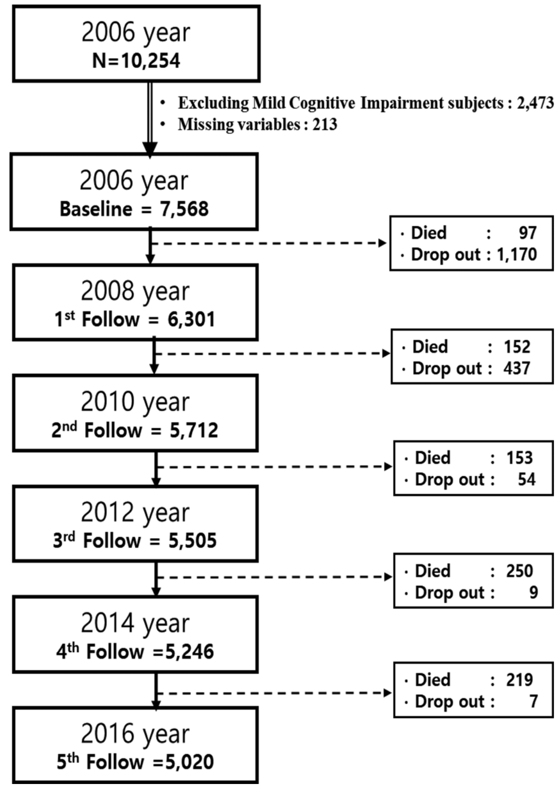

Figure 1. Flow diagram of identification and selection processes.

2.2. Mastication assessment

Mastication was measured using a self-report format.[19] A trained examiner presented patients with the following question: "Do you feel discomfort when chewing hard food, such as apples or meat?" Participants were required to select from among the following responses: "very uncomfortable," "somewhat uncomfortable," "average," "not uncomfortable," and "not uncomfortable at all." Ultimately, participants who responded with "very uncomfortable," "somewhat uncomfortable," and "average" were classified into the poor chewing ability group, whereas those who responded with "not uncomfortable" and "not uncomfortable at all" were classified into the good chewing ability group.

2.3. Cognitive impairment assessment

The Mini Mental State Examination (MMSE) was used to assess levels of cognitive impairment.[20] The MMSE is widely used worldwide and includes items related to orientation, instant recall, attention, calculation, vocabulary recall, and language. Scores range from 1 to 30 points. The present study utilized the K-MMSE, a Korean-translated version of the MMSE. The correlation among different K-MMSE versions has been reported as 0.80 and 0.95.[21] In the present study, the cut-off value for MMSE scores was set to <24 and >=24 as used in previous studies.[22,23]

2.4. Covariate assessment

2.4.1. Socioeconomic factors. Variables presented as risk factors for dementia in systematic literature reviews were used as covariates for the analysis.[12] For all covariates, variables from the first wave were applied. Moreover, gender and age (in years) were used as demographic variables, and education level (0 = college or more: reference group, 1 = less than high school) was used as a socioeconomic factor.

2.4.2. Health factors. Hypertension, diabetes, and obesity as diagnosed by a doctor (1 = ever been diagnosed by a doctor, 0 = otherwise) were used as dichotomous variables. The Korean version of the Center for Epidemiologic Studies Depression Scale was used to evaluate levels of depression among participants.[24,25] In the present study, patients who responded that they had experienced depressive symptoms for 3 or more days on at least 4 questions were considered to have depression.[24] The reliability of the Korean version of the Center for Epidemiologic Studies Depression has been reported as 0.796.[25]

2.4.3. Health behavior factors. The health behavior variables included in the analysis are exercise behavior and smoking status. A trained investigator asked all subjects, "How many times a week do you exercise regularly?." The subjects who responded to the question were divided into 2 groups: "No (1 = not exercising at all)" and "Yes (0 = doing regular exercise more than once)". Smoking status was assessed by the following questions: (1) Do you smoke cigarettes now? With responses yes, no; (2) if not a current cigarette smoker, did you smoke in the past with yes or no response options. And 3 variables of smoking status were used in the final analysis (0 = no smoking, 1 = ever, 2 = current smoking).

