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**Assessment of subjective and objective
masticatory function among elderly
individuals with mild cognitive impairment**

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Department of Dentistry

**Assessment of subjective and objective
masticatory function among elderly
individuals with mild cognitive impairment**

Directed by Professor Bock-Young Jung

A Dissertation Thesis

Submitted to the Department of Dentistry

and the Graduate School of Yonsei University

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Doctor of Philosophy in Dental Science

Nan-Ju Lee

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This certifies that the Doctoral dissertation
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감사의 글

수련의 생활을 마치고 나와 학위과정을 계속 이어나간다는 것은, 주변의 수많은 유혹들과 안일함을 이겨내야 했고 나 자신과의 긴 싸움을 해야 했습니다. 하지만 그러한 시간을 버텨내니 마침내 박사과정이라는 도착지를 앞에 두게 되었습니다. 그 기나긴 싸움에서 도움을 주신 많은 분들께 감사의 말을 전하고 싶습니다.

결혼과 출산으로 제가 헤이해져 있을 때, 학업과 진료로 바쁜신 와중에도 저를 끊임없이 격려해주시고 때로는 채찍질로 마음을 다잡을 수 있게 도와주신 정복영 지도교수님께 고개 숙여 깊은 감사를 드립니다. 연구년임에도 불구하고 논문 마무리를 위해 꼼꼼하게 지도해 주시고 아낌없는 조언을 해주신 덕에 부족한 실력이었지만 논문을 완성할 수 있었습니다. 또한 부족한 논문임에도 심사를 위해 바쁜 시간을 쪼개어 많은 조언을 주신 김기덕, 방난심 교수님께 감사 드리고 존경을 표하며, 뒤에서 묵묵히 저의 길을 응원해 주시고 힘이 되는 말씀으로 살뜰히 신경 써주신 박원서 교수님께도 감사 드립니다. 그리고 연구의 설계부터 연구방법에 대한 아낌없는 조언으로 논문의 완성도를 높일 수 있게 지도해주신 김백일 교수님의 가르침에 깊은 감사를 드립니다. 연구시작부터 연구진행을 도와준 후배 김택빈 선생님을 비롯한 후배

수련의 선생님들, 여러모로 논문 진행에 많은 도움을 준 최이슬/박경미
선생님, 그리고 예방치과 김효정/김 별 선생님께 고마움을 전합니다.

늘 막내딸이 잘 되길 응원해주시고 학위과정 잘 마칠 수 있게 물심양면
뒷바라지 해주신 저의 큰 버팀목인 이동열 아버님, 김복자 어머니님,
그리고 늘 따뜻하게 품어주신 조병만 아버님, 김경숙 어머니님께 모두
감사의 뜻을 전하며, 무엇보다도 가장 가까이서 아내의 길을 응원하고
묵묵히 육아와 가사를 도와준 사랑하는 나의 남편에게도 한없는 사랑과
고마움을 전합니다. 마지막으로 엄마의 손길이 많이 필요한 시기임에도
불구하고 논문 준비한다고 많은 시간을 같이 보내주지 못해 미안하고,
그럼에도 불구하고 너무나 건강하고 예쁘게 자라준 사랑하는 나의 아들
성현이에게 이 기쁨을 나누고자 합니다.

두서없이 적었지만, 이 모든 과정에서 힘이 되고 응원해주신 모든 분들께
다시 한 번 감사를 전합니다.

2021년 12월
이 난 주 올림

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ABSTRACT

**Assessment of subjective and objective masticatory
function among elderly individuals with
mild cognitive impairment.**

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(Directed by Professor Bock-Young Jung, D.D.S., M.S.D., Ph.D.)

Mild cognitive impairment (MCI) is the stage between the expected cognitive decline of normal aging and the more serious decline of dementia and recently, many research results have shown that cognitive decline is highly related to masticatory function including the number of teeth or chewing ability. Therefore in this cross-sectional study, we aimed to confirm the association between cognitive decline and masticatory function and to determine which specific indicators, including both subjective and objective

factors, are significantly associated with cognitive decline in elderly individuals.

A total of 123 elderly participants (mean age 76.5 ± 6.5 years; 82 females (66.7%) and 41 males (33.3%)) were included in this cross-sectional study. Cognitive function was evaluated by the Korean version of the Mini-Mental State Examination (KMMSE), which is a general screening tool for cognitive impairment, and oral examinations were performed. Questionnaires for subjective evaluations were administered, and dynamic masticatory function evaluations, such as mixing ability tests and bite force measurements were performed. The number of remaining teeth and posterior teeth were significantly lower in the MCI group than in the normal cognition group ($P=0.0296$, 0.0097). Also, bite force and the MAI were significantly lower in the MCI group ($P=0.0479$, <0.0001), and posterior support status showed significant differences between normal cognition and MCI groups ($P=0.0147$). However, only the MAI, representing dynamic masticatory performance, in the MCI group was 13.81 points lower than that in the normal cognition group (CI: -17.19, -10.43), and showed significant association with MCI regardless of sex, age and the presence of removable prostheses (RPs) ($P<0.0001$). This significant association was also confirmed in each group according to the presence or absence of RPs ($P<0.0001$).

In conclusion, among the masticatory factors assessed, the MAI was significantly associated with MCI in elderly patients after adjusting for sex, age and the presence of RPs. The findings of this study suggest that functional treatment that allows a new prosthesis to harmonize well with the surrounding structures and improves the masticatory performance is important.

Key Words : Masticatory function, Mild cognitive impairment (MCI), Mixing ability index (MAI), Mixing ability test (MAT), Korean Mini Mental State Examination (KMMSE)

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I . INTRODUCTION

As the aging population is growing rapidly worldwide, aging-related health problems such as cognitive impairment and dementia have begun to stand out as social issues in terms of welfare, because cognitive impairment makes it difficult for elderly individuals to live independently and harms not only the patients themselves but also the family members who take care of them. The World Health Organization(WHO) reported that there were 50 million dementia patients around the world in 2018 and that the number would be predicted to reach 82 million in 2030 (Organization 2019). The

cognitive impairment prevalence rate was reported to be over 40% according to recent community-based surveys in Japan. In Korea, 750,000 elderly people over 65 years old suffer from dementia, and the number is predicted to double every 17 years. Additionally, the Korean Ministry of Health and Welfare forecasts that the number of dementia patients will grow to 2.71 million by 2050 (Kim et al. 2011; Saito et al. 2013).

