Shimane J. Med. Sci., Vol.42 pp.59-72, 2025

Relationship Between Oral Function and Cognitive Status Among Community-dwelling Older Adults: An Observational Cross-sectional Study

Kumi IKEBUCHI[1)], Yuhei MATSUDA[1)], Mayu TAKEDA[1)], Takafumi ABE[2)], Kazumichi TOMINAGA[2,3)], Hisaaki SAITO[2,3)], Shozo YANO[2,4,5)], Minoru ISOMURA[2,6)], Takahiro KANNO[1,2)]

[1)] Department of Oral and Maxillofacial Surgery, Shimane University Faculty of Medicine, Izumo, Shimane 693-8501, Japan

[2)] Center for Community-Based Healthcare Research and Education (CoHRE), Head Office for Research and Academic Information, Shimane University, Izumo, Shimane 693-8501, Japan

[3)] Shimane Dental Association, Matsue, Shimane 690-0884, Japan

[4)] Department of Laboratory Medicine, Shimane University Faculty of Medicine, Izumo, Shimane 693-8501, Japan

[5)] The Center for Integrated Kidney Research and Advance (IKRA), Faculty of Medicine, Shimane University, Izumo, Shimane 693-8501, Japan

[6)] Faculty of Human Sciences, Shimane University, Matsue, Shimane 690-8504, Japan

（Received October 2, 2025; Accepted October 16, 2025; Published online February 16, 2026）

This study aimed to explore the relationship between oral and cognitive functions in community-dwelling older adults who underwent dental and oral health examinations and health check-ups conducted by the Shimane Extended Union of the Medical Care System for Latter-Stage Elderly People between April 2020 and March 2022. Data on general background, oral health status, and cognitive function were collected. Logistic regression analysis was performed as the primary analysis with cognitive function as the objective variable. The participants included 4,338 cases, excluding 1,757 with missing data. The analysis of forgetfulness revealed significant correlations with age, sex, lower leg circumference, masticatory function, swallowing function, oral hygiene status, current smoking status, social participation, and orthopedic disease. Significant correlations were found between age, lower leg circumference, oral dryness, social participation, stroke, and orthopedic disease（$p < 0.05$）. Cognitive function may be associated with declines in oral function and hygiene status in community-dwelling older adults.

Keywords: oral function, oral frailty, oral hypofunction, cognitive function, older adults

INTRODUCTION

The incidence of dementia has been increasing globally, posing a serious public health challenge for aging societies［1］. An international report in 2022 estimated that the number of people with dementia will exceed 55 million globally and is projected to reach 152 million by 2050［2］. The onset of dementia is influenced by a combination of genetic predisposition, chronic diseases, social isolation, and lifestyle factors［1］. Social and lifestyle factors are particularly important modifiable risk factors. Indeed, social isolation and loneliness are independent risk factors for cognitive decline and dementia; reduced social interactions impair neuroplasticity and trigger chronic stress responses［3］. Therefore, strengthen-

Corresponding author: Takahiro KANNO, D.D.S., Ph.D.
Department of Oral and Maxillofacial Surgery, Shimane University Faculty of Medicine, 89-1 Enya-cho, Izumo, Shimane 693-8501, Japan
Tel: +81-853-20-2301
Email: tkanno@med.shimane-u.ac.jp

ing social relationships and promoting social participation are crucial strategies for dementia prevention, contributing to cognitive maintenance and alleviation of loneliness [4].

Lifestyle habits play a pivotal role in the onset and progression of dementia. Hypertension, obesity, diabetes, physical inactivity, smoking, and unhealthy dietary patterns have been identified as risk factors [5]. Improvements in these lifestyle factors can contribute to the prevention of cognitive decline through neuroinflammation suppression and vascular function enhancement, with interventional studies confirming reductions in dementia risk [6]. Diseases related to cognitive function and lifestyle, such as hypertension, diabetes, and dyslipidemia, are also associated with poor oral function. A large-scale cluster randomized trial including over 33,000 participants in China reported that intensive blood pressure control was associated with a 15% reduction in the incidence of dementia over 4 years [7]. The Honolulu-Asia Aging Study, a historical community-based cohort study of Japanese American men born between 1900 and 1919, also demonstrated that "midlife" systolic blood pressure was the strongest predictor of dementia onset among Asians [8]. A meta-analysis of diabetes and dementia risk reported that diabetes might increase the risk of dementia [9]. Another meta-analysis of dyslipidemia suggested a potential causal association between lipid-related factors and dementia [10]. All lifestyle-related diseases (hypertension, diabetes, and dyslipidemia) are associated with oral function. Decline in masticatory ability and lack of denture use have been linked to hypertension in older adults with tooth loss [11], and so has the loss of posterior occlusion to an increased risk of cardiovascular diseases. The relationship between diabetes and periodontitis has long been recognized, and a Cochrane systematic review and meta-analysis of randomized controlled trials published in 2022 reported a moderately certain association [12]. In addition, a lower number of functional tooth units (FTUs) is significantly associated with higher HbA1c values, independent of age, body mass index, and diabetes medication, suggesting an association between diabetes and oral function [13]. Moreover, reduced masticatory function increases the risk of metabolic syndrome and its components, including hypertension, hypertriglyceridemia, and hyperglycemia [14]. Based on these associations, we hypothesized that oral function may be related to cognitive function.

The relationship between oral and cognitive functions has attracted significant attention [15]. In 2016, the Japanese Society of Gerodontology proposed the assessment of seven major oral functions in older adults: oral bacterial count, oral dryness, tongue pressure, occlusal force, masticatory function, and swallowing function [16]. Supporting our overarching hypothesis, previous studies have suggested that deterioration in oral function influences cognitive decline through mechanisms such as poor nutritional status, systemic inflammation, and reduced social interaction [17, 18]. A literature review on the association between oral and cognitive functions identified four domains: masticatory function, swallowing function, oral hygiene status, and oral dryness. Masticatory function, the ability to grind food into a swallowable form, depends on the number of teeth, occlusal condition, and occlusal force [19]. Occlusal stimulation by mastication increases cerebral blood flow and promotes hippocampal neurogenesis [20]. Conversely, tooth loss and ill-fitting dentures, which lead to impaired masticatory function, are associated with reduced cerebral blood flow and cognitive decline [21].