2.5. Statistical analysis

Initially, our analysis included data for 7568 people with normal baseline cognitive function, who were followed up in subsequent years (6301, 5712, 5505, 5246, and 5020 in 2008, 2010, 2012, 2014, and 2016, respectively; Fig. 1). Differences in socioeconomic, health, and health behavior factors from the first to the final wave were analyzed using *t* tests and chi-square tests (Table 1). In Model I (Table 2), baseline chewing function (first wave) was defined as the major explanatory variable, and the incidence of cognitive impairment at the final wave (sixth wave) was defined as the outcome variable. Following this, logistic regression analysis was performed after controlling for all covariates from the first wave. The analysis of model1 was analyzed by applying weights. In Model II (Table 3), chewing function at the first and sixth waves was measured, and dummy variables (good-good, good-poor, poor-good, and poor-poor) were created to define 4 groups based on changes in chewing function. Cognitive states, the major dependent variable, was measured from the second to sixth waves and entered into a general estimated equation model.[26] The covariates in the general estimated equation model reflected the measured values from the first wave, while time was also applied to the covariates. Because the measured values of the dependent variables of cognitive function from the second to sixth waves represent data repeatedly measured from the same participant, correlations may exist. In such cases, the correlations between the dependent variables must be considered in the analysis. Figure 2 shows the cognitive function mean scores from each wave for Models I and II obtained using *t* tests and analyses of variance. The collected data were analyzed using IBM SPSS (IBM SPSS 20.0 for windows, SPSS Inc, Chicago, IL).

3. Results

The numbers of participants for each year are shown in Figure 1. Among the initial survey population of 10,254 individuals, 213 people with missing answers to major explanatory variables and 2473 people with cognitive impairment were excluded. As a result, 7568 people (73.8%) with normal cognitive function were included in the first wave of the survey. The follow-up population in each wave consisted of the previous survey population minus those who were deceased or had dropped out. Totals of 7568, 6301, 5712, 5505, 5246, and 5020 people were followed up in 2006, 2008, 2010, 2012, 2014, and 2016, respectively. The mean age of participants at the first wave was 58.6 years, naturally increasing with each wave. The number of people with cognitive impairment was 0 (0%), 806 (12.8%), 1322 (23.1%), 993 (18.0%), 973 (18.3%), and 986 (19.6%) in the first to sixth waves, respectively. Among 10,254 people for whom baseline chewing function data were collected, approximately 15% (n=1.165) reported that they had poor chewing function. In subsequent waves, the number of people with chewing discomfort tended to decrease: 1076 (16.5%), 868 (14.5%), 697 (12.1%), 712 (13.0%), and 638 (12.2%). A comparison of the incidence of cognitive impairment according to chewing ability from baseline to 11 years is presented in Tables 2 and 3. In Model I, which was adjusted for all covariates, the odds ratio (OR) for developing cognitive impairment 11 years after baseline (sixth wave) in people with poor chewing ability in the first wave was 1.28 (95% confidence interval [CI] = 1.00–1.64), relative to people with good chewing ability in the first wave. The effect of interaction between chewing and time was 1.03 (95% CI=0.99–1.08), but it was not significant.

In Model II, the OR for cognitive impairment was higher among those with poorer chewing ability in the sixth wave than in the first wave. The OR for cognitive impairment in people who continued to report poor chewing ability from the first to sixth waves was 2.11 (95% CI=1.74–2.55). In addition, the OR for cognitive impairment in people who reported good chewing ability in the first wave but poor chewing ability in the sixth wave was 2.21 (95% CI=1.90–2.58). In contrast, the OR for cognitive impairment in people who reported poor chewing ability in the first wave but good chewing ability in the sixth wave were not significant. The OR for cognitive impairment over time was 1.41 (95% CI=1.39–1.43), corresponding to an approximately 40% risk of cognitive impairment every 2 years. The effect of interaction between chewing and time was significant (1.06 [95% CI=1.04–1.07]).

4. Discussion

The objective of this longitudinal study was to identify the effects of reduced chewing ability on the incidence of cognitive impairment in subjects aged 45 years and over with normal cognitive function. In our study, the decline in cognitive function impairment was clearly identified in the poor (poor-poor and good-poor) chewing ability group. Therefore, reduction of chewing function may contribute to deterioration of cognitive impairment. The good-poor group, which had good chewing function at the first wave and poor at sixth, was vulnerable. This group must be given more attention in prevention programs.

