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Author(s)	Hironaka, Sanae; Kugimiya, Yoshihiro; Watanabe, Yutaka; Motokawa, Keiko; Hirano, Hirohiko; Kawai, Hisashi; Kera, Takeshi; Kojima, Motonaga; Fujiwara, Yoshinori; Ihara, Kazushige; Kim, Hunkyung; Obuchi, Shuichi; Kakinoki, Yasuaki
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## Association between oral, social, and physical frailty in community-dwelling older adults

Sanae Hironaka<sup>a,b</sup>, Yoshihiro Kugimiya<sup>c</sup>, Yutaka Watanabe<sup>b,d</sup>, Keiko Motokawa<sup>b</sup>, Hirohiko Hirano<sup>b,e</sup>,  
Hisashi Kawai<sup>f</sup>, Takeshi Kera<sup>f,g</sup>, Motonaga Kojima<sup>h</sup>, Yoshinori Fujiwara<sup>i</sup>, Kazushige Ihara<sup>j</sup>, Hunkyung  
Kim<sup>b</sup>, Shuichi Obuchi<sup>f</sup>, Yasuaki Kakinoki<sup>a</sup>

<sup>a</sup>Department of Special Needs and Geriatric Dentistry, Kyushu Dental University, Kitakyushu, Japan

<sup>b</sup>Research Team for Promoting Independence and Mental Health, Tokyo Metropolitan Institute of Gerontology, Tokyo, Japan

<sup>c</sup>Department of Removable Prosthodontics and Gerodontology, Tokyo Dental College, Tokyo, Japan

<sup>d</sup>Gerodontology, Department of Oral Health Science, Faculty of Dental Medicine, Hokkaido University, Sapporo, Japan

<sup>e</sup>Department of Oral Surgery and Dentistry, Tokyo Metropolitan Geriatric Hospital, Tokyo, Japan

<sup>f</sup>Research Team for Human Care, Tokyo Metropolitan Institute of Gerontology, Tokyo, Japan

<sup>g</sup>Department of Physical Therapy, Takasaki University of Health and Welfare, Takasaki, Japan

<sup>h</sup>Department of Physical Therapy, University of Tokyo Health Sciences, Tokyo, Japan

<sup>i</sup>Research Team for Social Participation and Community Health, Tokyo Metropolitan Institute of Gerontology, Tokyo, Japan

<sup>1</sup>Department of Social Medicine, Hirosaki University Graduate School of Medicine, Hirosaki City,  
Aomori, Japan

Corresponding author:

Yutaka Watanabe DDS, PhD

Associate Professor

Gerodontology, Department of Oral Health Science, Faculty of Dental Medicine,

Hokkaido University

Nishi-7, Kita-13, Kita-ku, Sapporo, Hokkaido 060-8586, Japan.

Phone & Fax: 81-11-706-4582

Email: [ywata@den.hokudai.ac.jp](mailto:ywata@den.hokudai.ac.jp)

Research Team for Promoting Independence and Mental Health, Tokyo Metropolitan Institute of

Gerontology

35-2 Sakae-cho, Itabashi-ku, Tokyo 173-0015, Japan.

## **Abstract**

**Objectives** Oral frailty (OF) has been shown to be a predictor of disability. Therefore, it is important to be able to identify factors associated with OF in order to prevent long-term dependence. The purpose of this study was to clarify the relationships between OF, social frailty (SF), and physical frailty (PF) in community-dwelling older adults, with the overarching aim of informing the future development of effective measures to prevent frailty.

**Methods** Oral, physical, and social function, nutritional and psychological status, and medical history were examined in 682 community-dwelling individuals (267 men, 415 women) aged  $\geq 65$  years. Ordinal logistic regression analysis with SF and PF as independent variables was performed with path analysis to determine the relationship between the different types of frailty.

**Results** Logistic regression analysis revealed significant associations between OF and decline in social function, physical function, and nutritional status, and an increase in the number of medications used. Path analysis showed that SF was directly related to OF and that OF and SF were directly related to PF.

**Conclusions** These findings suggest that a decline in social function may directly influence a decline in oral and physical function. The results of this study provide initial evidence, that may guide the future development of measures that aim to prevent and manage OF.