The swallowing function refers to the ability to transport a food bolus from the oral cavity to the pharynx and esophagus, requiring the coordinated activity of multiple muscles and neural systems [22]. Dysphagia has been implicated in aspiration pneumonia, malnutrition, and possibly an increased risk of dementia [23]. Oral hygiene status, which is evaluated by the presence of dental plaque, calculus, periodontitis, and tongue coating, is also associated with cognition [24]. Periodontal disease, driven by pathogens such as *Porphyromonas gingivalis*, induces systemic inflammation and neuroinflammation through the invasion of bacterial components into the brain [25]. These inflammatory processes are associated with amyloid-β deposition and tau protein hyperphosphorylation, both of which are implicated in dementia [26]. Oral dryness, caused by decreased salivary secretion, impairs mastication, swallowing, and oral microbiota balance [27]. Saliva

exerts antimicrobial and mucosal protective effects, and its reduction increases the risk of inflammation and infection [28]. A cohort study reported an association between oral dryness, tooth loss, denture use, and the onset of subjective cognitive decline [29, 30].

In Japan, oral hypofunction was registered in 2018 as a new condition covered by the National Health Insurance, highlighting its role as a target for interventions to extend both physical and mental health and life expectancy. However, comprehensive large-scale investigations assessing multiple domains of oral function remain limited. Accordingly, this study aimed to investigate the association between various oral and cognitive functions in community-dwelling older adults. We hypothesized that older adults with higher oral function would demonstrate higher cognitive function. This study may provide evidence to support that oral function maintenance in older adults contributes to dementia prevention.

PARTICIPANTS AND METHODS

This study was approved by the ethics committee of Medical Research Ethics Committee of Shimane University Faculty of Medicine (approval number 20220723-1).

Participants

In Japan, all individuals aged ≥ 75 years are covered by the long-life medical care insurance system and eligible for a free annual oral health checkup. In this study, data were obtained from the Shimane Extended Union of the Medical Care System for Latter-Stage Elderly People, and oral health checkup records were processed to ensure anonymity. This cross-sectional study targeted residents of Shimane Prefecture, Japan, who were ≥ 75 years old and received at least one oral health checkup between April 1, 2020, and March 31, 2022. The exclusion criteria were as follows: (1) individuals who did not complete the health assessment questionnaire for older adults, and (2) those with missing values in the dental and oral health examination data. During the two years, 55,528 participants underwent a general health checkup (Shimane Extended Union of Medical Care System for Latter-Stage Elderly People), and 14,431 underwent an oral health checkup. Among them, 6,095 underwent both checkups during the study period and were initially included. After data cleaning and exclusion of participants with multiple checkups or missing data, the final study population consisted of 4,338 individuals.

Data collection

Background data

We collected data on age (years), sex (male/female), body mass index (BMI), lower leg circumference (cm), and smoking status (current smoker or non-smoker).

Data on the oral cavity

The oral assessments included the number of remaining teeth, periodontal tissue status, masticatory function, articulation, swallowing function, oral hygiene status, subjective oral dryness. All the examinations were performed by dentists and dental hygienists.

Number of remaining teeth

The remaining teeth were determined by visual examination and palpation.

Periodontal tissue status

The condition of periodontal tissues was evaluated by a dentist. Tooth mobility was assessed by palpation and classified into four grades (M0–M3). Visual inspection was performed for signs of redness, swelling, bleeding, suppuration, and calculus accumulation. Based on these findings, sites with the most advanced periodontal involvement within the oral cavity were rated as normal, mild, moderate, severe, or no target teeth (edentulous jaw). These evaluations were conducted independently of the number of teeth present in the edentulous jaw.

Masticatory function

Masticatory function was evaluated using "Sugarless Fine Gummy jellies" (Fine Co., Ltd., Tokyo, Japan). One gummy was chewed for 15 s, and the number of crushed pieces of 3 mm or larger was counted to obtain the gummy 15-s value.

Articulation

The dentist or dental hygienist asked the patient to read the sentence "panda-no-takara-mono" and conducted a monosyllabic listening test of "pa," "ta," "ka," and "ra." The patient was judged as deficient if there was one indistinct syllable.

Swallowing function

Swallowing function was evaluated by recording the total time taken to complete three consecutive dry swallows following a sip of water taken just before the test began (integrated time for three consecutive swallows).

Oral hygiene status

Oral hygiene status was assessed using a four-point scale (good, needs attention, not so good, and poor) based on the overall condition of the dental plaque, tongue coating, breath odor, and denture cleanliness. Dental plaque was graded as clean, moderate, abundant, or no remaining teeth; tongue coating as clean, moderate, or abundant; breath odor as not noticeable, mild, or strong; denture hygiene as clean, moderate, dirty, or no dentures. If any category was rated as having the lowest cleanliness level, the overall status was classified as defective.

Subjective oral dryness

Dry mouth was diagnosed according to one of the following three criteria: (1) a positive response to at least two items in the questionnaire ("mouth feels dry," "tongue pain," or "reduced taste"); (2) use of more than five medications daily or poor nutritional status, combined with at least one positive response to the above items; (3) a positive response to "mouth feels dry" in the questionnaire, together with clinical suspicion of xerostomia based on visual and palpatory examination by a dentist.

Social participation

Health assessment questionnaires for older adults, which were used by local governments throughout Japan in April 2020, were used to conduct interviews. The social participation item in the questionnaire was "do you go out at least once a week?". Living out was validated in a previous qualitative study as a question related to older adults' social participation [31].

Cognitive status

Health assessment questionnaires for older adults, which were used by local governments throughout Japan in April 2020, were used to conduct interviews. The cognitive status item in the questionnaire was, "Do people around you comment on your forgetfulness, e.g., say to you, You are always asking the same thing" (forgetfulness) and "There are times when you don't remember today's date" (accurate date recall) [32, 33]. "Cognitive status" was validated in a previous qualitative study as a question related to the social participation of older adults.

Medical history

Data regarding the presence or absence of a medical history of hypertension, diabetes mellitus, stroke, heart disease, cancer, lung disease, osteoporosis, or orthopedic diseases were collected.

Statistical analysis

Descriptive statistics were calculated as means and percentages for each variable. Participants were categorized into two groups: (1) those with forgetfulness (forgetfulness group) and those without (non-forgetfulness group), and (2) those who forgot dates (impaired date recall group) and those who did not (non-impaired date recall group). Logistic regression was used for both the univariate and multivariate analyses. Multicollinearity was assessed using the variance inflation factor (VIF) with a cutoff value of 10. When multicollinearity was detected, the correlated variable was included in the model. Based on previous studies, factors strongly associated with oral diseases were identified and used to select explanatory variables in a multivariate model. The outcome variable was cognitive status, and a variable reduction method was applied. Statis-tical analyses were conducted using SPSS version 27, with statistical significance set at $p < 0.05$.