Table 1

Demographic characteristics of the included participants.

Variable	Baseline (1st wave)		Follow-up (6th wave)	
	N	(%)	N	(%)
MMSE, n (%)				
Good	7568	(100.0)	4034	(80.4)
Poor	0	(0.0)	986	(19.6)
Total	7568	(100.0)	5020	(100.0)
MMSE score (Mean ± SD)	27.93 ± 1.880	26.33 ± 4.280		
Chewing, n (%)				
Good	6403	(84.6)	4595	(87.8)
Poor	1165	(15.4)	638	(12.2)
Total	7568	(100.0)	5233	(100.0)
Age (Mean ± SD)	58.63 ± 9.633	69.02 ± 8.838		
Age, n (%)				
<65	5370	(71.0)	3892	(74.4)
≥65	2198	(29.0)	1341	(25.6)
Total	7568	(100.0)	5233	(100.0)
Gender, n (%)				
Male	3714	(49.1)	2454	(46.9)
Female	3854	(50.9)	2779	(53.1)
Total	7568	(100.0)	5233	(100.0)
Education level, n (%)				
≤High school	996	(13.2)	633	(12.1)
≥College	6565	(86.8)	4597	(87.9)
Total	7561	(100.0)	5230	(100.0)
Hypertension, n (%)				
No	5706	(75.4)	2980	(56.9)
Yes	1862	(24.6)	2253	(43.1)
Total	7568	(100.0)	5233	(100.0)
Diabetes, n (%)				
No	6781	(89.6)	4246	(81.1)
Yes	787	(10.4)	987	(18.9)
Total	7568	(100.0)	5233	(100.0)
Obesity, n (%)				
No	3416	(45.5)	2371	(45.3)
Yes	4089	(54.5)	2862	(54.7)
Total	7505	(100.0)	5233	(100.0)
Depression, n (%)				
No	5654	(75.1)	3495	(66.8)
Yes	1878	(24.9)	1735	(33.2)
Total	7532	(100.0)	5230	(100.0)
Chronic disease (Mean ± SD)	0.64 ± 0.896	1.25 ± 1.202		
Smoking, n (%)				
No	5146	(68.0)	3465	(66.2)
Ever	787	(10.4)	1169	(22.3)
Yes	1635	(21.6)	599	(11.4)
Total	7568	(100.0)	5233	(100.0)
Regular exercise, n (%)				
No	4214	(55.7)	3244	(62.0)
Yes	3354	(44.3)	1989	(38.0)
Total	7568	(100.0)	5233	(100.0)

MMSE = Mini Mental State Examination.

The findings of the present study were similar to those of previous studies. A recent systematic literature review of 17 cross-sectional and 6 longitudinal studies regarding the association between chewing ability and cognitive function found that 15 cross-sectional and 5 longitudinal studies reported that poor chewing ability affected the incidence and prevalence of cognitive impairment, including dementia, among older adults.[16,27] In a study that analyzed secondary data for the middle-aged population in each country, including 14 European countries, people with chewing discomfort exhibited poorer word memory, vocabulary ability, and computation ability than those with good chewing ability. In particular, this study suggested that, as cognitive impairment progresses, it becomes more difficult to use an expanded vocabulary than to make numerical calculations.[28] Another study measured blood oxygen concentration and activation of the cortex and frontal lobe during chewing in 17 healthy adults aged 20 to 34 years. In this study, the group that performed gum chewing exhibited

Table 2

Incidence of mild cognitive impairment in participants with poor chewing ability.