**Key words:** oral frailty, social frailty, physical frailty, path analysis, oral function, polypharmacy

### **Abbreviations list**

GFI, goodness of fit index

IADL, instrumental activities of daily living

JST-IC, Japan Science and Technology Agency Index of Competence

LTCL, Japanese public long-term care insurance system

MMSE, Mini-Mental State Examination

MNA-SF, Mini Nutritional Assessment-Short Form

NFI, normed fit index

ODK, oral diadochokinesis

OF, oral frailty

PF, physical frailty

RMSEA, root mean square error of approximation

SF, social frailty

## 1. Introduction

Frailty is an important consideration in the development of strategies that aim to optimize a healthy life expectancy in the super-aged population of Japan. Frailty is defined as “a clinical state in which there is an increase in an individual's risk of dependence and/or mortality when exposed to a stressor that can be reduced by taking appropriate measures” (Morley et al., 2013). Risk factors for frailty include chronic disease (Danon-Hersch, Rodondi, Spagnoli, & Santos-Eggimann, 2012; Denfeld et al., 2017), poor nutritional status (Soysal et al., 2019), and polypharmacy (Saum et al., 2017). There is also evidence suggesting a relationship between frailty, number of teeth present, and oral function (Hakeem, Bernabé, & Sabbah, 2019; Tanaka et al., 2018).

Previous studies assessed oral function with only a single measure (e.g., tongue pressure or occlusal force) (Nakagawa et al., 2017; Tsuga, Maruyama, Yoshikawa, Yoshida, & Akagawa, 2011). Minakuchi et al. (2018) suggested that a multidimensional approach is necessary to evaluate oral function, which includes mastication, swallowing, and phonation. No recent studies have demonstrated that a combination of oral functional impairments can predict a decline in general function and disability.

Tanaka et al. (2018) coined the term “oral frailty” (OF) to recognize the multidimensional nature of poor oral health status. In their longitudinal study on community-dwelling older adults, they found that OF was a predictor of physical frailty (PF), dependency, and mortality.

Establishing management for OF appears to be important for the prevention of dependency. The relation factor of OF requires clarification before obtaining the basic information needed to establish appropriate management for OF. Moreover, there is an association between a decline in social function and decreases in subjective masticatory performance, number of teeth present, and tongue pressure (Mikami et al., 2019; Nagayoshi et al., 2017; Takeuchi, Aida, Kondo, & Osaka, 2013). Disability in social role functioning and intellectual activity were also identified as predictors of low performance in instrumental activities of daily living (IADL) (Fujiwara et al., 2003). This is of concern given that poor social relationships are recognized as a risk factor for mortality (Holt-Lunstad, Smith, & Layton, 2010). Makizako et al. (2015b) devised the term “social frailty” (SF) in a longitudinal study, that found a higher risk of disability in individuals with multiple indicators of social decline (e.g., living alone and decreased frequency of going out).

Although two longitudinal studies in community-dwelling older adults have confirmed that both, OF (Tanaka et al., 2018) and SF (Makizako et al., 2015b) negatively impact health status, the relationship between OF and SF remains unclear. In the meantime, the effect seems to be limited in the alone measure for frailty, which is a multifaceted concept. If the relationship between OF, SF, and PF, which is a predictor of dependency, is clarified, more multifaceted and effective correspondence may be possible.

We hypothesized that there would be associations between OF, SF, and PF. Therefore, in this study, we investigated the relationships between OF, SF, and PF in community-dwelling older adults using the definitions established for each type of frailty and a comprehensive range of variables, including nutritional status, sex, and medical history.

## 2. Materials and Methods

## 2.1 Study Design

This study had a cross-sectional design, and included subjects' data collected from comprehensive health checkups conducted annually by the Tokyo Metropolitan Institute of Gerontology (Tokyo, Japan) as a part of the Otasha Kenshin study initiated in 2011. The subjects in these health checkups were selected from a total of 7,162 older adults (aged 65–84 years) residing in nine towns in the Itabashi ward of Tokyo in 2011. Invitations for health checkups were sent to 6,699 older people, excluding those who were residing in long-term care institutions and those who had been subjects in previous research. In 2012, invitations for health checkups were sent to 7,015 older adults, excluding those who had reached 65 years of age or did not reside at the same address (according to the inhabitant registry) in the preceding fiscal year. Subsequent invitations for health checkups were sent in 2013–2018 to new study subjects, who had reached 65 years of age and to older adults who had participated in previous health checkups. In 2018, invitations were mailed to a total of 2,440 older adults, including 1,463 who had participated in previous health checkups (in 2011–2017) and 977 new study subjects, who had reached 65 years of age.