RESULTS

Participants' characteristics

Table 1 lists the baseline characteristics of the study

Table 1. Demographic characteristics (n = 4,338)

Variables	Categories	n (%)	Mean [SD]
Age (years)			79.5 [2.8]
Sex	Male	1,909 (44.0)	
	Female	2,429 (56.0)	
Body mass index (kg/m^2)			22.6 [3.1]
Lower leg circumference (cm)			33.3 [3.0]
Current smoker (yes)		146 (3.4)	
Number of remaining teeth			18.2 [9.0]
Periodontal tissue status			2.3 [1.0]
Masticatory function (gummy; 15 s)			16.4 [12.7]
Articulation pa	Good	4,327 (99.7)	
	Unclear	11 (0.3)	
Articulation ta	Good	4,318 (99.5)	
	Unclear	20 (0.5)	
Articulation ka	Good	4,324 (99.7)	
	Unclear	14 (0.3)	
Articulation ra	Good	4,315 (99.5)	
	Unclear	23 (0.5)	
Swallowing function			15.8 [10.1]
Oral hygiene status			1.5 [0.6]
Subjective oral dryness (yes)		418 (9.6)	
Social participation (going out, yes)		4,041 (93.2)	
Cognitive status	Forgetfulness (yes)	612 (14.1)	
	Accurate date recall (yes)	997 (23.0)	
Medical history	Hypertension	2,008 (46.3)	
	Diabetes mellitus	514 (11.8)	
	Stroke	36 (0.8)	
	Heart disease	384 (8.9)	
	Cancer	112 (2.6)	
	Lung disease	115 (2.7)	
	Osteoporosis	569 (13.1)	
	Orthopedic diseases	799 (18.4)	

SD, standard deviation

participants. The mean age was 79.5 years (SD 2.8), with 1,909 males (44.0%) and 2,429 females (56.0%). Regarding physical indicators, the mean BMI was 22.6 (SD 3.1), mean calf circumference was 33.3 cm (SD 3.0). In terms of lifestyle habits, 568 participants (13.1%) reported smoking. Regarding oral function, the mean number of remaining teeth was 18.2 (SD 9.0), mean periodontal tissue status was 2.3 (SD 1.0), 1,655 participants (38.1%) had masticatory dysfunction, participants with good articulation of "pa" was 4,327 (99.7%), "ta" was 4,318 (99.5%), "ka" was 4,324 (99.7%), and "ra" was 4,315 (99.5%), 485 (11.2%) had swallowing dysfunction, 1,144 (26.4%) had oral dryness, and 1,300 (29.9%) had poor oral hygiene status. In addition, 4,041 participants (93.2%) reported going out at least once a week, 612 participants (14.1%) reported being told they forget things, 997 participants (23.0%) reported sometimes being unable to recall today's date. Regarding medical history, 2,008 participants (46.3%) had hypertension, 514 (11.8%) had diabetes mellitus, 36 (0.8%) had stroke, 384 (8.9%) had heart disease, 112 (2.6%) had cancer, 115 (2.7%) had lung disease, 569 (13.1%) had osteoporosis, and 799 (18.4%) had orthopedic disorders.

Group comparison between the forgetfulness group and the non-forgetfulness group

Table 2 compares the forgetfulness and non-forgetfulness groups. Participants in the forgetfulness group (N = 612) were significantly older (80.1 ± 2.9 years) than those in the non-forgetfulness group (79.4 ± 2.8 years, $p < 0.001$). Lower leg circumference was slightly smaller in the forgetfulness group (33.1 ± 3.0 cm) than in the non-forgetfulness group (33.4 ± 3.0 cm, $p = 0.023$). The proportion of current smokers was slightly lower in the forgetfulness group (3.1%) than in the non-forgetfulness group (3.4%, $p = 0.018$). The number of remaining teeth was lower in the forgetfulness group (16.8 ± 9.5) than the non-forgetfulness group (18.4 ± 8.9, $p < 0.001$), and periodontal tissue status was poorer (2.5 ± 1.1 vs. 2.3 ± 1.0, $p = 0.024$). Masticatory function, measured by gummy chewing for 15 s, was reduced in the forgetfulness group (14.0 ± 12.7 g) compared to the non-forgetfulness group (16.8 ± 12.7 g, $p < 0.001$). Similarly, swallowing function was lower (17.3 ± 10.6 vs. 15.6 ± 10.0, $p < 0.001$), and oral hygiene status was slightly worse (1.6 ± 0.7 vs. 1.5 ± 0.6, $p < 0.001$). Subjective oral dryness was more frequently reported in the forgetfulness group (13.2%) than in the non-forgetfulness group (9.0%, $p = 0.002$). Social participation, defined as going out, was less common in the forgetfulness group (87.7%) than in the non-forgetfulness group (94.0%, $p < 0.001$). Regarding

Table 2. Comparison between the forgetfulness group and the non-forgetfulness group

Variables	Categories	N (%) or mean [SD]		p-value
		Forgetfulness group (N = 612)	Non-forgetfulness group (N = 3,726)	
Age (years)		80.1 [2.9]	79.4 [2.8]	< 0.001*
Sex	Male	286 (46.7)	1,623 (43.6)	0.147
	Female	326 (53.3)	2,103 (56.4)	
Body mass index (kg/m^2)		22.7 [3.0]	22.6 [3.1]	0.416
Lower leg circumference (cm)		33.1 [3.0]	33.4 [3.0]	0.023*
Current smoker (yes)		19 (3.1)	127 (3.4)	0.018*
Number of remaining teeth		16.8 [9.5]	18.4 [8.9]	< 0.001*
Periodontal tissue status		2.5 [1.1]	2.3 [1.0]	< 0.024*
Masticatory function (gummy; 15 s)		14.0 [12.7]	16.8 [12.7]	< 0.001*
Articulation pa	Good	609 (14.1)	3 (27.3)	0.194
	Unclear	3,718 (85.9)	8 (72.7)	
Articulation ta	Good	606 (14.0)	6 (30.0)	0.052
	Unclear	3,712 (86.0)	14 (70.0)	
Articulation ka	Good	609 (14.1)	3 (21.4)	0.434
	Unclear	3,715 (85.9)	11 (78.6)	
Articulation ra	Good	608 (14.1)	4 (17.4)	0.555
	Unclear	3,707 (85.9)	19 (82.6)	
Swallowing function		17.3 [10.6]	15.6 [10.0]	< 0.001*
Oral hygiene status		1.6 [0.7]	1.5 [0.6]	< 0.001*
Subjective oral dryness (yes)		81 (13.2)	337 (9.0)	< 0.002*
Social participation (going out, yes)		537 (87.7)	3,504 (94.0)	< 0.001*
Medical history	Hypertension	274 (44.7)	1734 (46.5)	0.431
	Diabetes mellitus	82 (13.4)	432 (11.6)	0.200
	Stroke	6 (1.0)	30 (0.8)	0.630
	Heart disease	68 (11.1)	316 (8.5)	0.038*
	Cancer	17 (2.8)	95 (2.5)	0.682
	Lung disease	22 (3.6)	93 (2.5)	0.134
	Osteoporosis	84 (13.7)	485 (13.0)	0.651
	Orthopedic diseases	156 (25.5)	643 (17.3)	< 0.001*