Variables	Mild cognitive impairment*			
	Odds ratio* (95% confidence interval)			
MMSE score at baseline	**1.413 (1.349–1.479)**	**1.295 (1.232–1.360)**	**1.281 (1.218–1.347)**	**1.277 (1.214–1.344)**
Chewing				
Good	ref	ref	ref	ref
Poor	**1.753 (1.395–2.202)**	**1.405 (1.109–1.779)**	**1.302 (1.021–1.659)**	**1.282 (1.004–1.635)**
Age				
<65		ref	ref	ref
≥65		**4.661 (3.857–5.632)**	**4.503 (3.698–5.483)**	**4.477 (3.665–5.468)**
Gender				
Male		ref	ref	ref
Female		**1.498 (1.241–1.808)**	**1.467 (1.212–1.775)**	**1.697 (1.326–2.173)**
Education				
≥High school		ref	ref	ref
<High school		**2.009 (1.336–3.019)**	**1.970 (1.314–2.952)**	**1.880 (1.248–2.831)**
Hypertension				
No			ref	ref
Yes			1.099 (0.883–1.368)	1.103 (0.886–1.372)
Diabetes				
No			ref	ref
Yes			**1.481 (1.072–2.045)**	**1.472 (1.067–2.033)**
Obesity				
Normal			ref	ref
Obesity			0.838 (0.695–1.010)	0.838 (0.695–1.010)
Depression				
No			ref	ref
Yes			**1.247 (1.008–1.543)**	1.226 (0.990–1.517)
Smoking				
Never smoker				ref
Past smoker				**1.539 (1.062–2.230)**
Current smoker				1.115 (0.819–1.519)
Regular exercise				
No				ref
Yes				**1.209 (1.002–1.459)**
Chewing * Time				1.033 (0.988–1.080)

* (Model I): obtained from logistic regression model adjusted for MMSE score, age, gender, education level, hypertension, diabetes, obesity, depression, regular exercise, and smoking status at baseline. The outcome variable was cognitive state obtained from the 6th wave.
Bold denotes statistical significance at $P < .05$.
MMSE = Mini Mental State Examination.

higher brain activation and accuracy associated with exercise ability. While there were no major differences in behaviors such as warning or collision, short-term chewing alone was able to increase exercise speed and accuracy, in addition to blood oxygen levels, demonstrating that oral function can control cognitive and physical functions.[29]

In the present study, the OR for cognitive impairment was about 1.28 times as high in people with poor chewing function than in those with good chewing function (Model I). In Model II, which identified changes in chewing function from the first wave to the last wave (sixth wave), ORs were 2.21 (95% CI = 1.90–2.58) in the good-poor group and 2.11 (95% CI = 1.74–2.55) in the poor-poor group. In a recent cross-sectional study involving Korean adults age 65 years and over, the OR for chewing and cognitive impairment was 1.28 (95% CI = 1.17–1.40).[30] Because it is difficult to compare cross-sectional studies to longitudinal studies, we also analyzed cross-sectional ORs for each wave that included individuals with cognitive impairment who were excluded at baseline. ORs for each wave were as follows: first wave: 1.25 (95% CI = 1.08–1.44); second wave: 1.27 (95% CI = 1.09–1.48); third wave: 1.48 (95% CI = 1.27–1.73); fourth wave: 2.05 (95% CI = 1.72–2.46), fifth wave: 2.37 (95% CI = 1.96–2.87); and sixth wave: 2.17 (95% CI = 1.77–2.65). ORs for the first and second waves were similar in the present study. In another cross-sectional Korean study involving adults over 70 living in rural areas, the authors reported an association between severe chewing discomfort and cognitive impairment, with an OR of 3.87 (95% CI = 1.20–12.49), which was higher than that observed in the present study.[15] This discrepancy may be explained by the fact that participants in the previous study were older and living in rural areas. Thus, they may not have received appropriate oral health care due to poor accessibility.

In Model II, people who had good chewing ability during the first wave but poor chewing ability during the sixth wave (OR = 2.21, 95% CI = 1.90–2.58) had higher ORs for cognitive impairment than those with continued poor chewing ability from the first to sixth waves (OR = 2.11, 95% CI = 1.74–2.55). Therefore, we speculate that the progression of cognitive impairment may be more rapid in people who report sudden

Table 3

Incidence of mild cognitive impairment in participants with poor chewing ability.

