



Association Between Dental Implants and Cognitive Function in Community-dwelling Older Adults in Korea

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Objectives: This study aimed to evaluate the association between dental implants and cognitive function in community-dwelling older adults.

Methods: Data were collected from the baseline survey (2016-2017) of the Korean Frailty and Aging Cohort Study. The study sample comprised 1115 community-dwelling people aged 70 years to 84 years who had 0-19 natural teeth. Dental implants and natural teeth were identified by panoramic radiography, while the cognitive function was assessed by the Korean version of the Mini-Mental State Examination (MMSE-KC). The association between dental implants and cognitive function was analyzed by multiple linear regression. Sensitivity analysis was performed to test for potential bias.

Results: The mean number of natural teeth in the study population was 9.50 (standard deviation [SD], 6.42), and the mean MMSE-KC score was 24.93 (SD, 3.55). In the simple univariate analysis, tooth replacement, age, sex, smoking status, alcohol consumption, body mass index, osteoporosis, number of natural teeth, periodontitis, chewing discomfort, tooth-brushing frequency, education level, monthly household income, participation in economic activity, living alone, and marital status had a significant impact on the association. After adjusting for confounders, the association between dental implants and cognitive function remained significant (B, 0.85; standard error, 0.40; $p < 0.05$). Age, body mass index, periodontitis, tooth-brushing frequency, and education level were also significantly associated with cognitive function. The results of the sensitivity analyses were consistent with those of the primary analysis.

Conclusions: Dental implants were associated with cognitive function in older adults living in the community. Dental implants as tooth replacements may play a role in preserving cognitive function.

Key words: Dental implant, Cognition, Cognitive reserve, Prosthesis and implants, Cognitive dysfunction, Aged

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INTRODUCTION

Cognitive decline is highly prevalent in old age. Studies have suggested 2 significant approaches to coping with cognitive decline. One is through improvements in modifiable factors such as drinking, smoking, diet, and exercise, and the other is through the appropriate management of chronic conditions such as hypertension and diabetes mellitus [1]. However, the effectiveness of these options is questionable. In geriatrics, how to change modifiable factors is among the critical areas of focus [2]. Managing chronic conditions is also not easy in

older adults, as doing so depends on medication intake, which in turn is challenging to ensure due to visual impairment, reduced fine motor function, and poor health literacy [3].

Implants or implantable devices provide new perspectives in this regard. They are medical devices made of 1 or more biomaterials that are intentionally placed in the body, completely or partially buried beneath the surface of the epithelium [4]. Implants can complement or replace body organs damaged due to aging [5]. Implants have less impact on an individual's lifestyle and require less direct action or complex skills. Therefore, implants can be an effective intervention with more modifiability than lifestyle modifications.

Several studies have reported a significant association between tooth loss and cognitive function [6-8]. A recent meta-analysis reported that older adults with <20 teeth had a 20% higher risk of cognitive decline [9]. Nevertheless, studies have rarely investigated the association between dental implants and cognitive function.

A previous study reported that dental implants could increase cerebral blood volume [10] and brain function in those with impaired brain regions [11], and reduce the imbalance and asymmetry of brain function [12]. To the best of our knowledge, no epidemiological study to date has assessed the association between dental implants and cognitive function.

We aimed to examine the association between dental implants and cognitive function in community-dwelling older adults. After determining the appropriate categories of natural teeth through a literature review, we examined the association between implants and cognitive function and tested the robustness of the results through sensitivity analyses.

METHODS

Data Source

In this cross-sectional study, we analyzed baseline data from the Korean Frailty and Aging Cohort Study (KFACS). The KFACS is a nationwide multicenter study that aimed to detect and analyze the causes and effects of frailty. The baseline survey, including 3014 community-dwelling people aged 70-84 years, was conducted in 2016-2017 with follow-up surveys planned every 2 years. Details of the design of the KFACS have been presented elsewhere [13].

We identified participants with panoramic radiography ($n=2609$) in whom the dental anatomy could be investigated at baseline ($n=3014$), after the exclusion of those with no

panoramic radiography ($n=315$) and illegible panoramic radiography ($n=90$). The number of natural teeth was investigated based on panoramic radiography and calculated, excluding retained tooth roots, pontics, and implants. Wisdom teeth were included as natural teeth.