Mild cognitive impairment (MCI) is the stage between the expected cognitive decline of normal aging and the more serious decline of dementia. MCI is characterized by problems with memory, language, thinking or judgment. MCI is clinically very important when considering that MCI may likely progress to dementia, and the study of individuals with MCI may provide insight into the pathogenesis of dementia as a predementia stage. According to the findings of a previous long-term (i.e., 6 years) follow-up, 80% of individuals with MCI developed dementia (Petersen 2003). Various risk factors for cognitive impairment and dementia have been suggested. These factors, including demographic (e.g., increasing age, sex especially the female sex, lower education level), genetic, lifestyle (e.g., smoking, drinking alcohol, diet, exercise) and medical (e.g., cardiovascular disease, heart failure, hypertension, high cholesterol, diabetes mellitus) factors are intricately related to each other and form a complex model (Lexomboon et al. 2012; Qiu, De Ronchi, and Fratiglioni 2007). Recently, many studies on

the relationship between masticatory and cognitive function have reported that masticatory function is mutually associated with cognitive impairment, and although which comes first is not yet known, masticatory dysfunction is one of the risk factors for cognitive decline in elderly individuals and is thus a confounding factor related to cognitive impairment.

Masticatory dysfunction refers to the decrease in or deterioration of masticatory function caused by a structural factor (e.g., number of remaining teeth, posterior occlusal contact), functional factor (e.g., masticatory performance, bite force) or both factors combined (Alvarenga et al. 2019). In fact, many studies have found a significant association between tooth loss and cognitive impairment (Nilsson, Berglund, and Renvert 2014; Park et al. 2013), and an increasing number of studies have supported the link between tooth loss and cognitive decline by explaining the possible mechanism, such as an increase in proinflammatory mediators that cause neuroinflammation and malnutrition due to tooth loss (Fang et al. 2018). In investigations on masticatory function, Kimura et al. (Kimura et al. 2013) and Kim et al. (Kim et al. 2017) found that a poor chewing ability was significantly associated with cognitive impairment, and Takeshita et al. (Takeshita et al. 2016) and Ikebe et al. (Ikebe et al. 2018) reported that the maximal bite force was positively associated with cognitive function by evaluating a large group of 1962 older adults. Several mechanisms underlying this relationship between

mastication and cognitive function have been suggested. Cognitive impairment is due to brain neurophysiological changes, including cortical atrophy and the deterioration of neurons, cells and synapses, especially when intraneuronal changes, such as beta-amyloid deposition and neuritic plaque formation take place in brain regions controlling learning, memory and emotional behavior, which is also known to be related to chewing function (Mattson 2004; Thal, Griffin, and Braak 2008). In addition, Momose et al. (Momose et al. 1997) showed that functional movement for mastication increased regional blood flow and cerebral blood flow by using functional magnetic resonance imaging and positron-emission tomography to measure brain activity. Additionally, researchers found that mastication changed the blood flow within the internal carotid artery, stimulating the oxygenation and perfusion of the brain area related to memory, especially the hippocampus, and focused on the association between mastication and the activation of different parts of the brain including the prefrontal cortex (PFC) (Onozuka et al. 2003; Oue et al. 2013). Onozuka et al. (Onozuka et al. 2003) reported that chewing gum increased neuronal activity and oxygenation in various parts of the brain and contributed to memory and learning. Although it is still unclear which mechanism directly affects the brain function activated by mastication, the fact that mastication activates brain function has reached a broad consensus.

Cognitive function has been assessed using various methods including a neuropsychological test for extensive assessment and the Mini-Mental State Examination (MMSE) and Montreal Cognitive Assessment (MoCA) for general assessment (Fujiwara et al. 2010). The MMSE is a standardized, widely used tool for the evaluation of cognitive function and has the advantage of being able to quantitatively evaluate the degree of cognitive impairment in 5 to 10 minutes, including tests of orientation, attention, memory, language and visual-spatial skills (Kang et al. 2016). Folstein et al. (Folstein et al. 1985) demonstrated that the MMSE is fairly sensitive and has reasonably good positive predictive value in relation to diagnoses of cognitive impairment. The MoCA is a brief cognitive screening tool developed for detecting MCI in older people and demonstrates reliable validity (Nasreddine et al. 2005). These tests were modified and translated to fit the customs of each population, for example, the Korean version of the Mini-Mental State Examination (KMMSE) in Korea (Kang et al. 2016) and the Japanese version of the MoCA (MoCA-J) in Japan.

In addition to the relevant objective masticatory factors, which can be determined by the dynamic masticatory function (sieving method, chewing gum, mixing ability test) and the static masticatory function (number of teeth, posterior occlusal contact, bite force) (Takagi et al. 2017), subjective factors, such as the mental or psychological condition of participants, could

influence masticatory function (Ikebe et al. 2018; Kim et al. 2017; Kimura et al. 2013; Nilsson, Berglund, and Renvert 2014; Park et al. 2013; Takagi et al. 2017; Takeshita et al. 2016). And some studies have shown that prosthetic treatment, such as with removable prostheses (RPs), implants and implant overdentures is effective in preserving the cognitive function of individuals by improving masticatory function, such as masticatory performance or efficiency (Boven et al. 2015; Campos et al. 2017).

Many previous studies have revealed the relationship between masticatory function and cognitive function in elderly individuals (Lin 2018; Shin et al. 2020), and Alvarenga et al. (Alvarenga et al. 2019) confirmed that masticatory dysfunction is positively associated with an increased risk of cognitive decline. However, few studies have identified which specific factors, including both subjective and objective factors of masticatory function, are significantly related to cognitive function.

In this cross-sectional study, both cognitive function and masticatory function were evaluated in elderly individuals and the difference in each masticatory function between the normal cognition and MCI groups was investigated. The aim of this study was to identify which subjective and objective confounding factors of masticatory function are significantly associated with MCI and to suggest a guide for prosthetic treatment to delay or prevent the onset of cognitive decline in elderly individuals.

II. MATERIALS & METHODS

2.1. Study participants

This cross-sectional study was approved by the institutional review board committee of the Yonsei School of Dentistry (No. 2-2019-0009). Among the patients over 65 years old who visited Yonsei University Dental Hospital of Advanced General Dentistry from March 2019 to February 2020, participants who were able to communicate, answer the questions and fill out the questionnaires on their own were included. In consideration of the period of adaptation to new prostheses, participants who had completed prosthetic treatment at least 6 months prior and had no problems chewing were included.