We excluded individuals receiving long-term care via the Japanese public long-term care insurance (LTCI) system and those with cognitive impairment (as indicated by a Mini-Mental State Examination [MMSE] score  $\leq 18$ ) to ensure the reliability of the subjective assessments, which included a self-administered questionnaire (Tanaka et al., 2018). We also excluded individuals with missing cognitive or oral function assessment data. All study investigators received training, that included measurement methods (using standardized evaluation criteria) and the use of evaluation instruments. The study protocol was approved by the Ethics Committee of the Tokyo Metropolitan Institute of Gerontology (Approval No. 48 in 2011; Approval No. 16 in 2018) and conducted in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology statement.

## 2.2 Measurements

### 2.2.1 Basic characteristics

Information on sex, age, years of education, smoking status, and alcohol consumption was collected using a self-administered questionnaire. We used the Japan Science and Technology Agency Index of Competence (JST-IC) score to assess the ability to perform IADL (Iwasa et al., 2018).

### 2.2.2 Nutritional status

Any one of three registered dietitians evaluated the nutritional status of each subject. Body mass index was calculated from height and weight using the standard formula. Limb muscle mass was measured by the bioelectrical impedance method using an InBody 770 system (Biospace, Seoul, Korea). Skeletal muscle mass index was calculated by dividing the sum of limb muscle mass by the square of height in meters (Murakami et al., 2015). Nutritional status was assessed using the Mini Nutritional Assessment-Short Form (MNA-SF), on which a score of  $\leq 11$  is considered to indicate a risk of malnutrition (Soysal et al., 2019).

### 2.2.3 Physical function

Any one of four specialist researchers assessed physical function. Grip strength was measured using a Smedley-type hand dynamometer (Yagami, Nagoya, Japan) and gait speed by the 5-m walk test (Kera et al., 2018). Researchers asked subjects to stand and grip the hand dynamometer as tightly as possible using their preferred hand. Tests were carried out twice, and the higher value was selected. To evaluate subjects' gait, their usual walking speed was measured on a 5-m course, with 3-m acceleration and deceleration courses placed at each end of the courses. Researchers asked subjects to walk at their usual speed.

#### *2.2.4 Cognitive psychological function*

Any one of three nurses or two psychologists assessed cognitive function using the Japanese version of the MMSE (Folstein, Folstein, & McHugh, 1975; Sakuma et al., 2017). MMSE scores  $\geq 19$  were classified into three groups ( $\leq 24$ , moderate cognitive impairment;  $\leq 27$ , mild cognitive impairment; and  $\geq 28$ , preserved cognitive function) (Kaufer et al., 2008; Sakuma et al., 2017). Following the method devised by Fujisawa et al. (2005), the tendency for depression was investigated using a self-administered questionnaire containing the following five items: "Is your life pretty full? (last 2 weeks)" (yes); "Do you still enjoy doing the things you used to do? (last 2 weeks)" (yes); "Do you think it is too much trouble to do the things you used to do? (last 2 weeks)" (yes); "Do you feel that you are a useful person who is needed by others?" (yes); and "Do you feel tired without any specific reason? (last 2 weeks)" (yes). Subjects who met two or more criteria were considered to be depressed (Ihara et al., 2016).