We conducted a literature review to determine the appropriate threshold for categorizing participants as having natural teeth. The presence of ≥ 20 natural teeth reportedly ensures optimal oral function through adequate chewing capacity and efficiency [14], and in many studies, was used as a threshold to categorize people as having natural teeth [15,16]. A recent meta-analysis reported that the risk of cognitive decline was 20% higher in individuals with <20 teeth than those with ≥ 20 teeth. [9] Thus, we set the upper limit of natural teeth as 19.

Accordingly, subjects with 0-19 natural teeth ($n=1285$) were identified from the cohort, and finally, eligible participants ($n=1115$) were selected after the exclusion of those with missing values ($n=170$). The following flow chart shows the participation selection process (Figure 1).

Measurements

Tooth replacement

Tooth replacement was investigated using panoramic radiography. Dentists performed the readings. We focused on the function of the teeth and considered dental prostheses as a fixed substitute for tooth loss [6]. A pontic is an artificial tooth

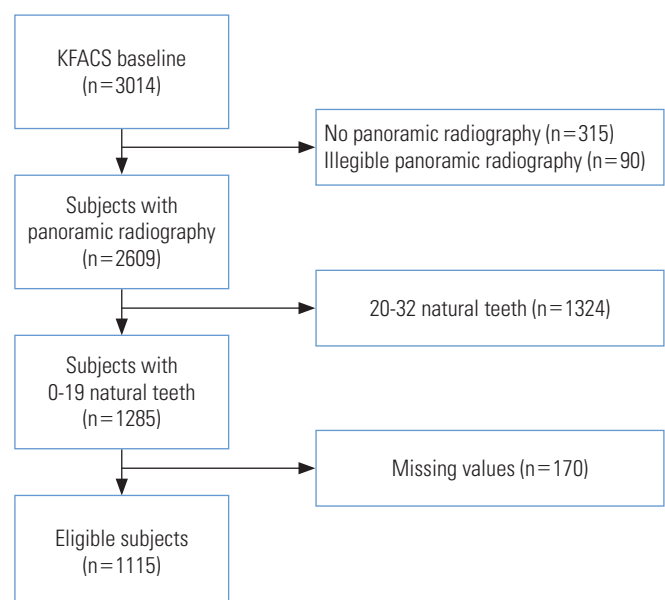


Figure 1. Flow chart of participant selection. KFACS, Korean Frailty and Aging Cohort Study.

on a fixed partial denture that replaces a missing natural tooth, restoring its function [18]. Whereas a dental implant has its own artificial tooth root anchored into the bone, a pontic has no tooth root and is connected to the abutment teeth on either side [18]. Therefore, pontics were included as tooth replacements. As a result, tooth replacement status was classified into 4 categories: none, pontics only, pontics and implants, and implants only.

Cognitive function

The Mini-Mental State Examination (MMSE) evaluates orientation, registration, attention and calculation, recall, and language [19]. In this study, cognitive function was measured using the MMSE in the Korean version of the Consortium to Establish a Registry for Alzheimer's Disease assessment packet (MMSE-KC) [20]. The MMSE-KC differs from the original MMSE in 3 items: orientation, attention and calculation, and language. Considering the high illiteracy rate among elderly Korean people, 'reading and writing' was replaced with 'judgment' and the '100-7 calculation' was replaced with 'speaking backward' [21]. This is a validated screening test with an area under the curve of >0.9 for Alzheimer disease [22]. Well-trained clinical research coordinators measured the MMSE-KC scores.

Covariates

Covariates were selected based on the possible mechanism of the effect of dental implants on cognitive function. However, due to the lack of epidemiological studies, we reviewed studies on tooth loss and cognitive function [7-9]. The proposed mechanisms of the effect of tooth loss on cognitive function can be classified into 4 categories: inflammation [23-25], abnormal mastication [7,10-12,26,27], reverse or bidirectional causality [28,29], and residual confounding in the socioeconomic domain [30]. As dental implants restore tooth function, it is expected that the abnormal mastication mechanism would be blocked. Therefore, the covariates related to the other 3 mechanisms were collected.