Variables	Mild cognitive impairment* Odds ratio* (95% confidence interval)			
MMSE score at baseline	**1.333 (1.301–1.366)**	**1.245 (1.215–1.277)**	**1.236 (1.205–1.268)**	**1.247 (1.214–1.281)**
Chewing				
Good-Good	ref	ref	ref	ref
Poor-Good	**1.215 (1.047–1.411)**	1.058 (0.912–1.227)	1.015 (0.873–1.180)	1.005 (0.858–1.177)
Good-Poor	**2.659 (2.308–3.064)**	**2.132 (1.852–2.456)**	**2.077 (1.800–2.396)**	**2.212 (1.899–2.578)**
Poor-Poor	**3.100 (2.620–3.668)**	**2.183 (1.839–2.592)**	**1.999 (1.674–2.388)**	**2.106 (1.739–2.550)**
Age				
<65		ref	ref	ref
≥65		**2.715 (2.455–3.003)**	**2.649 (2.388–2.939)**	**2.787 (2.494–3.114)**
Gender				
Male		ref	ref	ref
Female		**1.459 (1.327–1.604)**	**1.428 (1.296–1.573)**	**1.434 (1.252–1.643)**
Education				
≥High school		ref	ref	ref
<High school		**2.365 (1.916–2.919)**	**2.346 (1.901–2.897)**	**2.306 (1.851–2.873)**
Hypertension				
No			ref	ref
Yes			1.089 (0.976–1.215)	1.107 (0.987–1.243)
Diabetes				
No			ref	ref
Yes			**1.163 (0.993–1.362)**	**1.192 (1.008–1.409)**
Obesity				
Normal			ref	ref
Obesity			0.923 (0.840–1.015)	0.926 (0.839–1.023)
Depression				
No			ref	ref
Yes			**1.135 (1.021–1.261)**	**1.129 (1.009–1.262)**
Smoking				
Never smoker				ref
Past smoker				**1.047 (0.865–1.268)**
Current smoker				0.943 (0.800–1.111)
Regular exercise				
No				ref
Yes				**1.305 (1.182–1.442)**
Time				**1.407 (1.383–1.432)**
Chewing * Time				**1.055 (1.039–1.072)**

* (Model II): obtained from general estimated equation model adjusted for MMSE score, age, gender, education level, hypertension, diabetes, obesity, depression, regular exercise, and smoking status at baseline.
The outcome variables were all cognitive states obtained from the 2nd, 3rd, 4th, 5th, and 6th waves.
Bold denotes statistical significance at $P < .05$.
MMSE = Mini Mental State Examination.

decreases in chewing function within a short period (i.e., within 2 years). Moreover, people who reported poor chewing ability in the first wave but good chewing ability in the sixth wave exhibited changes in cognitive impairment similar to those observed in people who reported continued good chewing ability from the first to sixth waves.

In the aging population, the chewing ability resembles the pattern of physical dysfunction and the incidence of physical disability. A healthy individual (with independent physical function) suffering an acute disease such as pneumonia has a higher risk of permanent disability or death than that of an individual with a gradual muscle atrophy from aging.[31] A reduction in functional reserve from aging accelerates other progressed hypofunction in association with aging.[32] From out study, once the chewing function starts to decreases the cognitive function subsequently decreases within a short period of time. It is more suitable to draw the chewing ability and the cognitive function has an association rather than direct causal inferences as the reduction in functional reserve from aging is a result of various organ systems.

These results indicated that chewing function did not affect cognitive impairment in these 2 groups, suggesting that recovery of initial chewing difficult can delay or prevent cognitive impairment. The present study is the first population-based long-term follow-up study to report results similar to those of previous animal studies, which reported that the use of dental crowns or chewing-inducing food can recover chewing and cognitive function in animals with poor chewing ability.[33,34] Taken together, these findings indicate that chewing ability is not simply the ability to chew and break down food, but can be a marker of cognitive function. Moreover, recovery of chewing function can be a major factor in preventing or delaying