#### *2.2.5 Medical history and number of medications*

Either of two nurses recorded the medical history and number of medications taken. Information was sought about the following diseases, each of which has been associated with PF: hypertension (Danon-Hersch et al., 2012), heart disease (Denfeld et al., 2017), diabetes mellitus (Danon-Hersch et al., 2012), hyperlipidemia (Ramsay et al., 2015), osteoporosis (Li et al., 2017), chronic obstructive pulmonary disease (Lee, Auyeung, Leung, Kwok, & Woo, 2014), osteoarthritis (Castell et al., 2015), spinal stenosis (Yagi et al., 2018), malignant neoplasm (Calado et al., 2016), anemia (Danon-Hersch, Rodondi, Spagnoli, & Santos-Eggimann, 2016), stroke (Calado, Ferriolli, Moriguti, Martinez, & Lima, 2016), chronic kidney disease (Walker et al., 2013), and fracture after 60 years of age (Kojima, 2016). Subjects were asked how many medications they were taking (0, 1, 2, 3, 4, or  $\geq 5$ ). The use of five or more medications related to PF was defined as polypharmacy (Saum et al., 2017).

#### *2.2.6 Oral function*

Any one of four dentists or four dental hygienists assessed oral function. The parameters measured were the number of teeth present, masticatory performance, tongue pressure, and oral diadochokinesis (ODK), which represents the dexterity of the tongue. The number of teeth present was defined as the number of



erupted teeth in the oral cavity, excluding retained roots and teeth with severe periodontitis. Masticatory performance was assessed using color-changeable chewing gum (Masticatory Performance Evaluating Gum Xylitol; Lotte Co., Ltd., Tokyo, Japan). The  $a^*$  value for the gums after 1 minute of mastication was measured in three places using a color-difference meter (CR-20 Color Reader; Konica Minolta, Tokyo, Japan), with the mean value defined as the masticatory performance (Kugimiya et al., 2020). Tongue pressure was assessed using a JMS tongue pressure device (JMS Co., Ltd., Hiroshima, Japan). The tongue pressure probe was pinched between the tongue and palate, and tongue pressure was applied with maximal voluntary muscular effort for approximately 7 seconds. Three measurements were recorded, and the mean value was defined as the tongue pressure (Tsuga et al., 2011). ODK was assessed using an oral functions measurement device (Kenkokun Handy; Takei Scientific Instruments Co., Ltd., Niigata, Japan). The study subjects were asked to repeat each given syllable /ta/ sequentially as fast as possible for 5 seconds. The number of pronunciations per second was recorded (Watanabe et al., 2017).

### 2.3 Definitions of frailty

#### 2.3.1 Oral frailty

Referencing the report by Tanaka et al. (2018), the cut-off values for the individual components were defined as follows: number of teeth present ( $< 20$ ); masticatory performance (men,  $< 14.2$ ; women,  $< 10.8$ ); tongue pressure (men,  $< 27.4$  kPa; women,  $< 26.5$  kPa); and ODK (men,  $< 5.2$  times/second; women,  $< 5.4$  times/second). As a subjective evaluation, subjects who responded “yes” to "Do you have any difficulties eating tough foods compared to 6 months ago?" were considered to have decreased masticatory performance, and those who responded “yes” to "Have you choked on your tea or soup recently?" were considered to have decreased swallowing function. OF was evaluated according to the responses to six objective and subjective items, as previously described (Tanaka et al., 2018). Individuals who did not respond positively to any relevant items were regarded as robust. Those who responded positively to 1–2 items and  $\geq 3$  items were categorized as having as oral prefrailty (preOF) and OF, respectively.

#### 2.3.2 Social frailty

SF was evaluated as in the report by Makizako et al. (2015b). Cut-offs were set for each of the five items as follows: “Do you go out less frequently compared with last year?” (yes), “Do you sometimes visit your friends?” (no), “Do you feel you are helpful to friends or family?” (no), “Do you live alone?” (yes), and “Do you talk with someone every day?” (no). Individuals who did not have any relevant items were regarded as robust. Those who had 1 item and  $\geq 2$  items were categorized as having social prefrailty (preSF) and SF, respectively.

#### 2.3.3 Physical frailty

As in the report by Makizako, Shimada, Doi, Tsutsumimoto, and Suzuki (2015a), PF was assessed for each of the five categories with the following cut-off values: (1) unintentional weight loss, “Have you lost 2 kg or more in the past 6 months?” (yes); (2) exhaustion, “In the last 2 weeks, have you felt tired for no reason?”