SD, standard deviation

medical history, the prevalence of heart disease was higher in the forgetfulness group (11.1%) than in the non-forgetfulness group (8.5%, p = 0.038), and orthopedic disease was more common (25.5% vs. 17.3%, p < 0.001).

Group comparison between the accurate and non-accurate date recall groups

Table 3 shows comparisons between the accurate and inaccurate date recall groups. Participants in the accurate date recall group (N = 997) were significantly older (80.0 ± 3.0 years) than those in the non-accurate recall group (79.3 ± 2.8 years, p < 0.001). The number of remaining teeth was lower in the accurate recall group (17.3 ± 9.4) than the non-accurate group (18.5 ± 8.9, p < 0.001). Masticatory function was also reduced (15.2 ± 12.8 vs. 16.7 ± 12.7, p < 0.01), while swallowing function was slightly better in the accurate recall group (16.5 ± 10.7 vs. 15.6 ± 9.9, p = 0.007). Oral hygiene status was marginally worse in the accurate recall group (1.6 ± 0.7) than in the non-accurate group (1.5 ± 0.6, p = 0.006). Subjective oral dryness was more prevalent (12.4% vs. 8.8%, p < 0.001), and the proportion of current smokers was higher (4.9% vs. 2.9%, p = 0.001). Social participation was lower in the accurate recall group (89.6%) than in the inaccurate recall group (94.2%; p < 0.01). Diabetes

Table 3. Comparison between the accurate date recall group and the non-accurate date recall group

Variables	Categories	N (%) or mean [SD]		p-value
		Impaired date recall group (N = 997)	Non-impaired date recall group (N = 3,341)	
Age (years)		80.0 [3.0]	79.3 [2.8]	< 0.001*
Sex	Male	422 (42.3)	1,487 (44.5)	0.230
	Female	575 (57.7)	1,854 (55.5)	
Body mass index (kg/m^2)		22.5 [3.0]	22.7 [3.1]	0.055
Lower leg circumference (cm)		32.9 [3.0]	33.4 [2.9]	< 0.001*
Current smoker (yes)		49 (4.9)	97 (2.9)	0.001*
Number of remaining teeth		17.3 [9.4]	18.5 [8.9]	< 0.001*
Periodontal tissue status		2.4 [1.1]	2.3 [1.0]	0.054
Masticatory function (gummy; 15 s)		15.2 [12.8]	16.7 [12.7]	< 0.001*
Articulation pa	Good	994 (99.7)	3,333 (99.8)	0.723
	Unclear	3 (0.3)	8 (0.2)	
Articulation ta	Good	992 (99.5)	3,326 (99.6)	0.792
	Unclear	5 (0.5)	15 (0.4)	
Articulation ka	Good	992 (99.5)	3,332 (99.7)	0.335
	Unclear	5 (0.5)	9 (0.3)	
Articulation ra	Good	993 (99.6)	3,322 (99.4)	0.627
	Unclear	4 (0.4)	19 (0.6)	
Swallowing function		16.5 [10.7]	15.6 [9.9]	0.007*
Oral hygiene status		1.6 [0.7]	1.5 [0.6]	0.006*
Subjective oral dryness (yes)		124 (12.4)	294 (8.8)	< 0.001*
Social participation (going out, yes)		893 (89.6)	3,148 (94.2)	< 0.001*
Medical history	Hypertension	445 (44.6)	1,563 (46.8)	0.247
	Diabetes mellitus	140 (14.0)	374 (11.2)	0.016*
	Stroke	16 (1.6)	20 (0.6)	0.004*
	Heart disease	87 (8.7)	297 (8.9)	0.899
	Cancer	27 (2.7)	85 (2.5)	0.734
	Lung disease	28 (2.8)	87 (2.6)	0.736
	Osteoporosis	141 (14.1)	428 (12.8)	0.285
	Orthopedic diseases	210 (21.1)	589 (17.6)	0.015*

SD, standard deviation

mellitus was more common in the accurate recall group (14.0% vs. 11.2%, p = 0.02), as was stroke (1.6% vs. 0.6%, p = 0.004), and orthopedic diseases (21.1% vs. 17.6%, p = 0.015).

Relationship between oral function and forgetfulness

Table 4 presents the relationship between oral function and forgetfulness. Multivariate logistic regression analysis revealed that increasing age was significantly associated with higher odds of the outcome (odds ratio [OR] = 1.08, 95% CI: 1.05–1.11, p < 0.001). Female sex was associated with lower odds compared to males (OR = 0.78, 95% CI: 0.64–0.96, p = 0.019). Lower leg circumference showed a protective effect (OR = 0.96, 95% CI: 0.92–0.99, p = 0.031), current smokers was associated (OR = 1.31, 95% CI: 1.06–1.31, p = 0.012). Masticatory function was inversely associated with the outcome (OR = 0.99, 95% CI: 0.98–0.99, p < 0.001), swallowing function was related (OR = 1.01, 95% CI: 1.00–1.02, p = 0.014), and poorer oral hygiene status increased the odds (OR = 1.15, 95% CI: 1.02–1.31, p = 0.027). Social participation, defined as going out, was significantly protective (OR = 0.53, 95% CI: 0.40–0.70, p < 0.001). Among medical history variables, orthopedic diseases were significantly associated with increased odds (OR = 1.55, 95% CI: 1.26–1.90, p < 0.001).

Table 4. Factors associated with forgetfulness using logistic regression analysis.