Participants 1) with a history of a congenital or acquired diseases, such as cerebral infarction, or psychiatric illness, including depression and dementia, that could make it difficult to communicate with researchers and perform their daily activities independently (Cardoso et al. 2019; Park et al. 2013); 2) with difficulty performing dynamic masticatory function tests with maximal effort because of their health problems, such as cardiovascular disease, general weakness after surgery (including ward patients) and Parkinson's disease (Takagi et al. 2017); and 3) with temporomandibular joint pain or 3 degrees of mobility for multiple teeth were excluded from this study to avoid bias from nonmasticatory function-related factors. Out of 129 participants, 6 participants with incomplete data were excluded, and a total of 123 participants were

finally included in this study. Informed consent was obtained from each individual. The sample size was calculated using G*power 3.1 software (Kiel University, Kiel, Germany) with an α of 0.05, a power of 0.99 and an effect size of 1.68.

2.2. Study design

Cognitive and masticatory function assessments were performed on all participants. Cognitive function was assessed by 1 trained researcher using the K-MMSE. For masticatory function evaluation, both subjective and objective assessments were performed. The subjective masticatory ability assessment was conducted using a simple questionnaire, the Key Food Intake Ability (KFIA) questionnaire, to determine the participant's masticatory ability. Additionally, a chewing test and bite force measurement were performed to assess the participant's dynamic objective masticatory function while wearing an RP and the number of remaining teeth, the number of posterior teeth, posterior occlusal support and the presence of RPs were recorded for static objective masticatory function assessment.

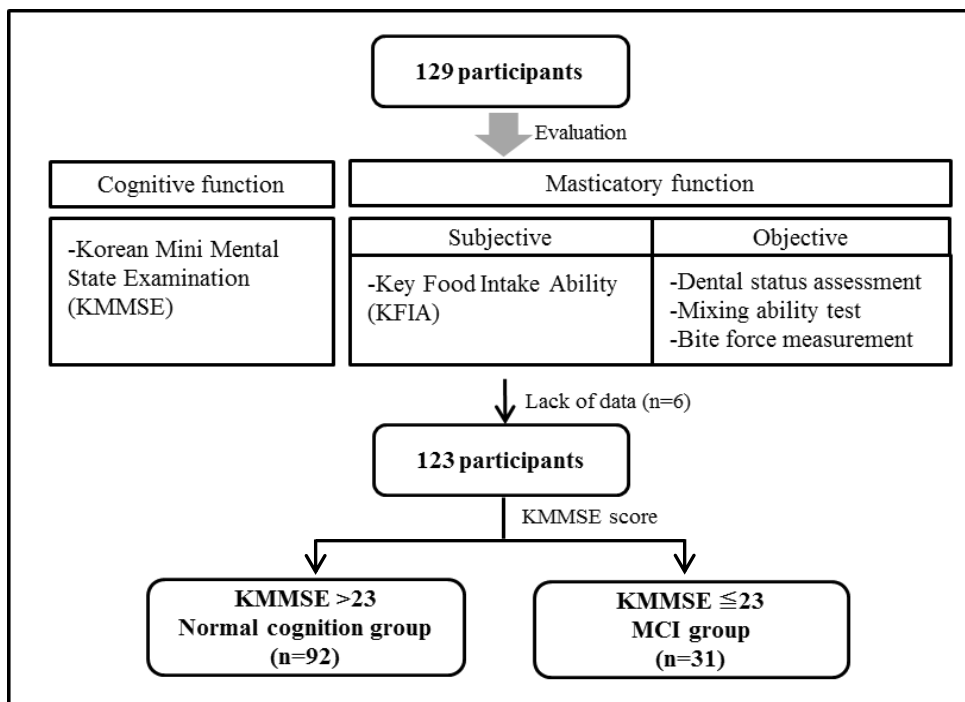
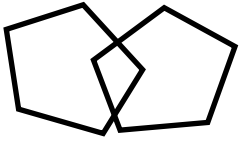


Figure 1. Study design.

2.2.1. Evaluation of cognitive function

The K-MMSE consists of 30 questions in the following 6 domains: registration, attention and calculation, recall, language, ability to follow simple commands and orientation. Each question is rated as 0 or 1 point and those points are summed to create a total K-MMSE score that ranges from 0 to 30, in which lower scores indicate more severe cognitive impairment. In this study, the MCI group included participants with a KMMSE score of 23 based on the reference scores reported in previous studies, whereas Kramer et al divided their participants into a ‘MCI’ group with a KMMSE score of 23 points or less and a ‘normal’ group with a KMMSE score of 24 points or more (Kramer et al. 1985). In this study, participants in the MCI group were recommended to visit a neurologist for further evaluation.

Table 1. Test form of the Korean Mini-Mental State Examination (K-MMSE).

항 목		점 수	
A. 지남력 (시간)	년	0 1	
	월	0 1	
	일	0 1	
	요일	0 1	
	계절	0 1	
B. 지남력 (장소)	나라	0 1	
	시, 도	0 1	
	무엇 하는 곳	0 1	
	현재 장소 명	0 1	
	몇 층	0 1	
C. 기억등록	비행기	0 1	
	연필	0 1	
	소나무	0 1	
D. 주의집중 및 계산	100 -7	0 1	
	-7	0 1	
	-7	0 1	
	-7	0 1	
	-7	0 1	
E. 기억회상	비행기	0 1	
	연필	0 1	
	소나무	0 1	
F. 언어 및 시공간구성	이름대기	시계	0 1
		볼펜	0 1
	명령시행	종이를 뒤집기	0 1
		반으로 접은 다음	0 1
		저에게 주세요	0 1
	따라 말하기	백문이 불여일견	0 1
	오각형 그리기		0 1
	읽기	눈을 감으세요	0 1
	쓰기		0 1
	Total score :		

2.2.2. Dental status assessment

The number of remaining teeth was determined by counting the teeth that were natural or restored, except third molars and root rests. In the case of implants, if they were restored with a fixed prosthesis, they were counted as remaining teeth. However, in the case of implant-retained RPs, the implants were excluded from the number of remaining teeth because they represented RPs, and the presence of RPs was recorded separately. Posterior occlusal support was recorded using the Eichner index based on the condition of posterior occluding contacts between the maxilla and the mandible, with 3 classifications as follows: Eichner A, occluding pairs in four bilateral posterior supports; Eichner B, one to three occluding pairs or occluding contacts in the anterior region; and Eichner C, no occluding pair (Ikebe et al. 2010).