(yes); (3) low activity, “Do you engage in moderate levels of physical exercise or sports aimed at health?” and “Do you engage in low levels of physical exercise aimed at health?” (subjects who answered “no” to both of these questions were classified as having low activity); (4) weakness, decreased grip strength (men, < 26.0 kg, women, < 18.0 kg), and (5) slowness, decreased gait (< 1.0 m/s). Individuals who did not have any relevant items were regarded as robust. Those who had 1–2 items and  $\geq 3$  items were categorized as having physical prefrailty (prePF) and PF, respectively.

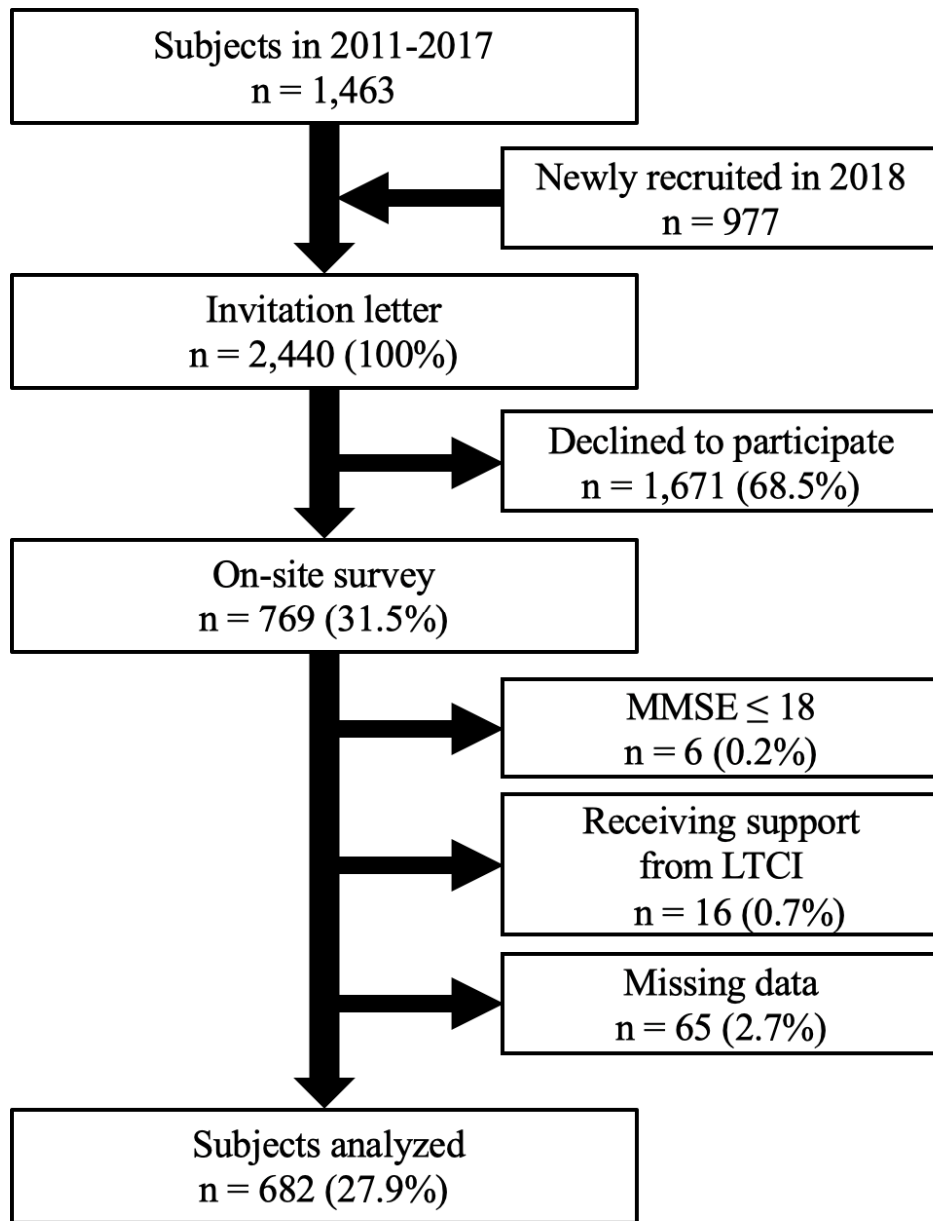
## 2.4 Statistical analysis

Sex-related differences were analyzed using the Mann-Whitney *U* test for continuous variables and the chi-square test for categorical variables. Continuous variables were Bonferroni-corrected after the Jonckheere-Terpstra trend test to examine trends in the robust OF, preOF, and OF groups. Categorical variables were analyzed using the chi-square test. Ordinal logistic regression analyses were then performed, treating the three OF groups as objective variables to identify factors associated with OF. Currently, there are few reports on factors associated with OF, but there is a report on the association between OF and PF (Tanaka et al., 2018). Therefore, the factors related to PF were treated as independent variables. The number of medications was analyzed as a continuous variable with a cut-off value of five. Next, path analysis of the results of the ordinal logistic regression analysis was performed in order to examine the relationship between OF, SF, and PF. The fit of the models in the path analysis was evaluated using the goodness of fit index (GFI), normed fit index (NFI), and root mean square error of approximation (RMSEA). All statistical analyses were performed using SPSS Statistics version 23 and SPSS Amos version 23 (IBM Corp., Armonk, NY, USA) with a significance level of less than 5%.