Variables	Categories	Univariate		Multivariate	
		Odds (95% CI)	p-value	Odds (95% CI)	p-value
Age (years)		1.10 (1.07–1.13)	< 0.001*	1.08 (1.05–1.11)	< 0.001*
Sex	Male	1 (ref)	0.143	1 (ref)	0.019*
	Female	0.88 (0.74–1.04)		0.78 (0.64–0.96)	
Body mass index (kg/m^2)		1.01 (0.98–1.04)	0.416	1.04 (0.99–1.08)	0.054
Lower leg circumference (cm)		0.97 (0.94–1.00)	0.046*	0.96 (0.92–0.99)	0.031*
Current smoker (yes)		1.30 (1.07–1.57)	0.009*	1.31 (1.06–1.31)	0.012*
Number of remaining teeth		0.98 (0.97–0.99)	< 0.001*		
Periodontal tissue status		1.14 (1.05–1.23)	< 0.001*		
Masticatory function (gummy; 15 s)		0.98 (0.97–0.99)	< 0.001*	0.99 (0.98–0.99)	< 0.001*
Articulation pa	Good	1 (ref)	0.222		
	Unclear	2.29 (0.61–8.65)			
Articulation ta	Good	1 (ref)	0.049*		
	Unclear	2.63 (1.01–6.86)			
Articulation ka	Good	1 (ref)	0.436		
	Unclear	1.66 (0.46–5.98)			
Articulation ra	Good	1 (ref)	0.651		
	Unclear	1.28 (0.44–3.79)			
Swallowing function		1.02 (1.01–1.02)	< 0.001*	1.01 (1.00–1.02)	0.014*
Oral hygiene status		1.29 (1.14–1.46)	< 0.001*	1.15 (1.02–1.31)	0.027*
Subjective oral dryness (yes)		1.53 (1.18–1.99)	< 0.001*		
Social participation (going out)		0.45 (0.34–0.60)	< 0.001*	0.53 (0.40–0.70)	< 0.001*
Medical history	Hypertension	0.93 (0.78–1.10)	0.417		
	Diabetes mellitus	1.18 (0.92–1.52)	0.201		
	Stroke	1.22 (0.51–2.94)	0.658		
	Heart disease	1.35 (1.02–1.78)	0.034*		
	Cancer	1.09 (0.65–1.84)	0.742		
	Lung disease	1.46 (0.91–2.34)	0.119		
	Osteoporosis	1.06 (0.83–1.36)	0.630		
	Orthopedic diseases	1.64 (1.34–2.01)	< 0.001*	1.55 (1.26–1.90)	< 0.001*

CI: Confidence interval, *p < 0.05

Relationship between oral function and accurate date recall

Table 5 shows the relationship between oral function and accurate data recall. Multivariate logistic regression analysis revealed that increasing age was significantly associated with higher odds of the outcome (OR = 1.07, 95% CI: 1.05–1.10, p < 0.001). Lower leg circumference showed a protective effect (OR = 0.96, 95% CI: 0.93–0.98, p < 0.001), while subjective oral dryness was positively associated (OR = 1.30, 95% CI: 1.04–1.64, p = 0.023). Social participation, defined as going out, was significantly protective (odds ratio [OR]: 0.58; 95% CI: 0.45–0.74, p < 0.001). Among medical history variables, diabetes mellitus showed an association (odds ratio = 1.30, 95% confidence interval: 1.05–1.61, p = 0.014), and stroke showed a strong association with increased odds (OR = 2.80, 95% CI: 1.43–5.51, p = 0.003).

DISCUSSION

The major finding of this study was that four domains of oral function (masticatory function, swallowing function, oral hygiene status, and oral dryness) were significantly associated with subjective cognitive decline in community-dwelling older adults. Furthermore, this study demonstrates novelty in indicating that specific oral functions, among multiple oral functions, may be associated with cognitive

Table 5. Factors associated with accurate date recall using logistic regression analysis

Variables	Categories	Univariate		Multivariate	
		Odds (95% CI)	p-value	Odds (95% CI)	p-value
Age (years)		1.09 (1.06–1.12)	< 0.001*	1.07 (1.05–1.10)	< 0.001*
Sex	Male	1 (ref)	0.224		
	Female	1.09 (0.95–1.26)			
Body mass index (kg/m^2)		0.98 (0.96–1.00)	0.110		
Lower leg circumference (cm)		0.94 (0.92–0.97)	< 0.001*	0.96 (0.93–0.98)	< 0.001*
Current smoker (yes)		1.02 (0.87–1.20)	0.825		
Number of remaining teeth		0.99 (0.98–0.99)	< 0.001*		
Periodontal tissue status		1.10 (1.03–1.17)	0.008*		
Masticatory function (gummy; 15 s)		0.99 (0.99–1.00)	0.001*		
Articulation pa	Good	1 (ref)	0.735		
	Unclear	1.26 (0.33–4.75)			
Articulation ta	Good	1 (ref)	0.830		
	Unclear	1.12 (0.41–3.08)			
Articulation ka	Good	1 (ref)	0.264		
	Unclear	1.87 (0.62–5.58)			
Articulation ra	Good	1 (ref)	0.525		
	Unclear	0.70 (0.24–2.08)			
Swallowing function		1.01 (1.00–1.02)	0.008*		
Oral hygiene status		1.12 (1.01–1.25)	0.030*		
Subjective oral dryness (yes)		1.47 (1.18–1.84)	< 0.001*	1.30 (1.04–1.64)	0.023*
Social participation (going out)		0.53 (0.41–0.68)	< 0.001*	0.58 (0.45–0.74)	< 0.001*
Medical history	Hypertension	0.92 (0.80–1.06)	0.232		
	Diabetes mellitus	1.30 (1.05–1.60)	0.015*	1.30 (1.05–1.61)	0.014*
	Stroke	2.71 (1.40–5.25)	0.003*	2.80 (1.43–5.51)	0.003*
	Heart disease	0.98 (0.76–1.26)	0.873		
	Cancer	1.07 (0.69–1.65)	0.775		
	Lung disease	1.08 (0.70–1.66)	0.724		
	Osteoporosis	1.12 (0.91–1.38)	0.274		
	Orthopedic diseases	1.25 (1.05–1.49)	0.014*	1.18 (0.98–1.41)	0.074