2.2.3. Mixing ability test

The mixing ability test was developed by Sato et al. (Sato et al. 2003), and was used to measure and evaluate chewing ability and masticatory performance in this study. The mixing ability index (MAI) was calculated by analyzing the degree of color mixing and the shape and wideness of a chewed wax specimen, which were integrated into one-dimensional values. A two-color wax cube ($12 \times 12 \times 12 \text{ mm}^3$) was used, and participants were instructed to chew the wax specimen ten times with a normal chewing pattern using their own habitual masticatory side while seated with the head upright and in an unsupported natural position.

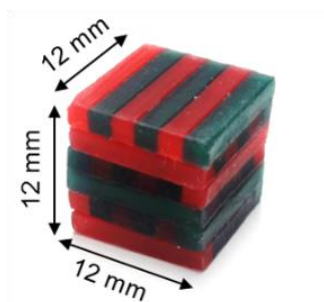


Figure 2. Wax specimen

This chewing test was repeated two times per participant and analyzed within three days. All chewed wax specimens were photographed on both sides using a digital single-lens reflex camera (D80, Nikon Co., Tokyo, Japan) under standardized conditions of distance and light and those images were saved as JPEG files (Kim et al. 2019). In each image, using a digital image

analyzer (Image-Pro Plus® version 6.0, Media Cybernetics, Inc., Bethesda, MD, USA), the total projection area, area above 50 Mm in thickness, maximum length, maximum width, and area without color mixing were selected and calculated by a single independent examiner to eliminate measurement error.

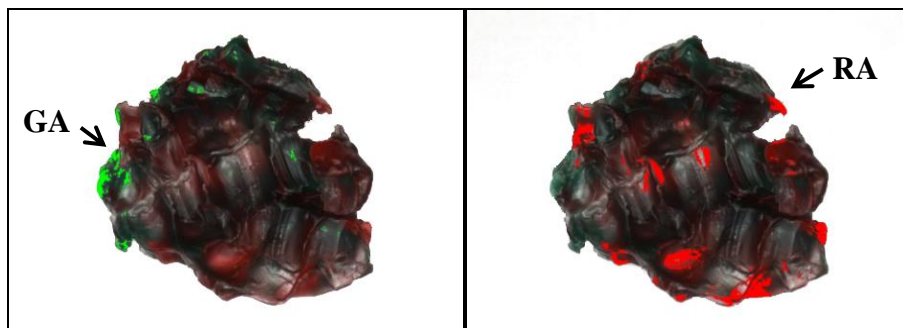


Figure 3. Identification of the area without color mixing in color images

Example of color image analysis using a digital image analyzer (Image-Pro Plus® version 6.0, Media Cybernetics Inc., Bethesda, MD, USA). The unmixed areas were identified and are marked with GA (green area) and RA (red area). The unselected areas were judged to be mixed (i.e., the combination of the two colors of wax).

All measured data were used to calculate the MAI, on a scale of 0–100 points, by using a modified method suggested by Jeong et al. (Jeong et al. 2010), and the average of two specimens for each participant was obtained. A higher score indicated better masticatory performance, and a relative comparison of the MAI between the participants was conducted (Kim et al. 2019).

2.2.4. Bite force measurement

Prior to measurement, participants were instructed and trained to bite with their own maximum force several times at the maximal intercuspal position for 3 seconds. Participants were asked to sit in a comfortable position and look forward with their head upright while keeping Frankfort's horizontal plane parallel to the ground. A pressure-sensitive film (Dental Prescale 50H, GC, Japan) was positioned into the mouth, and the film size was checked to ensure that all teeth were adequately covered. Bite force measurements were conducted and analyzed using a bite force analyzer (OCCLUSER 709, GC, Japan).

2.2.5. KFIA

Subjective masticatory ability (Takagi et al. 2017) was assessed by the self-assessed questionnaires, devised and suggested by Kim et al. (Kim et al. 2009); these questionnaires asked participants whether they had any difficulties chewing five key foods, including peanuts, carrots, caramel, dried squid, and diced radish kimchi. Responses were based on a five-point Likert scale depending on the degree of discomfort. The average score for the five key foods was recorded as the KFIA score, with a higher score indicating better subjective masticatory function.

Table 2. Questionnaire for evaluation of the KFIA score.

Food list	Cannot chew at all(1)	Difficult to chew(2)	Cannot say either(3)	Can chew some(4)	Can chew well(5)
1. Peanut					
2. Carrot					
3. Dried squid					
4. Caramel					
5. Radish Kimchi					
Total score	Average				

2.5. Statistical analysis

All statistical analyses were carried out using SAS 9.4 software (SAS Institute Inc., Cary, NC, USA.) and were judged based on the significance level of 0.05. The Wilcoxon rank sum test was used to determine differences between the groups in terms of continuous dependent variables and the chi-square test was used for categorical variables. To determine the statistical correlation between cognitive function and masticatory function, multiple generalized linear and logistic regression analyses were performed. The dependent variables were age, the KFIA score, the number of teeth, the number of posterior teeth, bite force, the MAI and the Eichner index, and the independent variable was the KMMSE score.