## 3. Results

### 3.1 Subject characteristics

Figure 1 shows a flow chart outlining the process used to select subjects for this study. Invitations for health checks were mailed to a total of 2,440 older adults, of whom 769 (31.5%) eventually participated. Individuals with an MMSE score  $\leq 18$  ( $n=6$ , 0.2%), those receiving LTCI support ( $n=16$ , 0.7%), and those with missing cognitive or oral function data ( $n=65$ , 2.7%) were excluded, leaving 682 (27.9%) subjects (267 men, 415 women; mean age  $73.3 \pm 6.6$  years) for inclusion in the analyses. The OF, PF, and SF rates are compared according to sex in Table 1. There was no significant sex-related difference in the OF or PF rate; however, SF was found to be more common in men. Table 2 shows the results for the study endpoints according to OF status. Three hundred and eighty (55.7%) of the 682 subjects had preOF and 65 (9.5%) had OF. Subjects with OF were older, were less independent in IADL, had lower physical and cognitive function, and tended to be depressed. Appendices A1-A3 show the respective correspondence rate for each item potentially associated with OF, SF, and PF.



**Figure 1.** Flow chart demonstrating the process used to select the study subjects.

LTCI, Japanese Public Long-Term Care Insurance System; MMSE, Mini-Mental State Examination.

**Table 1.** Characteristics of the study population

Variable	Overall (n = 682)		Men (n = 267)		Women (n = 415)		P-value
	Mean ± SD	Median, [Q1, Q3]	Mean ± SD	Median, [Q1, Q3]	Mean ± SD	Median [Q1, Q3]	
	n (%)		n (%)		n (%)		
Age, years	73.3 ± 6.6	72.0 [68.0, 78.0]	72.8 ± 6.6	71.0 [67.0, 78.0]	73.6 ± 6.5	73.0 [68.0, 79.0]	0.101
Education, years	13.4 ± 2.8	12.0 [12.0, 16.0]	14.2 ± 2.8	16.0 [12.0, 16.0]	12.9 ± 2.7	12.0 [12.0, 14.0]	<0.001
Current or past smoker, n (%)	248 (36.4)		183 (68.5)		65 (15.7)		<0.001
Drinks alcohol, n (%)	321 (47.1)		182 (68.2)		139 (33.5)		<0.001
JST-IC score	12.1 ± 2.8	12.0 [11.0, 14.0]	12.0 ± 2.9	12.0 [10.0, 14.0]	12.2 ± 2.7	13.0 [11.0, 14.0]	0.222
BMI	22.8 ± 3.3	22.7 [20.6, 24.7]	23.6 ± 3.2	23.3 [21.7, 25.4]	22.3 ± 3.4	22.1 [20.1, 24.2]	<0.001
SMI	6.5 ± 1.0	6.3 [5.7, 7.3]	7.5 ± 0.7	7.5 [7.0, 7.9]	5.9 ± 0.7	5.8 [5.4, 6.3]	<0.001
MNA-SF score	12.8 ± 1.3	13.0 [12.0, 14.0]	13.0 ± 1.3	13.0 [12.0, 14.0]	12.6 ± 1.3	13.0 [12.0, 14.0]	<0.001
≤ 11, n (%)	126 (18.5)		39 (14.6)		87 (21.0)		0.037
Handgrip strength, kg	27.9 ± 8.5	26.0 [22.0, 34.0]	35.5 ± 6.9	36.0 [31.0, 40.0]	22.9 ± 5.1	23.0 [19.0, 26.0]	<0.001