CI: Confidence interval, *p < 0.05

function. This result supports the findings of previous studies indicating that impaired oral function is a risk factor for cognitive decline [30]. Several cohort studies have demonstrated that older adults with reduced masticatory function are at an increased risk of cognitive decline and dementia [34]. Moreover, masticatory activities, such as chewing gum, have been suggested to improve the processing speed and memory task performance [35]. Functional magnetic resonance imaging (fMRI) studies have further reported that mastication enhances activation in the hippocampus and prefrontal cortex, leading to improvements in memory recognition, suggesting that chewing activates cognitive networks [36]. Thus, although the cross-sectional design of this study allowed for only inferences, our findings suggest that reduced masticatory function negatively influences cognitive decline. Among community-dwelling older males, a decline in swallowing function has been reported to reflect cognitive deterioration [37]. Older adults with cognitive impairment have an approximately 3.2-fold increased risk of developing dysphagia, suggesting cognitive decline as a risk factor for impaired swallowing [37]. Therefore, although swallowing function and cognition were associated in our study, the causal direction may differ from that of masticatory function, as many studies have indicated that cognitive impairment influences the decline in swallowing. Poor oral hygiene promotes neuroinflammation and neurodegeneration through periodontal pathogens and inflammatory mediators that reach the brain through systemic circulation [25]. *Porphyromonas gingivalis* infection has been identified in the brain of patients with Alzheimer's disease, and gingipain inhibition has been shown to ameliorate pathological changes [25]. Although direct evidence of the association between oral hygiene and cognition remains limited, poor oral hygiene may contribute to cognitive decline through pathways involving tooth loss and subsequent deterioration of masticatory function. Oral dryness can impair mastication, swallowing, taste perception, and conversation, thereby reducing social interaction and diminishing cognitive reserve [38]. An observational study in Spain reported that older adults with cognitive impairment exhibit oral dryness more frequently, with dementia pharmacotherapy potentially contributing to this symptom [39]. Conversely, a cross-sectional study in China that investigated the overall oral function, including oral dryness, did not detect a clear association between oral dryness alone and cognition [40]. In our study, medication use was not considered an adjustment factor; further research is required to clarify the relationship between oral dryness and cognitive function.

Age, sex, lower leg circumference, smoking, social participation, diabetes mellitus, cerebrovascular disease, and orthopedic disorders are associated with cognitive function. Several factors influence cognitive performance. Age was the greatest risk factor, with the risk of cognitive decline markedly increasing with advancing age [41]. Sex differences have also been reported, with females having a higher risk of developing Alzheimer's disease than males [42]. Lower leg circumference reflects sarcopenia and nutritional status, with muscle loss associated with cognitive deterioration [43]. Among lifestyle factors, smoking contributes to cognitive decline through oxidative stress and vascular damage [44].

Reduced social participation increases the risk of dementia through isolation and decreased mental engagement [45]. In addition, diabetes mellitus promotes neurodegeneration through hyperglycemia and insulin resistance, and is strongly associated with cognitive impairment [46]. Cerebrovascular diseases contribute to dementia by causing neuronal injury through blood flow disturbances and infarction [47]. Orthopedic disorders, by limiting physical activity, may adversely affect cognition through mechanisms such as inactivity and frailty [48]. Thus, the non-oral factors associated with cognition in this study are reasonable and consistent with existing evidence.

For cognitive function assessment, we used two questions: "Have others pointed out your forgetfulness?" and "Do you sometimes fail to recall today's date?". Both have been validated as simple, subjective measures of cognitive function in prior studies [32, 33]. The former reflects not only self-awareness but also memory deficits recognized in a social context and has been linked to social participation and the quality of interpersonal relationships. Conversely, the latter, which captures temporal orientation through data recall, is more strongly associated with biological factors such as aging and cerebro-

vascular disease. The differences in the associated factors observed in this study may be explained by the former reflecting social stimulation and environmental factors, whereas the latter measures cognitive domains more directly linked to neurological substrates. The greater number of associations between oral functions and the former measure may be because oral functions, such as mastication, swallowing, and speech, are closely tied to social interaction and daily living, making their decline more noticeable to others and reflected in subjective cognitive assessments. In contrast, impairments in date recall may capture neurological changes more directly, rendering them less sensitive to the indirect influences of oral function. Together, our findings and the findings of previous studies suggest that maintaining and improving oral hygiene and function through regular dental visits may help prevent cognitive decline. Therefore, a high-risk approach aimed at improving oral function is necessary for older adults with impaired oral function through collaboration with administrative agencies.

This study had three limitations. First, the participants were relatively healthy older adults who underwent community health examinations. The enrollment criteria did not exclude individuals certified as requiring long-term care under Japan's National Health Insurance system, and such participants were included. Although cognitive impairment was not an exclusion criterion, participants were required to complete the questionnaires, which likely excluded individuals with overt dementia. Moreover, long-term hospitalized or institutionalized individuals not eligible for health checkups were excluded from the study. This limitation represents a form of bias known as the "healthy volunteer effect," which is difficult to statistically control. In addition, the survey period coincided with the onset of the coronavirus disease 2019 pandemic, and thus it is important to consider the possibility that uncontrollable biases may have affected participants' behavior. Nevertheless, our findings may be generalizable to other Japanese regions with analogous aging populations, because the results of this study are consistent with those of other similar reports. Second, this was a cross-sectional study, and causality could not be established. Third, the recommended assessment of oral function was based on the diagnostic criteria for oral hypofunction introduced in the National Health Insurance database in 2018. However, we used data from group health examinations conducted in 2015 by the Shimane Dental Association. Although these examinations provide a simple and comprehensive assessment of oral function with cutoff values derived from community-based data, concerns remain regarding the reliability and validity of individual measures. While our study applied cross-sectional analyses, future research should employ longitudinal designs to examine the causal relationships.

CONCLUSIONS

The results of this study suggest an association between masticatory function, swallowing function, oral hygiene status, and dryness with cognitive function. Oral healthcare providers should develop oral healthcare activities while providing opportunities for the social participation of older adults, such as comprehensive community care, to maintain and promote oral health status and function.

Ethical approval

Medical Research Ethics Committee of Shimane University Faculty of Medicine (approval number 20220723-1)

Author Contributions

Conceptualization, T.A. and T.K.; methodology, K.I., Y.M., M.T., T.A., K.T., S.Y. and T.K.; software, K.I., Y.M. and M.T.; validation, K.I., Y.M., M.T., T.A. and T.K.; formal analysis, K.I., Y.M. and Y.A.; investigation, T.A., K.T., H.S., J.S., N.M., R.M. and Y.I.; resources, T.A., K.T., H.S., J.S., N.M., R.M. and Y.I.; data curation, K.I., Y.M., M.T., T.A. and K.T.; writing—original draft preparation, K.I. and Y.M.; writing—review and editing, T.A. and T.K.; visualization, K.I. and Y.M.; supervision, Y.A., S.Y., M.I. and T.K.; project administration, T.A., M.I. and T.K.; funding acquisition, T.A. All authors have read and agreed to the published version of the manuscript.