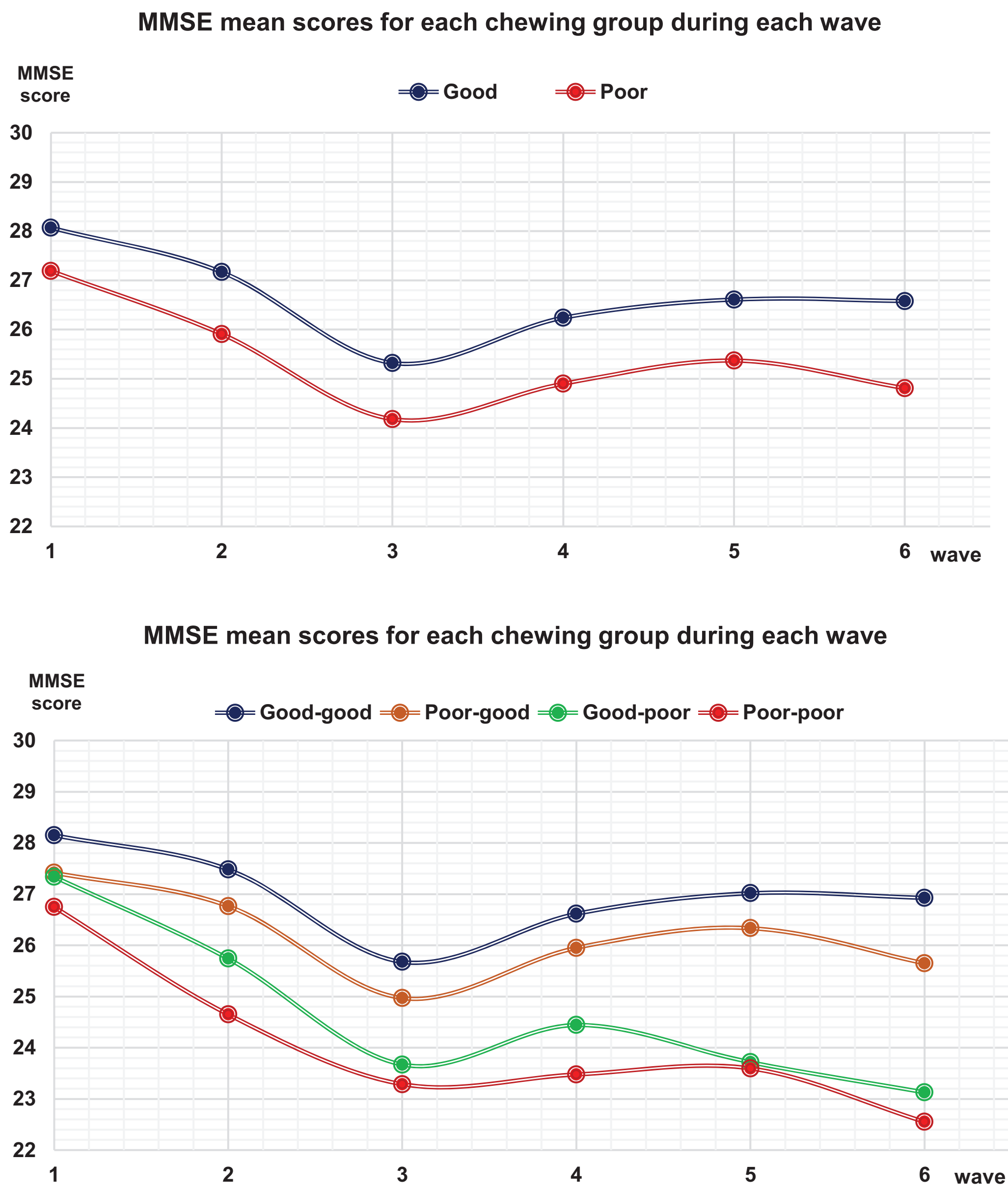

Figure 2. MMSE mean scores for each chewing group during each wave. MMSE = Mini Mental State Examination.

cognitive impairment. Therefore, loss of chewing function should be monitored and treated to delay and/or prevent age-induced cognitive impairment.

To date, many previous studies have performed analyses by considering loss of chewing function to be the same as the number of missing teeth. However, considering only the association between the number of missing teeth and cognitive function is insufficient given the findings of the present study. Many previous studies have reported that the number of missing teeth exhibits no association with cognitive impairment in people with missing teeth who improved their chewing ability with proper prosthesis or dentures. In a 6-year follow-up study involving facility-dwelling older adults, tooth number was not a significant factor.[35] Furthermore, in a population-based study involving participants age 65 and over, the length of time without proper restoration of missing teeth was the only factor that exhibited an association with cognitive impairment.[36] A 4-year follow-up study involving adults age 65 and older living in rural areas also confirmed that, even with missing teeth, use of dentures was not associated with the onset of dementia.[37] Moreover, in a study that investigated adults age 75 and over, loss of chewing ability was associated with cognitive impairment, whereas the number of teeth was not.[38] Notably, the brain is especially sensitive to morphological and biological changes that occur with aging.[39] Therefore, older adults may be more sensitive to loss of chewing ability than younger individuals. Taken together, these findings indicate that restoration of chewing ability in older adults with appropriate prostheses or dentures may delay or prevent the deterioration of brain function.