III. RESULTS

3.1. Characteristics of participants according to KMMSE scores

A total of 123 participants ranging from 65 to 93 years old participated in this study. The participants consisted of 82 women (66.7%) and 41 men (33.3%) with a mean age of 76.5 ± 6.5 years old, with 31 out of 123 participants in the MCI group and the remainder in the normal cognition group. Table 3 shows the demographic characteristics and the comparison of objective and subjective masticatory function assessments between the MCI and normal cognition groups. Regarding the sex distribution, the proportion of females was high in both the MCI and normal cognition groups, but there was no significant difference in the sex distribution between these two groups ($P=0.5569$). The mean age in the MCI group was significantly older than that in the normal cognition group ($P=0.0108$). The KMMSE score in the MCI group (20.06 ± 3.65) was also significantly lower than that in the normal cognition group (27.88 ± 1.47) ($P < 0.0001$). The difference in the KFIA score, reflecting subjective masticatory function, between the normal cognition (3.60 ± 1.07) and MCI groups (3.33 ± 0.81) was not significant ($P=0.0764$), even though the MAI, representing objective masticatory function, was significantly different between the two groups. The number of remaining teeth and posterior teeth was significantly lower in the MCI group than in the normal cognition group ($P=0.0296, 0.0097$). Among objective factors of masticatory function,

the bite force in the MCI group was 529.90 ± 361.16 , which was significantly lower than that in the normal cognition group (683.22 ± 389.95) ($P=0.0479$), and the MAI, representing chewing ability, was significantly lower in the MCI group (56.60 ± 8.59) than in the normal cognition group (70.10 ± 7.41) ($P < 0.001$). For the Eichner index, the Eichner A proportion was higher in the normal cognition group and the Eichner B+C proportion was higher in the MCI group; these differences were significant ($P=0.0041$). The percentage of overall participants wearing RPs was 36.6%, which was more than one third, and the difference in the percentage of participants wearing RPs between the normal cognition and MCI groups was significant ($P=0.0147$).

Table 3. Characteristics of participants according to KMMSE scores (n=123).

Dependent variable	Total	Normal cognition group	MCI group	P-value*
N	123	92	31	
Sex M:F N(%)	41(33.33) :81(66.67)	32(34.78) :60(65.22)	9(29.03) :22(70.97)	0.5569†
Age	76.54±6.53, 76.00(11.00)	75.51±5.59, 75.50(8.00)	79.61±8.08, 82.00(17.00)	0.0108
MMSE score	25.91±4.06, 27.00(6.00)	27.88±1.47, 28.00(2.00)	20.06±3.65, 21.00(5.00)	<.0001
KFIA score	3.53±1.02, 3.60(1.40)	3.60±1.07, 3.60(1.40)	3.33±0.81, 3.20(1.00)	0.0764
Number of remaining teeth	19.73±7.88, 22.00(10.00)	20.58±7.59, 22.50(9.00)	17.23±8.30, 19.00(12.00)	0.0296
Number of posterior teeth	10.29±4.88, 12.00(6.00)	10.87±4.87, 12.00(6.50)	8.58±4.57, 9.00(7.00)	0.0097
Bite force	644.58±387.25, 560.80(503.50)	683.22±389.95, 600.55(517.2)	529.90±361.16, 509.00(462.10)	0.0479
MAI	66.70±9.68, 68.43(11.89)	70.10±7.41, 71.10(8.87)	56.60±8.59, 58.40(11.94)	<.0001
Eichner A:B+C N(%)	67(54.47) :56(45.53)	57(61.96) :35(38.04)	10(32.26) :21(67.74)	0.0041†
Non- RP: RP N(%)	78(63.41) :45(36.59)	64(69.57) :28(30.43)	14(45.16) :17(54.84)	0.0147†

Mean±SD, Median(IQR).

*Wilcoxon rank sum test.

†Chi-square test

3.2. Comparison of masticatory function according to the presence of RPs

All participants (n=123) were classified according to the presence of RPs, and the results of the subjective and objective masticatory function evaluations in the MCI and normal cognition groups are shown in Table 4. In the non-RP group, the differences in the sex distribution, KFIA score, number of remaining teeth, number of posterior teeth and bite force between the normal cognition and MCI groups were not significant. However, the differences in age and the MAI between the normal cognition and MCI groups were statistically significant ($P < 0.05$). In the RP group, the differences in the sex distribution, age, KFIA score, number of remaining teeth, number of posterior teeth and bite force were not significant, but the MAI was significantly different between the normal cognition and MCI groups ($P = 0.0001$). That is, the MAI showed significant differences between the MCI and normal cognition groups regardless of the presence of RPs.

Table 4. Comparison of masticatory function according to the presence of RPs (n=123).

Dependent variable	Non-RP group		p-value*	RP group		p-value*
	Normal cognition group	MCI group		Normal cognition group	MCI group	
N	64	14		28	17	
Sex M:F N	24:40	4:10	0.5281†	8:20	5:12	0.9999†
Age	74.45±5.93, 74(8.5)	81.71±7.86, 84(12)	0.0025	77.93±3.84, 78(5)	77.88±8.07, 78(14)	0.9628
KMMSE score	27.78±1.58, 28(2)	19.79±3.42, 20.5(5)	<.0001	28.11±1.17, 28(2)	20.29±3.92, 22(3)	<.0001
KFIA score	3.85±0.88, 3.8(1.2)	3.69±0.70, 3.5(1)	0.3329	3.03±1.25	3.04±0.80	0.9999
Number of remaining teeth	24.45±3.53, 25.5(5)	23.07±3.45, 23.5(4)	0.1359	11.71±6.93, 12.5(11)	12.41±8.05, 12(10)	0.8795
Number of posterior teeth	13.44±2.36, 14(3)	12.21±2.36, 12.5(2)	0.0736	5±3.94, 4(7)	5.59±3.68, 6(6)	0.6317
Bite force	746.46±374.39, 707.25(542.5)	602.93±406.69, 525.35(419.4)	0.1334	538.66±392.81, 441.1(467.6)	469.76±318.87, 391(487.5)	0.6419
MAI	70.6±7.66, 71.26(8.04)	56.07±9.8, 58.8(11.81)	<.0001	68.96±6.79, 70.18(9.88)	57.05±7.75, 56.42(11.34)	0.0001
Eichner A:B+C N	55:9	9:5	0.0558†	2:26	1:16	0.9999†

Mean±SD, Median(IQR).

*Wilcoxon rank sum test

†Fisher's exact test

3.3. Association between MCI and masticatory function factors

Table 5 shows the results of simple and multiple linear regression analyses for investigating the association of MCI with the results of several subjective and objective masticatory function assessments. Model 1 is the crude simple generalized linear model. The KFIA score and bite force were not significantly different between the MCI and normal cognition groups in the crude model. The number of remaining teeth in the MCI group was 3.35 less than that in the normal cognition group (confidence interval (CI): -6.55, -0.16), and this difference was statistically significant ($P=0.0400$). The number of posterior teeth, in the MCI group was 2.29 less than that in the normal cognition group (CI: -4.26, -0.32), and this difference was statistically significant ($P=0.0233$). In the case of the MAI, which represents dynamic objective masticatory function, the MAI in the MCI group was 13.50 points lower than that in the normal cognition group (CI: -16.67, -10.32), a statistically significant difference ($P<0.0001$). Thus, according to Model 1* of the simple logistic regression, the odds ratio of having incomplete posterior occlusal support was significantly (3.42 times) higher in the MCI group than in the normal cognition group in the crude model ($P=0.0052$).