Demographic variables included age and sex. Health behaviors included smoking status (non-smoker, former smoker, or current smoker), alcohol consumption (none, ≤ 1 /wk, or >1 /wk), and body mass index (<23.0 kg/m², 23.0-24.9 kg/m², or ≥ 25.0 kg/m²). Comorbidities included hypertension, cerebrovascular disease, coronary artery disease, asthma or chronic obstructive pulmonary disease, osteoporosis, diabetes mellitus, depression, and other psychiatric disorders. Among laboratory

markers, high-sensitivity C-reactive protein (hs-CRP) (<1.0 mg/L, 1.0-3.0 mg/L, or >3.0 mg/L) was selected. Oral health-related variables included the number of natural teeth, periodontitis (normal, mild, moderate, severe, or edentulous), chewing discomfort (not at all, mild, moderate, or severe), and tooth-brushing frequency (0-1 time/d, 2 times/d, or ≥ 3 times/d). Socio-economic position (SEP) variables included education level (no formal education, primary school, middle school, or high school or higher), monthly household income ($<1\,000\,000$ Korean won [KRW], 1 000 000-3 000 000 KRW, or $\geq 3\,000\,000$ KRW), participation in economic activity, living alone, and marital status (married or widowed/separated/divorced/never married).

Statistical Analysis

In the descriptive analysis, quantitative data were expressed as mean \pm standard deviation, and qualitative data were expressed as frequency (%). Comparisons of the response variable and covariates among the tooth replacement groups were performed using analysis of variance and the chi-square test. Simple univariate analyses were performed with simple linear regression for quantitative data, and the Student *t*-test and analysis of variance for qualitative data. The association between dental implants and cognitive function was analyzed by multiple linear regression. Tooth replacement was set as the explanatory variable, the MMSE-KC score as the response variable, and the covariates described above were adjusted for. A value of *p*-value <0.05 was considered to indicate statistical significance. Statistical analysis was performed using SAS version 9.4 (SAS Institute Inc., Cary, NC, USA).

Sensitivity analysis

Multiple sensitivity analyses were conducted. A sensitivity analysis for natural tooth categorization was conducted to adjust for selection bias. Multiple linear regression analysis was performed by changing the upper limit ($n=19$) of the category in the range of ± 5 . A sensitivity analysis of tooth replacement was also conducted. The pontic and implant group contained various types of tooth replacements (pontics and implants) in varying combinations. Therefore, multiple linear regression analysis was performed with the exclusion of this group.

Ethics Statement

The study protocol was approved by the Institutional Review Board of Ajou University Hospital (AJIRB-MED-MDB-19-158). All participants provided written informed consent. This article

Table 1. Characteristics of the study population (n=1115)