Gait speed, m/s	1.4 ± 0.3	1.4 [1.2, 1.6]	1.4 ± 0.3	1.4 [1.2, 1.6]	1.4 ± 0.3	1.4 [1.2, 1.6]	0.643
MMSE score	28.6 ± 1.6	29.0 [28.0, 30.0]	28.4 ± 1.7	29.0 [28.0, 30.0]	28.7 ± 1.5	29.0 [28.0, 30.0]	0.028
≤ 23, n (%)	10 (1.5)		5 (1.9)		5 (1.2)		
24–27, n (%)	126 (18.5)		57 (21.3)		69 (16.6)		0.218
≥ 28, n (%)	546 (80.1)		205 (76.8)		341 (82.2)		
Depression, n (%)	153 (22.4)		51 (19.1)		102 (24.6)		0.094
Oral function							
Present teeth, n	21.6 ± 7.9	24.0 [18.0, 27.0]	22.5 ± 7.3	25.0 [20.0, 27.0]	21.1 ± 8.2	24.0 [18.0, 27.0]	0.046
Masticatory performance	22.0 ± 4.9	22.8 [19.6, 25.4]	23.3 ± 4.2	23.9 [21.1, 26.3]	21.1 ± 5.1	22.16 [18.8, 24.8]	<0.001
Tongue pressure, kPa	33.0 ± 7.5	32.9 [28.1, 37.8]	33.7 ± 8.4	33.3 [27.8, 38.9]	32.6 ± 6.9	32.6 [28.3, 36.9]	0.109
ODK, times/s	6.4 ± 0.7	6.4 [6.0, 6.8]	6.4 ± 0.7	6.4 [6.0, 6.8]	6.4 ± 0.7	6.4 [6.0, 6.8]	0.853
Subjective difficulty in eating	147 (21.6)		42 (15.7)		105 (25.3)		0.003

Subjective difficulty in swallowing	182	(26.7)	67	(25.1)	115	(25.7)	0.451
Medical history							
Hypertension, n (%)	282	(41.3)	129	(48.3)	153	(36.9)	0.003
Heart disease, n (%)	109	[16.0)	51	(19.1)	58	(14.0)	0.075
Diabetes mellitus, n (%)	74	(10.9)	38	(14.2)	36	(8.7)	0.023
Hyperlipidemia, n (%)	256	(37.5)	90	(33.7)	166	(40.0)	0.098
Osteoporosis, n (%)	113	(16.6)	11	(4.1)	102	(24.6)	<0.001
Chronic obstructive pulmonary disease, n (%)	3	(0.4)	3	(1.1)	0	(0.0)	0.030
Osteoarthritis, n (%)	98	(14.4)	19	(7.1)	79	(19.0)	<0.001
Spinal stenosis, n (%)	68	(10.0)	25	(9.4)	43	(10.4)	0.671

Malignant neoplasm, n (%)	98	(14.4)	35	(13.1)	63	(15.2)	0.451
Anemia, n (%)	20	(2.9)	8	(3.0)	12	(2.9)	0.937
Stroke, n (%)	40	(5.9)	25	(9.4)	15	(3.6)	0.002
Chronic kidney disease, n (%)	3	(0.4)	1	(0.4)	2	(0.5)	0.836
Fracture, n (%)	122	(17.9)	31	(11.6)	91	(21.9)	0.001
Medications $\geq 5$ , n (%)	174	(25.5)	81	(30.3)	93	(22.4)	0.020
Oral frailty							
Robust, n (%)	237	(34.8)	100	(37.5)	137	(33.0)	
Prefrailty, n (%)	380	(55.7)	147	(55.1)	233	(56.1)	0.238
Frailty, n (%)	65	(9.5)	20	(7.5)	45	(10.8)	
Social frailty							
Robust, n (%)	287	(42.1)	123	(46.1)	164	(39.5)	
Prefrailty, n (%)	237	(34.8)	71	(26.6)	166	(40.0)	0.001