Model 2 is a multiple generalized linear model adjusted by age, sex and the presence of RPs, and the results showed that the KFIA score, number of remaining teeth, number of posterior teeth and bite force were not significantly

different between the MCI and normal cognition groups. However, the MAI in the MCI group was 13.81 points lower than that in the normal cognition group (CI: -17.19, -10.43), and this difference was statistically significant ($P < 0.001$). The odds ratio of incomplete posterior occlusal support was 3.12 times higher in the MCI group than in the normal cognition group, with no statistical significance ($P = 0.1124$) in Model 2*.

Table 5. Association between MCI and masticatory function factors.

Dependent variable	Model 1(crude)				Model 2(adjusted)			
	beta	95% CI		P-value	beta	95% CI		P-value
KFIA score	-0.27	-0.69	0.15	0.2042	-0.03	-0.45	0.38	0.8723
Number of remaining teeth	-3.35	-6.55	-0.16	0.0400	-0.74	-3.03	1.55	0.5238
Number of posterior teeth	-2.29	-4.26	-0.32	0.0233	-0.22	-1.53	1.10	0.7439
Bite force	-153.32	-310.79	4.16	0.0563	-98.71	-258.17	60.75	0.2227
MAI	-13.50	-16.67	-10.32	<.0001	-13.81	-17.19	-10.43	<.0001

	Model 1*			Model 2*				
	OR	95% CI		P-value	OR	95% CI		P-value
Eichner index B+C (ref. A)	3.42	1.44	8.10	0.0052	3.12	0.77	12.72	0.1124

The independent variable was the MCI group (ref: normal cognition group)

Model 1 is a simple generalized linear model

Model 1* is a simple logistic regression model

Model 2 is a multiple generalized linear model adjusted by sex, age and the presence of RPs

Model 2* is a multiple logistic regression model adjusted by sex, age and the presence of RPs

3.4. Association between MCI and masticatory function factors according to the presence of RPs.

Table 6 shows whether there was a difference between the normal cognition and MCI groups according to the presence of RPs, because wearing RPs to replace missing teeth has the potential to improve chewing efficiency and hypothetically has an effect on cognitive impairment.(Boven et al. 2015; Campos et al. 2017; Krall, Hayes, and Garcia 1998; Polzer et al. 2012; Van der Bilt 2011) The KFIA score, number of remaining teeth, number of posterior teeth and bite force had no statistically significant association with MCI regardless of RP use. However, in the MCI group, the MAI was 14.06 points lower (CI: -19.86, -9.35) in the non-RP group and 11.85 points lower (CI: -15.87, -7.83) in the RP group than the MAI in the normal cognition group regardless of the presence of RPs ($P < 0.0001$). For the Eichner index, the odds ratio of having incomplete posterior occlusal support was higher in the MCI group in both the non-RP group (OR: 4.03, CI: 0.81, 20.18) and the RP group (OR: 1.36, CI: 0.10, 18.85), but the difference was not significant.

Table 6. Association between MCI and masticatory function factors according to the presence of RPs.

Dependent variable	Multiple generalized linear model*							
	Non-RP group				RP group			
	Beta	95% CI	P-value*	Beta	95% CI	P-value*		
KFIA score	-0.10	-0.65	0.45	0.7203	0.01	-0.69	0.71	0.9883
Number of remaining teeth	-2.14	-4.40	0.12	0.0633	0.71	-3.94	5.36	0.7592
Number of posterior teeth	-0.98	-2.51	0.55	0.2077	0.59	-1.86	3.03	0.6293
Bite force	-114.87	-359.87	130.14	0.3532	-70.99	-287.91	145.94	0.5124
MAI	-14.60	-19.86	-9.35	<.0001	-11.85	-15.87	-7.83	<.0001

Dependent variable	Multiple logistic regression*							
	Non-RP group			RP group				
	OR	95% CI	P-value*	OR	95% CI	P-value*		
Eichner Index B+C (ref. A)	4.03	0.81	20.18	0.0900	1.36	0.10	18.85	0.8174

The independent variable was the MCI group (ref. normal cognition group).

*Adjusted by sex and age.

IV. DISCUSSION

Cognitive impairment and dementia make it difficult for elderly individuals to live independently and are the main causes of decreased quality of life (QOL), along with physical frailty. For this reason, recognizing the risk factors and preventing cognitive impairment and dementia is very important. The relationships between various risk factors for cognitive function can be mutual, confounded and mediated by each other, resulting in a complex causal pathway. To investigate the correlation between cognitive function and masticatory function and identify key factors to prevent or delay MCI in elderly individuals, both subjective and objective masticatory factors were investigated and measured in this study. The investigation of subjective masticatory function, generally self-assessed, showed other aspects of mastication such as adoptive and psychological factors that cannot be determined from the objective assessment. Most clinical studies on masticatory functions have performed both objective and subjective assessments, but for the study of the relationship between MCI and oral function, a subjective method has not been used due to the lack of a standardized method and the reliability of data obtained from participants with cognitive decline (Weijenberg et al. 2015). However, both subjective and objective methods were assessed in this study because the target participants were physically healthy and independent in their daily lives, and a previous

study reported that chewing ability measured using a subjective masticatory function assessment had a significantly positive association with cognitive impairment (Lexomboon et al. 2012). Therefore, it was expected that the results of the subjective and objective masticatory assessments may not necessarily agree to some degree (Komiyama et al. 2020), but a consistent tendency between them might be found. However, the difference in the KFIA score, reflecting subjective masticatory function, between the normal cognition and MCI groups in this study was not significant ($P=0.0764$), even though a significant difference in the MAI, reflecting objective masticatory function, was found between the MCI and normal cognition groups. This finding is supported by previous studies reporting that older people tend to overestimate their physical function without an awareness of latent declines (Komiyama et al. 2020), and 22.4%–39% disagreement between objective and subjective masticatory function has been reported (Kimura et al. 2013; Takagi et al. 2017). This phenomenon could be explained as ‘anosodiaphoria’, which is a condition indifferent to the existence of one’s handicap and a major symptom of MCI originating from the reduced neuronal response in the frontal and parietal cortical midline structures (Ries et al. 2007). Other previous cross-sectional studies showed that the results of both assessments were influenced by different factors, e.g., the subjective assessment was significantly associated with depression, cognitive function, bite force, and mouth dryness, while the

objective assessment was related to skeletal muscle mass, number of functional or remaining teeth and bite force (Komiyama et al. 2020; Takagi et al. 2017).