Variables	Total	Tooth replacement				p-value
		None	Pontics only	Pontics and implants	Implants only	
MMSE-KC score, mean ± SD	24.93 ± 3.55	24.22 ± 3.84	24.87 ± 3.57	25.67 ± 3.05	26.39 ± 2.47	<0.001
Age, mean ± SD (y)	76.81 ± 3.97	77.57 ± 3.97	76.99 ± 3.86	75.49 ± 3.82	76.51 ± 3.81	<0.001
Sex (female)	582 (52.2)	220 (52.6)	177 (51.2)	153 (56.3)	32 (40.5)	0.098
Smoking status						0.010
Non-smoker	652 (58.5)	230 (55.0)	203 (58.7)	177 (65.1)	42 (53.2)	
Former smoker	364 (32.6)	136 (32.5)	116 (33.5)	79 (29.0)	33 (41.8)	
Current smoker	99 (8.9)	52 (12.4)	27 (7.8)	16 (5.9)	4 (5.1)	
Alcohol consumption						0.086
None	345 (30.9)	138 (33.0)	108 (31.2)	83 (30.5)	16 (20.3)	
≤1/wk	246 (22.1)	102 (24.4)	68 (19.7)	61 (22.4)	15 (19.0)	
>1/wk	524 (47.0)	178 (42.6)	170 (49.1)	128 (47.1)	48 (60.8)	
Body mass index (kg/m ²)						0.055
Normal (<23.0)	394 (35.3)	158 (37.8)	137 (39.6)	74 (27.2)	25 (31.6)	
Overweight (23.0-24.9)	289 (25.9)	102 (24.4)	84 (24.3)	81 (29.8)	22 (27.8)	
Obese (≥25.0)	432 (38.7)	158 (37.8)	125 (36.1)	117 (43.0)	32 (40.5)	
Hypertension	637 (57.1)	243 (58.1)	195 (56.4)	153 (56.3)	46 (58.2)	0.944
Cerebrovascular disease	59 (5.3)	31 (7.4)	17 (4.9)	9 (3.3)	2 (2.5)	0.066
Coronary artery disease	102 (9.1)	46 (11.0)	27 (7.8)	22 (8.1)	7 (8.9)	0.413
Asthma or COPD	14 (1.3)	2 (0.5)	5 (1.4)	5 (1.8)	2 (2.5)	0.270
Osteoporosis	206 (18.5)	90 (21.5)	58 (16.8)	44 (16.2)	14 (17.7)	0.236
Diabetes mellitus	244 (21.9)	91 (21.8)	82 (23.7)	55 (20.2)	16 (20.3)	0.745
Depression	31 (2.8)	16 (3.83)	9 (2.6)	5 (1.8)	1 (1.3)	0.348
Other psychiatric disorder	37 (3.3)	15 (3.6)	7 (2.0)	12 (4.4)	3 (3.8)	0.396
hs-CRP (mg/L)						0.205
<1.0	660 (59.2)	234 (56.0)	211 (61.0)	164 (60.3)	51 (64.6)	
1.0-3.0	325 (29.1)	122 (29.2)	104 (30.1)	77 (28.3)	22 (27.8)	
>3.0	130 (11.7)	62 (14.8)	31 (9.0)	31 (11.4)	6 (7.6)	
No. of natural teeth	9.50 ± 6.42	5.11 ± 5.62	11.94 ± 4.95	12.75 ± 5.28	10.91 ± 6.75	<0.001
Periodontitis						<0.001
Normal	95 (8.5)	33 (7.9)	17 (4.9)	28 (10.3)	17 (21.5)	
Mild	108 (9.7)	29 (6.9)	36 (10.4)	32 (11.8)	11 (13.9)	
Moderate	345 (30.9)	102 (24.4)	124 (35.8)	103 (37.9)	16 (20.3)	
Severe	421 (37.8)	108 (25.8)	169 (48.8)	109 (40.1)	35 (44.3)	
Edentulism	146 (13.1)	146 (34.9)	0 (0.0)	0 (0.0)	0 (0.0)	
Chewing discomfort						<0.001
Not at all	352 (31.6)	103 (24.6)	102 (29.5)	117 (43.0)	30 (38.0)	
Mild discomfort	200 (17.9)	77 (18.4)	54 (15.6)	54 (19.9)	15 (19.0)	
Moderate discomfort	369 (33.1)	148 (35.4)	120 (34.7)	77 (28.3)	24 (30.4)	
Severe discomfort	194 (17.4)	90 (21.5)	70 (20.2)	24 (8.8)	10 (12.7)	
Tooth-brushing frequency (times/d)						0.002
0-1	169 (15.2)	81 (19.4)	56 (16.2)	27 (9.9)	5 (6.3)	
2	504 (45.2)	178 (42.6)	163 (47.1)	120 (44.1)	43 (54.4)	
≥3	442 (39.6)	159 (38.0)	127 (36.7)	125 (46.0)	31 (39.2)	

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Table 1. Continued from the previous page

Variables	Total	Tooth replacement				p-value
		None	Pontics only	Pontics and implants	Implants only	
Education level						<0.001
Uneducated	317 (28.4)	156 (37.3)	106 (30.6)	41 (15.1)	14 (17.7)	
Primary school	308 (27.6)	119 (28.5)	98 (28.3)	74 (27.2)	17 (21.5)	
Middle school	183 (16.4)	59 (14.1)	61 (17.6)	50 (18.4)	13 (16.5)	
High school or higher	307 (27.5)	84 (20.1)	81 (23.4)	107 (39.3)	35 (44.3)	
Monthly household income (10 ⁴ Korean won)						<0.001
≥300	123 (11.0)	23 (5.5)	30 (8.7)	54 (19.9)	16 (20.3)	
100-300	396 (35.5)	125 (29.9)	122 (35.3)	119 (43.8)	30 (38.0)	
<100	596 (53.4)	270 (64.6)	194 (56.1)	99 (36.4)	33 (41.8)	
Economic activity participation	327 (29.3)	127 (30.4)	117 (33.8)	63 (23.2)	20 (25.3)	0.027
Living alone	297 (26.6)	134 (32.1)	88 (25.4)	57 (21.0)	18 (22.8)	0.009
Marital status (widowed/ separated/divorced/ never married)	418 (37.5)	172 (41.1)	133 (38.4)	89 (32.7)	24 (30.4)	0.076

Values are presented as number (%).

SD, standard deviation; MMSE-KC, Korean version of the Mini-Mental State Examination; COPD, chronic obstructive pulmonary disease; hs-CRP, high-sensitivity C-reactive protein.

is compliant with the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) guidelines [17].