Acknowledgments

The authors thank all the participants who partici-

pated in this study. We would like to express our appreciation to the Center for Community-Based Health Research and Education (CoHRE) and Shimane Dental Association and all staff members of the Department of Oral and Maxillofacial Surgery of the Shimane University Faculty of Medicine for their kind assistance and support. We express our gratitude to those who participated in this study for their valuable contributions.

Funding

None

Conflict of Interest

None

REFERENCES

1) 2023 Alzheimer's disease facts and figures. *Alzheimers Dement*. 2023;19:1598-695. doi: 10.1002/alz.13016.

2) Collaborators GBDDF. Estimation of the global prevalence of dementia in 2019 and forecasted prevalence in 2050: an analysis for the Global Burden of Disease Study 2019. *Lancet Public Health*. 2022;7:e105-e25. doi: 10.1016/S2468-2667(21)00249-8.

3) Guarnera J, Yuen E, Macpherson H. The Impact of Loneliness and Social Isolation on Cognitive Aging: A Narrative Review. *J Alzheimers Dis Rep*. 2023;7:699-714. doi: 10.3233/ADR-230011.

4) Nakahara K, Yokoi K. Role of Meaningful Social Participation and Technology Use in Mitigating Loneliness and Cognitive Decline Among Older Adults. *Am J Occup Ther*. 2024;78:7806205150. doi: 10.5014/ajot.2024.050794.

5) Khan M, Jaiswal A, Wandile B. A Comprehensive Review of Modifiable Cardiovascular Risk Factors and Genetic Influences in Dementia Prevention. *Cureus*. 2023;15:e48430. doi: 10.7759/cureus.48430.

6) Muscat SM, Barrientos RM. Lifestyle modifications with anti-neuroinflammatory benefits in the aging population. *Exp Gerontol*. 2020;142:111144. doi: 10.1016/j.exger.2020.111144.

7) He J, Zhao C, Zhong S, *et al*. Blood pressure reduction and all-cause dementia in people with uncontrolled hypertension: an open-label, blinded-endpoint, cluster-randomized trial. *Nat Med*. 2025;31:2054-61. doi: 10.1038/s41591-025-03616-8.

8) Mogi M. Hypertension management to prevent dementia. *Hypertens Res*. 2022;45:573-5. doi: 10.1038/s41440-022-00869-5.

9) Cao F, Yang F, Li J, *et al*. The relationship between diabetes and the dementia risk: a meta-analysis. *Diabetol Metab Syndr*. 2024;16:101. doi: 10.1186/s13098-024-01346-4.

10) Zhao Y, Zhang H, Cheng J, Zou Y, Zhang D, Duan X. Association between Dyslipidaemia and Cognitive Impairment: A Meta-Analysis of Cohort and Case-Control Studies. *J Integr Neurosci*. 2024;23:40. doi: 10.31083/j.jin2302040.

11) Abe T, Tominaga K, Ando Y, *et al*. Reduced masticatory performance and not using dentures are associated with hypertension in older adults with tooth loss: the Shimane CoHRE study. *Hypertens Res*. 2022;45:1553-62. doi: 10.1038/s41440-022-00976-3.

12) Simpson TC, Clarkson JE, Worthington HV, *et al*. Treatment of periodontitis for glycaemic control in people with diabetes mellitus. *Cochrane Database Syst Rev*. 2022;4:CD004714. doi: 10.1002/14651858.CD004714.

13) Oohira M, Kitamura M, Higuchi K, *et al*. Association between total functional tooth unit score and hemoglobin A1c levels in Japanese community-dwelling individuals: the Nagasaki Islands study. *BMC Oral Health*. 2024;24:1254. doi: 10.1186/s12903-024-05043-6.

14) Fushida S, Kosaka T, Nakai M, *et al*. Lower Masticatory Performance Is a Risk for the Development of the Metabolic Syndrome: The Suita Study. *Front Cardiovasc Med*. 2021;8:752667. doi: 10.3389/fcvm.2021.752667.

15) Takahashi T, Hatta K, Ikebe K. Risk factors of cognitive impairment: Impact of decline in oral function. *Jpn Dent Sci Rev*. 2023;59:203-8. doi: 10.1016/j.jdsr.2023.06.006.

16) Minakuchi S, Tsuga K, Ikebe K, *et al*. Oral hypofunction in the older population: Position paper of the Japanese Society of Gerodontology in 2016. *Gerodontology*. 2018;35:317-24. doi: 10.1111/ger.12347.

17）Noble JM, Scarmeas N, Papapanou PN. Poor oral health as a chronic, potentially modifiable dementia risk factor: review of the literature. *Curr Neurol Neurosci Rep*. 2013;13:384. doi: 10.1007/s11910-013-0384-x.

18）Sherman DW, Alfano AR, Alfonso F, *et al*. A Systematic Review of the Relationship between Social Isolation and Physical Health in Adults. *Healthcare (Basel)*. 2024;12:1135. doi: 10.3390/healthcare12111135.

19）Kugimiya Y, Watanabe Y, Igarashi K, *et al*. Factors associated with masticatory performance in community-dwelling older adults: A cross-sectional study. *J Am Dent Assoc*. 2020;151:118-126. doi: 10.1016/j.adaj.2019.10.003.

20）Momose T, Nishikawa J, Watanabe T, *et al*. Effect of mastication on regional cerebral blood flow in humans examined by positron-emission tomography with （1）（5）O-labelled water and magnetic resonance imaging. *Arch Oral Biol*. 1997;42:57-61. doi: 10.1016/s0003-9969(96)00081-7.

21）Silva Ulloa S, Cordero Ordonez AL, Barzallo Sardi VE. Relationship between dental occlusion and brain activity: A narrative review. *Saudi Dent J*. 2022;34:538-43. doi: 10.1016/j.sdentj.2022.09.001.

22）Sasegbon A, Hamdy S. The anatomy and physiology of normal and abnormal swallowing in oropharyngeal dysphagia. *Neurogastroenterol Motil*. 2017;29. doi: 10.1111/nmo.13100.

23）Easterling CS, Robbins E. Dementia and dysphagia. *Geriatr Nurs*. 2008;29:275-85. doi: 10.1016/j.gerinurse.2007.10.015.

24）Lu JJ, Ma J, Wu JJ, *et al*. Tongue coating-dependent superior temporal sulcus remodeling in amnestic mild cognitive impairment. *Brain Res Bull*. 2024;214:110995. doi: 10.1016/j.brainresbull.2024.110995.