Many previous studies have reported that the dental status such as the number of teeth, number of occluding teeth, number of occluding pairs and occlusal contact area, is a factor that influences cognition (Miquel, Aspiras, and Day 2018; Van der Bilt 2011). These structural factors can affect functional masticatory performance and coordination with the neuromuscular system. A number of studies reported fewer teeth and greater difficulty chewing food in cognitively impaired participants than in participants with normal cognition (Alvarenga et al. 2019; Nilsson, Berglund, and Renvert 2014; Park et al. 2013). Teixeira et al. (Teixeira et al. 2014) proposed that the loss of teeth could be a factor provoking cognitive impairment and stressed the need to study the relationship between the two aspects. However, in the present study, there was a significant difference in the number of teeth and posterior teeth (Table 3) but there was no significant correlation between the number of remaining teeth or the number of posterior teeth alone and MCI (Table 5), even after adjusting for sex, age and the presence of RPs. The tooth number has been shown to be significantly associated with general cognitive function in a few studies, but most of their participants were edentulous or had fewer than 10 teeth (Scherder et al. 2008; Weijenberg et al. 2015). However, in

this study, mean number of both normal and MCI groups was 20.58 ± 7.59 and 17.23 ± 8.30 respectively, which number can be considered as functionally acceptable from the shortened dental arch concept (Fueki and Baba 2017), therefore no significant association between the number of teeth and cognitive ability might be seen in this study. On the other hand, elderly people are more likely to lose teeth and to undergo restorative treatment for missing teeth, and this tendency becomes more apparent as aging progresses, it is difficult to determine the validity of assessing the number of remaining teeth in investigating the association with cognitive function. Ikebe et al. (Ikebe et al. 2018) reported that the number of teeth was significantly related to the cognitive score in a group in their 70s, but not in a group in their 80s, and the occlusal force had a statistically significant association with cognitive function in both the group in their 70s and the group in their 80s. On the basis of these findings, it can be speculated that most of the participants in the group in their 80s had experienced tooth loss, resulting in a nonsignificant association with cognitive function, whereas the occlusal force showed a different aspect of objective masticatory function independent of the number of remaining teeth.

The posterior occlusal contact condition was assessed using the Eichner index, which demonstrates posterior occlusal support and provides a standard to determine the degree of morbidity of dentition (Eichner 1990). Since simply the number of teeth or the number of posterior teeth does not provide sufficient information on masticatory function, it was expected that a

correlation with cognitive function could be found by examining the occlusion of the posterior teeth, which is responsible for mastication. In a simple comparison, the Eichner A proportion was significantly higher in the normal cognition group, and the Eichner B+C proportion was significantly higher in the MCI group (Table 3. $P=0.0041$). Even the odds ratio for being Eichner B+C compared to Eichner A was 3.12 times higher in the MCI group in the multiple generalized logistic regression (Table 5, Model 2, $P=0.1124$), but a significant association between posterior occlusal contact and cognitive function could not be found. To our knowledge, this is the first study taking into account posterior support through the use of the Eichner index. Several studies have emphasized the importance of posterior occlusion in cognitive function (Han et al. 2020), and Takeuchi et al. (Takeuchi et al. 2015) demonstrated that compared with tooth loss, the loss of posterior functional tooth units (FTUs), which were defined as the number of pairs of opposing natural and artificial teeth, was significantly associated with cognitive decline. Although a significant association between posterior occlusion assessed by the Eichner index and MCI was not found in this study, those results may suggest that posterior support is important for cognitive function. Therefore, further studies of sufficient numbers of participants with varying oral conditions without RPs are needed for a more accurate investigation of the association between MCI and posterior occlusion using the Eichner index again by

dividing the participants into more 10 than subgroups (A1-A3, B1-B4, C1-C3) rather than Eichner A, B and C groups, or other specific methods to evaluate posterior occlusion, such as by FTUs or the occlusal contact area.

In addition to the dental status, it is also suggested that the bite force, as a key determinant of masticatory performance, is absolutely necessary to comminute food (Hatta et al. 2020; Ikebe et al. 2018) and is related to cognitive function. Based on these results, the bite force, as a static masticatory factor, and the MAI, as a dynamic masticatory factor, were measured to evaluate masticatory performance, but no significant association with cognitive function was found in this study.

In this study, among the objective variables, including the MAI, number of remaining teeth, number of posterior teeth, posterior occlusal support and bite force, only the MAI appeared to have a significant positive correlation with MCI regardless of sex, age and the presence of RPs ($P < 0.0001$), which is in accordance with the above previous reports, although there were methodological differences (Ikebe et al. 2018; Kimura et al. 2013; Lexomboon et al. 2012; Scherder et al. 2008). Additionally, because there is no academic reference for the standard cutoff score of the MAI, the MAI cut off score was set based on the overall data of the participants in this study, and it should be understood that a lower MAI score in the MCI group indicates a lower chewing ability in the MCI group than in the normal cognition group rather

than a lower MAI score itself. This result is in line with the physiological feature of mastication: mastication is a complex process involving surrounding structures and the neuromuscular system (Van der Bilt et al. 2006), and through a series of cooperative interactions among these elements, mastication provides considerable sensory input to the brain, especially related to cognition (Ono et al. 2010). Even though bite force is also exerted by and reflects the function of masticatory muscles and neuromuscular system, there could be an obvious difference between the MAI as a dynamic function and bite force as a static function (Jeong et al. 2010). Therefore, chewing is a series of processes in which the teeth, tongue, muscles, and the neuromuscular system continuously cooperate for a certain period of time, and bite force is representative of only the force temporarily exerted at a specific moment (Van der Bilt et al. 2006). Therefore, bite force, unlike the MAI, has a limitation as an objective masticatory functional factor to predict masticatory functional performance.