RESULTS

The characteristics of the study population are shown in Table 1. Of the 1115 eligible participants, 79 had implants only, 272 had both pontics and implants, 346 had pontics only, and 418 had none. The mean age was 76.81 ± 3.97 years, and the number of men was 533 (47.8%). The mean MMSE-KC score of all participants was 24.93 ± 3.55 . The mean MMSE-KC score was 24.87 ± 3.57 in the pontic group, 26.39 ± 2.47 in the implant group, and 25.67 ± 3.05 in the pontic and implant group, and 24.22 ± 3.84 in the no tooth replacement group.

The MMSE-KC score, age, smoking status, number of natural teeth, periodontitis, chewing discomfort, tooth-brushing frequency, education level, monthly household income, participation in economic activity, and frequency of living alone were significantly different among the tooth replacement groups.

Table 2 shows the number of natural teeth, pontics, and implants in each tooth replacement group. The pontic group had 11.94 ± 4.95 natural teeth and 2.92 ± 2.05 pontics, while the implant group had 10.91 ± 6.75 natural teeth and 4.57 ± 3.17 implants. The pontic and implant group had 12.75 ± 5.28 natural teeth, 4.06 ± 2.63 pontics, and 6.03 ± 3.62 implants.

In the simple univariate analysis (Table 3), tooth replace-

Table 2. Number of natural teeth, pontics, and implants by tooth replacement type

Group	n (%)	No. of natural teeth	No. of pontics	No. of implants
None	418	5.11 ± 5.62	-	-
Pontic only	346	11.94 ± 4.95	2.92 ± 2.05	-
Pontic and implant	272	12.75 ± 5.28	4.06 ± 2.63	6.03 ± 3.62
Implant only	79	10.91 ± 6.75	-	4.57 ± 3.17

Values are presented as mean \pm standard deviation.

ment, age, sex, smoking status, alcohol consumption, body mass index, osteoporosis, number of natural teeth, periodontitis, chewing discomfort, tooth-brushing frequency, education level, monthly household income, participation in economic activity, living alone, and marital status showed significant association with cognitive function ($p < 0.05$).

In multiple linear regression (Table 3), the association between the implant only group and cognitive function was significant (B, 0.85; standard error [SE], 0.40; $p = 0.034$). However, the association between the pontic only group and cognitive function was not significant (B, 0.31; SE, 0.26; $p = 0.229$). The association of the pontic and implant group was likewise not significant (B, 0.20; SE, 0.29; $p = 0.494$).

The covariates that demonstrated a significant association were age (B, -0.13; SE, 0.02; $p < 0.001$), obesity (B, 0.53; SE, 0.23; $p = 0.019$), severe periodontitis (B, -0.81; SE, 0.37; $p = 0.030$), tooth-brushing frequency (B, 0.60; SE, 0.28; $p = 0.031$ for 2 times/d; B, 0.56; SE, 0.28; $p = 0.049$ for ≥ 3 times/d) and education level

Table 3. Simple univariate analysis and multiple linear regression analysis of factors associated with cognitive function (n=1115)