25）Dominy SS, Lynch C, Ermini F, *et al*. Porphyromonas gingivalis in Alzheimer's disease brains: Evidence for disease causation and treatment with small-molecule inhibitors. *Sci Adv*. 2019;5:eaau3333. doi: 10.1126/sciadv.aau3333.

26）Kamer AR, Pushalkar S, Gulivindala D, *et al*. Periodontal dysbiosis associates with reduced CSF Abeta42 in cognitively normal elderly. *Alzheimers Dement (Amst)*. 2021;13:e12172. doi: 10.1002/dad2.12172.

27）Pei XM, Zhou LX, Tsang MW, Tai WC, Wong SC. The Oral Microbial Ecosystem in Age-Related Xerostomia: A Critical Review. *Int J Mol Sci*. 2024;25:12815. doi: 10.3390/ijms252312815.

28）Rosa L, Lepanto MS, Cutone A, *et al*. Lactoferrin and oral pathologies: a therapeutic treatment. *Biochem Cell Biol*. 2021;99:81-90. doi: 10.1139/bcb-2020-0052.

29）Xie Y, Xia X, Tian X, *et al*. The association between cognitive impairment and oral health or oral hygiene behaviors among multiethnic older adults in Western China: a cross-sectional multicenter study. *BMC Public Health*. 2025;25:259. doi: 10.1186/s12889-024-21158-5.

30）Mishima Y, Nakamura M, Matsuda Y, *et al*. Association Between Cognitive Impairment and Poor Oral Function in Community-Dwelling Older People: A Cross-Sectional Study. *Healthcare (Basel)*. 2025;13:589. doi: 10.3390/healthcare13060589.

31）Laliberte Rudman D, Gold D, McGrath C, Zuvela B, Spafford MM, Renwick R. "Why would I want to go out?": Age-related Vision Loss and Social Participation. *Can J Aging*. 2016;35:465-78. doi: 10.1017/S0714980816000490.

32）Hill NL, Bhargava S, Bratlee-Whitaker E, Turner JR, Brown MJ, Mogle J. Longitudinal Relationships Between Subjective Cognitive Decline and Objective Memory: Depressive Symptoms Mediate Between-Person Associations. *J Alzheimers Dis*. 2021;83:1623-36. doi: 10.3233/JAD-210230.

33）Kumai K, Kawabata N, Meguro K, Takada J, Nakamura K, Yamaguchi S. Mental and Physical Self-Awareness of Alzheimer Patients: Decreased Awareness of Amnesia and Increased Fear of Falling Compared to Views of Families: The Tajiri and Wakuya Projects. *Dement Geriatr Cogn Disord*. 2021;50:96-102. doi: 10.1159/000516656.

34）Tada A, Miura H. Association between mastication and cognitive status: A systematic review. *Arch Gerontol Geriatr*. 2017;70:44-53. doi: 10.1016/j.archger.2016.12.006.

35）Hirano Y, Obata T, Takahashi H, *et al*. Effects of chewing on cognitive processing speed. *Brain Cogn*. 2013;81:376-81. doi: 10.1016/j.bandc.2012.12.002.

36) Hirano Y, Obata T, Kashikura K, Nonaka H, Tachibana A, Ikehira H, *et al*. Effects of chewing in working memory processing. *Neurosci Lett*. 2008;436:189-92. doi: 10.1016/j.neulet.2008.03.033.

37) Dehaghani SE, Doosti A, Zare M. Association between swallowing disorders and cognitive disorders in adults: a systematic review and meta-analysis. *Psychogeriatrics*. 2021;21:668-74. doi: 10.1111/psyg.12704.

38) Lu TY, Chen JH, Du JK, *et al*. Dysphagia and masticatory performance as a mediator of the xerostomia to quality of life relation in the older population. *BMC Geriatr*. 2020;20:521. doi: 10.1186/s12877-020-01901-4.

39) Gil-Montoya JA, Barrios R, Sanchez-Lara I, *et al*. Prevalence of Drug-Induced Xerostomia in Older Adults with Cognitive Impairment or Dementia: An Observational Study. *Drugs Aging*. 2016;33:611-8. doi: 10.1007/s40266-016-0386-x.

40) Chen Y, Li C, Fan Y, Jiao L, Silverman M, Ishimaru M, *et al*. Associations of oral health status and swallowing function with cognitive impairment in the aging population: a cross-sectional study. *BMC Oral Health*. 2023;23:912. doi: 10.1186/s12903-023-03640-5.

41) Nalls MA, Blauwendraat C, Vallerga CL, *et al*. Identification of novel risk loci, causal insights, and heritable risk for Parkinson's disease: a meta-analysis of genome-wide association studies. *Lancet Neurol*. 2019;18:1091-102. doi: 10.1016/S1474-4422(19)30320-5.

42) Aggarwal NT, Mielke MM. Sex Differences in Alzheimer's Disease. *Neurol Clin*. 2023;41:343-58. doi: 10.1016/j.ncl.2023.01.001.

43) Ishii H, Makizako H, Doi T, Tsutsumimoto K, Shimada H. Associations of Skeletal Muscle Mass, Lower-Extremity Functioning, and Cognitive Impairment in Community-Dwelling Older People in Japan. *J Nutr Health Aging*. 2019;23:35-41. doi: 10.1007/s12603-018-1110-9.

44) Anstey KJ, von Sanden C, Salim A, O'Kearney R. Smoking as a risk factor for dementia and cognitive decline: a meta-analysis of prospective studies. *Am J Epidemiol*. 2007;166:367-78. doi: 10.1093/aje/kwm116.

45) Kuiper JS, Zuidersma M, Oude Voshaar RC, *et al*. Social relationships and risk of dementia: A systematic review and meta-analysis of longitudinal cohort studies. *Ageing Res Rev*. 2015;22:39-57. doi: 10.1016/j.arr.2015.04.006.

46) Akter K, Lanza EA, Martin SA, Myronyuk N, Rua M, Raffa RB. Diabetes mellitus and Alzheimer's disease: shared pathology and treatment? *Br J Clin Pharmacol*. 2011;71:365-76. doi: 10.1111/j.1365-2125.2010.03830.x.

47) Leys D, Erkinjuntti T, Desmond DW, *et al*. Vascular dementia: the role of cerebral infarcts. *Alzheimer Dis Assoc Disord*. 1999;13 Suppl 3:S38-48. doi: 10.1097/00002093-199912003-00007.

48) Tian J, Jones G, Lin X, *et al*. Association between chronic pain and risk of incident dementia: findings from a prospective cohort. *BMC Med*. 2023;21:169. doi: 10.1186/s12916-023-02875-x.