The results of the present study demonstrate that reduced chewing ability influences the incidence of cognitive impairment. Moreover, our results verified that degeneration and recovery of chewing function can accelerate or delay cognitive impairment, respectively. The findings of this large-scale population-based longitudinal study may help to establish the causal relationship between chewing ability and cognitive function.

Our study has some limitations. It is not an objective conclusion about association as a limitation of the survey. And unlike Model I, statistical analysis for Model II was performed without weighting. Because we considered the correlation from the second to sixth waves wave cognitive states measured repeatedly from the same participant, so we used GEE, which is difficult to apply weights. Notwithstanding these limitations, the authors opine that the results of our study are reliable enough to test the hypothesis that chewing ability is the causal relationship with mild cognitive impairment. Considering the limitations inherent in the present study, future longitudinal studies should use objective methods to assess oral and brain functions in order to more fully elucidate this causal relationship.

Acknowledgments

We would like to thank all the investigators, staff, and clinicians who participated in this study.

References

[1] United Nations. New York: United Nations; 2002. World Population Ageing, 1950-2050.
[2] Kim IK. Demographic transition and population aging in Korea. Korea J Popul Dev 1996;25:27–40.
[3] He W, Goodkind D, Kowal P. He W, Goodkind D, Kowal P. An aging world: 2015. U.S. Government Publishing Office, Washington, DC. 2016. An Aging World: 2015 Washington, DC: U.S. Census Bureau; 2016.
[4] Murray CJ, Atkinson C, Bhalla K, et al. The state of US health, 1990-2010: burden of diseases, injuries, and risk factors. JAMA 2013;310:591–608.
[5] Wimo A, Guerchet M, Ali GC, et al. The worldwide costs of dementia 2015 and comparisons with 2010. Alzheimers Dement 2017;13:1–7.
[6] Pankratz VS, Roberts RO, Mielke MM, et al. Predicting the risk of mild cognitive impairment in the Mayo Clinic Study of Aging. Neurology 2015;84:1433–42.
[7] Petersen RC, Doody R, Kurz A, et al. Current concepts in mild cognitive impairment. Arch Neurol 2001;58:1985–92.
[8] Jack CR, Petersen RC, Xu YC, et al. Prediction of AD with MRI-based hippocampal volume in mild cognitive impairment. Neurology 1999;52:1397–403.
[9] Prince M, Wimo A, Guerchet M, et al. Alzheimer's Disease International. World Alzheimer Report 2015: The Global Impact of Dementia: An Analysis of Prevalence, Incidence, Cost and Trend.
[10] Lee DW, Seong SJ. Korean national dementia plans: from 1st to 3rd. J Korean Med Assoc 2018;61:298–303.
[11] Kim S, Lee C. Status and Improvement Tasks of Dementia Management Plan. Seoul, South Korea: National Assembly Budget Office; 2014.
[12] Norton S, Matthews FE, Barnes DE, Yaffe K, Brayne C. Potential for primary prevention of Alzheimer's disease: an analysis of population-based data. Lancet Neurol 2014;13:788–94.
[13] Kato T, Usami T, Noda Y, et al. The effect of the loss of molar teeth on spatial memory and acetylcholine release from the parietal cortex in aged rats. Behav Brain Res 1997;83:239–42.
[14] Kimura Y, Ogawa H, Yoshihara A, et al. Evaluation of chewing ability and its relationship with activities of daily living, depression, cognitive status and food intake in the community-dwelling elderly. Geriatr Gerontol Int 2013;13:718–25.
[15] Kim EK, Lee SK, Choi YH, et al. Relationship between chewing ability and cognitive impairment in the rural elderly. Arch Gerontol Geriatr 2017;70:209–13.
[16] Tada A, Miura H. Association between mastication and cognitive status: a systematic review. Arch Gerontol Geriatr 2017;70:44–53.