Variable	Simple analysis		p-value	Multiple analysis		p-value
	n (%)	MMSE-KC score, mean ± SD		B ¹	SE	
Tooth replacement			<0.001			
None	418 (37.5)	24.22 ± 3.84		Reference		
Pontic only	346 (31.0)	24.87 ± 3.57		0.31	0.26	0.229
Pontic and implant	272 (24.4)	25.67 ± 3.05		0.20	0.29	0.494
Implant only	79 (7.1)	26.39 ± 2.47		0.85	0.40	0.034
Age, mean ± SD (y)	76.81 ± 3.97	24.93 ± 3.55	<0.001	-0.13	0.02	<0.001
Sex			<0.001			
Male	533 (47.8)	25.88 ± 3.06		Reference		
Female	582 (52.2)	24.06 ± 3.74		-0.67	0.36	0.064
Smoking status			<0.001			
Non-smoker	652 (58.5)	24.33 ± 3.73		Reference		
Former smoker	364 (32.6)	25.98 ± 2.88		0.62	0.32	0.054
Current smoker	99 (8.9)	25.00 ± 3.69		0.11	0.41	0.792
Alcohol consumption			0.002			
None	345 (30.9)	24.41 ± 3.76		Reference		
≤ 1/wk	246 (22.1)	24.90 ± 3.56		0.05	0.27	0.841
> 1/wk	524 (47.0)	25.28 ± 3.37		0.09	0.23	0.709
Body mass index (kg/m ²)			0.008			
Normal (<23.0)	394 (35.3)	24.51 ± 3.93		Reference		
Overweight (23.0-24.9)	289 (25.9)	24.99 ± 3.43		0.25	0.24	0.300
Obese (≥ 25.0)	432 (38.7)	25.27 ± 3.22		0.53	0.23	0.019
Hypertension			0.844			
No	478 (42.9)	24.91 ± 3.61		Reference		
Yes	637 (57.1)	24.95 ± 3.51		0.19	0.19	0.320
Cerebrovascular disease			0.449			
No	1056 (94.7)	24.91 ± 3.57		Reference		
Yes	59 (5.3)	25.27 ± 3.18		-0.09	0.41	0.829
Coronary artery disease			0.113			
No	1013 (90.9)	28.88 ± 3.57		Reference		
Yes	102 (9.1)	25.46 ± 3.31		0.39	0.32	0.222
Asthma or COPD			0.649			
No	1101 (98.7)	24.94 ± 3.56		Reference		
Yes	14 (1.3)	24.50 ± 3.35		0.02	0.83	0.982
Osteoporosis			<0.001			
No	909 (81.5)	25.11 ± 3.48		Reference		
Yes	206 (18.5)	24.16 ± 3.76		0.14	0.26	0.583
Diabetes mellitus			0.098			
No	871 (78.1)	24.84 ± 3.61		Reference		
Yes	244 (21.9)	25.26 ± 3.31		0.14	0.23	0.536
Depression			0.114			
No	1084 (97.2)	24.96 ± 3.55		Reference		
Yes	31 (2.8)	23.94 ± 3.49		-0.42	0.58	0.463
Other psychiatric disorder			0.463			
No	1078 (96.7)	24.92 ± 3.57		Reference		
Yes	37 (3.3)	25.35 ± 2.92		0.32	0.52	0.548

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Table 3. Continued from the previous page

Variable	Simple analysis		p-value	Multiple analysis		p-value
	n (%)	MMSE-KC score, mean ± SD		B ¹	SE	
hs-CRP (mg/L)			0.293			
<1.0	660 (59.2)	24.86 ± 3.64		Reference		
1.0-3.0	325 (29.1)	25.17 ± 3.32		0.15	0.21	0.466
>3.0	130 (11.7)	24.67 ± 3.67		-0.02	0.30	0.934
No. of natural teeth	9.50 ± 6.42	24.93 ± 3.55	<0.001	0.01	0.02	0.522
Periodontitis			<0.001			
Normal	95 (8.5)	25.74 ± 2.85		Reference		
Mild	108 (9.7)	24.70 ± 3.42		-0.74	0.44	0.089
Moderate	345 (30.9)	25.04 ± 3.45		-0.62	0.37	0.097
Severe	421 (37.8)	25.11 ± 3.48		-0.81	0.37	0.030
Edentulous	146 (13.1)	23.81 ± 4.23		-0.68	0.44	0.120
Chewing discomfort			<0.001			
Not at all	352 (31.6)	25.09 ± 3.58		Reference		
Mild discomfort	200 (17.9)	25.57 ± 3.18		0.50	0.27	0.065
Moderate discomfort	369 (33.1)	24.99 ± 3.43		0.38	0.23	0.099
Severe discomfort	194 (17.4)	23.87 ± 3.87		-0.07	0.28	0.793
Tooth-brushing frequency (times/d)			0.019			
0-1	169 (15.2)	24.22 ± 3.92		Reference		
2	504 (45.2)	25.03 ± 3.45		0.60	0.28	0.031
≥3	442 (39.6)	25.09 ± 3.49		0.56	0.28	0.049
Education level			<0.001			
Uneducated	317 (28.4)	22.35 ± 3.96		Reference		
Primary school	308 (27.6)	25.03 ± 3.06		2.25	0.26	<0.001
Middle school	183 (16.4)	26.21 ± 2.42		3.25	0.31	<0.001
High school or higher	307 (27.5)	26.74 ± 2.38		3.56	0.31	<0.001
Monthly household income (10 ⁴ Korean won)			<0.001			
≥300	123 (11.0)	26.76 ± 2.58		Reference		
100-300	396 (35.5)	25.60 ± 3.31		-0.07	0.33	0.827
<100	596 (53.5)	24.11 ± 3.65		-0.46	0.35	0.187
Economic activity participation			0.003			
No	788 (70.7)	25.14 ± 3.40		Reference		
Yes	327 (29.3)	24.41 ± 3.85		-0.32	0.21	0.134
Living alone			<0.001			
No	818 (73.4)	25.15 ± 3.55		Reference		
Yes	297 (26.6)	24.31 ± 3.50		0.23	0.31	0.457
Marital status			<0.001			
Married	697 (62.5)	25.32 ± 3.58		Reference		
Widowed/separated/ divorced/never married	418 (37.5)	24.29 ± 3.41		0.56	0.32	0.076