The significant association between the MAI and MCI was confirmed once again even after participants were divided according to the presence of RPs (Table 6, $P < 0.0001$), and this finding is in agreement with those of previous studies reporting that RPs could affect masticatory function, especially chewing efficiency or bite force (Boven et al. 2015; Campos et al. 2017; Krall, Hayes, and Garcia 1998; Polzer et al. 2012; Van der Bilt 2011). The reason

why only RPs were investigated is based on the results of these previous studies, because it was expected that there would be a difference in masticatory function between the group in which the partially edentulous region was restored with a RP and the group in which it was not. Additionally, because fixed prostheses such as implants always reside in the oral cavity, they were expected to have the same effect as natural or restored teeth during mastication. In this study, the MAI in the MCI group was significantly lower than that in the normal cognition group in both the non-RP and RP groups, and no difference was found in the association between cognitive and masticatory function according to the presence of RPs. However, it is necessary to accurately compare the difference in masticatory function according to cognitive function in the two groups by equalizing the number of participants in the non-RP and RP groups.

General cognitive function can be simply assessed using the MMSE, but an extensive neuropsychological test battery can be conducted to test other aspects of cognitive function including executive dysfunction, impaired judgment and various degrees of memory loss, through tests of verbal fluency, memory attention, visuospatial function and so on (Weijenberg et al. 2013). Weijenberg et al. (Weijenberg et al. 2015) reported that none of these aspects of cognitive function were significantly associated with masticatory function, although general condition and verbal fluency were positively associated with

masticatory performance. In this study, the KMMSE, a modified version of the MMSE used in Korea, was used for general screening for cognitive impairment, but an extensive assessment tool was not introduced. The MMSE was originally developed for general screening for cognitive impairment in the hospital setting. The set of questions within the MMSE is relatively simple, and the percentage of ‘false-negative’ responses was reported to be as high as 19.7–30% (Kang et al. 2016). For further investigation of cognitive function, the accuracy of testing should be improved by incorporating a more extensive testing tool for the aspects of cognitive function that cannot be covered by the MMSE.

This study has several limitations. First, although we found a significant association between the MAI and MCI, we could not establish a causal relationship between masticatory function and cognitive decline, because this was a cross-sectional study. Therefore, further longitudinal studies of participants with similar oral conditions are needed. Second, a number of studies regarding the effect of oral health on cognitive function have been reported, but they have shown conflicting results. Variations in the methodology used in each study are considered the main reason for these inconsistent findings and make a qualitative comparison impossible. Additionally, there are no standard data from a healthy population comprising various age groups to enable a quantitative comparison. A further study with a

better design should be performed using a standard method, and the results should be analyzed and compared with the data from a healthy population. Despite the comparably small number of participants, the power of this analysis for confirming the association between MCI and masticatory function was greater than 0.8, and the significance level was sufficiently high, so our results can be considered reliable. However, for more precise verification, a sufficient number of participants should be selected from the MCI group and the normal groups with uniform gender distribution. In addition, care must be taken to avoid possible bias in the result in selecting the target groups with varied oral condition by considering the posterior occlusal support and type of prosthesis.

V. CONCLUSION

The number of remaining teeth, number of posterior teeth, bite force, MAI and posterior support status showed significant differences between the MCI and normal cognition groups. However, among the masticatory factors assessed, only the MAI was significantly associated with MCI in elderly patients after the effects of sex, age and the presence of RP were excluded. The findings of this study suggest that it is more important to improve chewing efficiency by maintaining or improving posterior occlusal support through prosthetic rehabilitation than by simply increasing the number of teeth using dental implant or restorative treatments. In other words, more strategic and long-term treatment plans throughout the life span are required to prevent or delay MCI in the elderly population.

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국문요약

노인에게서 경도인지장애와 주관적, 객관적 저작기능의 평가

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지도 교수: 정 복 영

경도인지장애는 정상 노화과정과 치매의 중간 단계로서, 많은 선연구들에서 인지장애와 저작기능이 밀접한 연관성을 가지고 있음을 보고하였다. 본 연구의 목적은 노인에게서의 경도인지장애와 주관적, 객관적 저작기능간의 연관성을 파악하는 것이며, 더 나아가 저작기능 중에서도 어떠한 특정 요인이 경도인지장애와 유의한 연관성을 갖는지를 봄으로서, 노인의 치과치료 시 임상적으로 어떤 부분을 고려해야 하는지 고찰해보고자 함이다.

본 연구에서는 총 129 명의 노인 참가자에 대해 인지기능 선별검사인 한국판 간이정신검사 (Korean Mini-Mental State Examination, 이하 KMMSE)를 시행하여 23 점을 기준으로 정상그룹과 경도인지장애그룹으로

나누었고, 모든 참가자에 대해 주관적, 객관적 저작기능의 평가를 시행하였다. 주관적 평가는 식품섭취능 (Food Intake Ability, 이하 KFIA)을 설문지 형식으로 시행하였으며, 객관적 평가로는 구강검사, Mixing Ability Test, 교합력 등을 측정하고 기록하였다. 129 명의 참가자 중 하나이상의 자료가 부족한 6 명을 제외하고 최종 123 명에 대해 분석을 시행하였으며, 정상그룹은 92 명, 경도인지장애 그룹은 31 명 이었다.

전체치아개수, 구치부 치아개수는 모두 경도인지장애그룹에서 유의하게 적었으며 ($P=0.0296$, 0.0097), 교합력과 MAI 점수또한 유의하게 낮았다 ($P=0.0479$, <0.0001). 구치부 교합의 경우 두 그룹간의 분포차이가 통계적으로 유의하였다 ($P=0.0147$). 하지만 성별, 연령, 가철성 보철의 유무를 보정한 후에는 객관적 동적 저작기능의 평가지표인 MAI 점수만이 경도인지장애와 유의한 연관성을 가짐을 확인하였다 ($P<0.0001$).

본 연구의 한계 내에서, 저작기능 중 MAI 점수로 평가되는 객관적 저작효율만이 경도인지장애와 유의한 연관성을 가짐을 확인하였으며, 이는 임상에서 노인의 치과치료 시 저작효율을 증진시킬 수 있는 기능적인 치료가 필요함을 시사한다.

핵심되는 말: 저작기능, 경도인지장애, 한국판 간이정신검사 (KMMSE), 저작효율, Mixing Ability Test