[17] Kim MS, Oh BJ, Yoo JW, Han DH. The association between mastication and mild cognitive impairment in Korean adults. Medicine (Baltimore) 2020;99:e20653.
[18] Korean Longitudinal Study of Ageing. Seoul, South Korea: Korea Employment Information Service; 2018.
[19] Lexomboon D, Trulsson M, Wardh 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.
[20] Folstein MF, Folstein SE, McHugh PR. "Mini-mental state": a practical method for grading the cognitive state of patients for the clinician. J Psychiatr Res 1975;12:189–98.
[21] Kang Y, Na DL, Hahn S. A validity study on the Korean mini-mental state examination (K-MMSE) in dementia patients. J Korean Neurol Assoc 1997;15:300–8.
[22] Okamoto N, Morikawa M, Okamoto K, et al. Relationship of tooth loss to mild memory impairment and cognitive impairment: findings from the Fujiwara-kyo study. Behav Brain Funct 2010;6:1–8.
[23] Park H, Suk SH, Cheong JS, et al. Tooth loss may predict poor cognitive function in community-dwelling adults without dementia or stroke: the PRESENT project. J Korean Med Sci 2013;28:1518–21.
[24] Irwin M, Artin KH, Oxman MN. Screening for depression in the older adult: criterion validity of the 10-item Center for Epidemiological Studies Depression Scale (CES-D). Arch Intern Med 1999;159:1701–4.
[25] Cho MJ, Kim KH. Use of the Center for Epidemiologic Studies Depression (CES-D) scale in Korea. J Nerv Ment Dis 1998;186:304–10.
[26] Liang K, Zeger S. Longitudinal data analysis using generalized linear models. Biometrika 1986;73:13–22.
[27] Fang WL, Jiang MJ, Gu BB, et al. Tooth loss as a risk factor for dementia: systematic review and meta-analysis of 21 observational studies. BMC Psychiatry 2018;18:345.
[28] Listl S. Oral health conditions and cognitive functioning in middle and later adulthood. BMC Oral Health 2014;14:70.
[29] Hirano Y, Obata T, Takahashi H, et al. Effects of chewing on cognitive processing speed. Brain Cogn 2013;81:376–81.
[30] Park K, Hong GS. Predictors of chewing ability among community-residing older adults in Korea. Geriatr Gerontol Int 2017;17:78–84.
[31] Kim SJ, Lee JH, Han B, et al. Effects of hospital-based physical therapy on hospital discharge outcomes among hospitalized older adults with community-acquired pneumonia and declining physical function. Aging Dis 2015;6:174–9.
[32] Kim SJ, Lee JH, Nakagawa S, et al. Predictors of hospitalization among newly admitted skilled nursing facility residents: rethinking the role of functional decline. J Patient Care Res Rev 2014;1:70–6.
[33] Watanabe K, Ozono S, Nishiyama K, et al. The molarless condition in aged SAMP8 mice attenuates hippocampal Fos induction linked to water maze performance. Behav Brain Res 2002;128:19–25.
[34] Momose T, Nishikawa J, Watanabe T, et al. Effect of mastication on regional cerebral blood flow in humans examined by positron-emission tomography with ^{15}O-labelled water and magnetic resonance imaging. Arch Oral Biol 1997;42:57–61.
[35] Shimazaki Y, Soh I, Saito T, et al. Influence of dentition status on physical disability, mental impairment, and mortality in institutionalized elderly people. J Dental Res 2001;80:340–5.
[36] Li J, Xu H, Pan W, Wu B. Association between tooth loss and cognitive decline: a 13-year longitudinal study of Chinese older adults. PLoS One 2017;12:e0171404.
[37] Yamamoto T, Kondo K, Hirai H, Nakade M, Aida J, Hirata Y. Association between self-reported dental health status and onset of dementia: a 4-year prospective cohort study of older Japanese adults from the Aichi Gerontological Evaluation Study (AGES) project. Psychosom Med 2012;74:241–8.
[38] Elsig F, Schimmel M, Duvernay E, et al. Tooth loss, chewing efficiency and cognitive impairment in geriatric patients. Gerodontology 2015;32:149–56.
[39] Ono Y, Yamamoto T, Kubo KY, Onozuka M. Occlusion and brain function: mastication as a prevention of cognitive dysfunction. J Oral Rehabil 2010;37:624–40.