SD, standard deviation; SE, standard error; MMSE-KC, Korean version of the Mini-Mental State Examination; COPD, chronic obstructive pulmonary disease; hs-CRP, high-sensitivity C-reactive protein.

¹Regression coefficient.

(B, 2.25; SE, 0.26; $p < 0.001$ for primary school; B, 3.25; SE, 0.31, $p < 0.001$ for middle school; B, 3.56; SE, 0.31; $p < 0.001$ for high school or higher).

In the sensitivity analysis for natural tooth categorization, the implant only group showed a significant association with upper limits between 19 and 22. However, neither the pontic

group nor the pontic and implant group showed significant relationships in any category (Supplemental Material 1).

An additional sensitivity analysis was performed by linear regression, excluding the pontic and implant group (Supplemental Material 2). The implant group also showed a significant association (B, 0.92; SE, 0.42; $p=0.030$); the pontic group showed no significant association (B, 0.43; SE, 0.27; $p=0.120$).

DISCUSSION

In community-dwelling older adults with 0-19 natural teeth, cognitive function was significantly higher among those with implants than among those with neglected tooth loss (B, 0.85; SE, 0.40; $p=0.034$). However, the effects of implants should be carefully interpreted. The mean number of implants in the implant group was 4.57, making it difficult to interpret the regression coefficient merely according to the presence of an implant.

However, the pontic and implant groups did not show significant relationships with cognitive function despite the inclusion of implants. There may be 2 reasons for this finding. First, the pontic and implant group was heterogeneous. The abutments of a pontic can be either natural teeth or implants, and the number of abutments may be different even though the number of pontics is the same [18]. Therefore, it is challenging to classify older adults with both pontics and implants into a single group. Second, there is an interaction between the pontic and the implant. Due to the absence of a root, the load on the pontic is transmitted to the abutment. If the abutment is an implant, the load of the pontic is transmitted to the implant. The disequilibrium of force transmitted to the implant can be a cause of implant failure [31,32].

The mechanisms of implants on cognitive function are indissolubly linked with those of tooth loss on cognitive function. As already reviewed, the mechanisms through which tooth loss may be associated with cognitive function can be classified into 4 categories: (1) inflammation, (2) abnormal mastication, (3) reverse or bidirectional causality, and (4) residual confounding in the socioeconomic domain.

In terms of the inflammatory mechanism, increased levels of proinflammatory factors such as CRP, tumor necrosis factor α , interleukin (IL)-1, IL-6, and α -1-antichymotrypsin due to infections caused by poor oral health, including tooth loss and periodontitis, lead to chronic systemic inflammation, which plays a pivotal role in cognitive decline [23-25].

Abnormal mastication mechanisms may act through 3 pathways. First, since mastication stimulates the brain, reduced mastication leads to cognitive decline through a reduction in the strength of brain activation [11,26], and asymmetric mastication induces asymmetric brain activity [12]. Second, since mastication increases cerebral blood flow, abnormal mastication reduces cerebral blood flow [10]. Third, abnormal mastication leads to poor oral intake, resulting in cognitive decline [7,27].

Reverse causality or bidirectional causality may account for this association, in that when the cognitive decline occurs, the ability to perform activities of daily living (ADLs) such as oral hygiene and dental care may be impaired [28,29].

Residual confounding in the socioeconomic domain could play a role since tooth loss is a surrogate marker of SEP. It is impossible to assess the independent role of tooth loss in cognitive decline due to the strong link between tooth loss and SEP [30].

Based on the above review of the mechanism of tooth loss on cognitive function, a mechanism of dental implants on cognitive function can be proposed. First, dental implants can affect cognitive function by reducing the degree of abnormal mastication. Some previous studies showed that dental implants increase cerebral blood flow [10] and improve the asymmetry of brain function [12], providing support for this mechanism.

In terms of reverse causality, dental implants have significant implications. As dental implants function independently of the ability to perform ADLs, they are also useful in older adults with cognitive decline. Cognitive function was partially reversed when mastication was restored through artificial crowns in mice without molars [33]. Cognitive decline was alleviated through occlusion rehabilitation in long-term molar-free mice [34]. In humans, dental implants have been reported to enhance brain function in those with cognitive impairment [11].

The cognitive reserve could explain the effect of implants on cognitive function through the integration of these mechanisms. The concept of cognitive reserve explains the discrepancy between the degree of brain changes and the severity of clinical outcomes resulting from individual differences in reserve and compensation [35]. A person with a higher cognitive reserve can be more resistant to brain changes and can better maintain cognitive function. Cognitive reserve is an active phenomenon that can be supplemented through life ex-

periences such as education and occupational achievements [36], and it may prevent or reduce pathologic brain changes [37]. Individual differences in cerebral blood flow and the neural network have been presented as the underlying mechanisms of cognitive reserve [35,37]. In this context, dental implants could augment cognitive reserve through their role as adequate replacements for tooth loss.

This discussion can be extended to all implants, not just dental implants. That is, by complementing or replacing damaged body organs, implants can contribute to the preservation of cognitive reserve. Other implants, such as cochlear implants [38] and intraocular lens implants [39], have also been reported to elicit cognitive improvements in older adults through the replacement of damaged organs; however, those types of implants directly affect cognitive function, unlike dental implants.

However, there are also limitations to implants. Dental implants are more invasive than pontics. Because contraindications to dental implants include medical conditions such as acute illness and uncontrolled metabolic diseases [18], people with implants may be medically healthier than those without them. The same point holds for extending the discussion across implantable devices. It seems clear that implantable devices are less safe than other medical devices, such as wearable devices.

Our study has various strengths. First, it was designed and performed based on a mechanism associating tooth loss with cognitive function. We focused on the mechanism of abnormal mastication, which can be improved with dental implant use, and the factors related to the other mechanism were selected and adjusted for. The level of hs-CRP was adjusted as a confounder related to the inflammation mechanism. Reverse causality was adjusted using various oral health variables. We attempted to resolve the issue of residual socioeconomic confounding by adjusting for a significantly higher number of SEP items than previous studies.

Second, participants' oral condition was objectively evaluated based on panoramic radiography. Most previous studies were based on questionnaires, while those with objective evaluations had small study populations. Third, multiple sensitivity analyses were conducted to adjust for selection bias.

To the best of our knowledge, our study is the first epidemiological study to reveal the association between dental implants and cognitive function. While most previous studies only focused on the association between tooth loss and cogni-

tive function, the very few that concentrated on the association between dental implants and cognitive function were experimental and enrolled few participants [10-12]. Therefore, this study is valuable, in that it showed the effect of implants on cognitive function in a real-world setting based on data from a large study population.

However, our study has some limitations. First, it had a cross-sectional design, which did not allow for the sufficient inference of causality. A longitudinal study based on KFACS follow-up data should be conducted in the future. Next, there was no information on the position of tooth loss and tooth replacement. Further research should be based on a more detailed reading of panoramic radiography.

Implant use as a treatment to complement or replace damaged organs will increase in response to trends in aging [5]. Our study shows that implants have the potential to prevent cognitive decline by restoring the function of damaged organs. Furthermore, they can be combined with information technology such as biosignal monitoring, enabling them to play a more active role in the prevention of cognitive impairment [40].

In conclusion, our study showed that dental implants were associated with cognitive function in community-dwelling older adults. Dental implants as tooth replacements may contribute to the prevention of cognitive impairment by preserving cognitive reserve.

SUPPLEMENTAL MATERIALS

Supplemental materials are available at <https://doi.org/10.3961/jpmph.19.163>.

CONFLICT OF INTEREST

The authors have no conflicts of interest associated with the material presented in this paper.

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AUTHOR CONTRIBUTIONS

Conceptualization: SK, JY, YL. Data curation: SK, JK. Formal analysis: SK. Funding acquisition: SK, YL. Methodology: SK, JY, YL. Project administration: SK, JK. Visualization: SK. Writing - original draft: SK. Writing - review & editing: SK, JY, JK, YL.

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