Frailty, n (%)	158	(23.2)	73	(27.3)	85	(20.5)	
Physical frailty							
Robust, n (%)	346	(50.7)	136	(50.9)	210	(50.6)	
Prefrailty, n (%)	312	(45.7)	122	(45.7)	190	(45.8)	0.984
Frailty, n (%)	24	(3.5)	9	(3.4)	15	(3.6)	

Categorical variables are shown as the number (percentage) and were analyzed using the chi-square test. Continuous variables are expressed as the mean and standard deviation and were analyzed using the Mann-Whitney *U* test. A *P*-value of < 0.05 was considered statistically significant. The number of subjects taking more than five medications was not documented; therefore, the number of subjects on polypharmacy are shown as a proportion. BMI, body mass index; JST-IC, Japan Science and Technology Agency Index of Competence; MMSE, Mini-Mental State Examination; MNA-SF, Mini Nutritional Assessment-Short Form; ODK, oral diadochokinesis; Q1, first quartile; Q3, third quartile; SD, standard deviation; SMI, skeletal muscle mass index



**Table 2.** Evaluation of items potentially affecting oral frailty status

Variable	Robust (n = 237)		preOF (n = 380)		OF (n = 65)		<i>P</i> -value
	Mean ± SD	Median [Q1, Q3]	Mean ± SD	Median [Q1, Q3]	Mean ± SD	Median [Q1, Q3]	
	n (%)		n (%)		n (%)		
Age, years	71.1 ± 5.7	69.0 [67.0, 75.0]	74.0 ± 6.6	74.0 [68.0, 79.0]	77.1 ± 6.5	78.0 [73.0, 81.0]	<0.001
Men, n (%)	100 (42.2)		147 (38.7)		20 (30.8)		0.238
Education, years	13.9 ± 2.9	14.0 [12.0, 16.0]	13.2 ± 2.7	12.0 [12.0, 16.0]	12.5 ± 2.8	12.0 [10.5, 14.0]	<0.001
Current or past smoker, n (%)	72 (30.4)		150 (39.5)		26 (40.0)		0.060
Drinks alcohol, n (%)	123 (51.9)		182 (47.9)		16 (24.6)		<0.001
JST-IC score	12.8 ± 2.3	13.0 [11.0, 15.0]	12.0 ± 2.8	12.0 [10.0, 14.0]	10.6 ± 3.4	11.0 [7.5, 13.0]	<0.001
BMI	23.1 ± 3.4	23.0 [21.0, 24.9]	22.7 ± 3.3	22.6 [20.5, 24.5]	22.4 ± 3.4	22.3 [20.0, 24.7]	0.049
SMI	6.7 ± 1.1	6.6 [5.8, 7.5]	6.5 ± 1.0	6.3 [5.7, 7.3]	6.1 ± 0.9	5.9 [5.4, 6.6]	<0.001
MNA-SF score	13.0 ± 1.2	13.0 [12.0, 14.0]	12.7 ± 1.3	13.0 [12.0, 14.0]	12.4 ± 1.5	13.0 [11.0, 14.0]	0.002
≤ 11, n (%)	32 (13.5)		75 (19.7)		19 (29.2)		0.010

Handgrip strength, kg	29.7 ± 8.6	28.0 [24.0, 37.0]	27.5 ± 8.3	26.0 [22.0, 33.0]	23.5 ± 7.4	24.0 [17.0, 27.0]	<0.001
Gait speed, m/s	1.4 ± 0.2	1.5 [1.3, 1.6]	1.4 ± 0.3	1.4 [1.2, 1.5]	1.2 ± 0.3	1.3 [1.1, 1.4]	<0.001
MMSE score	28.9 ± 1.4	29.0 [28.0, 30.0]	28.5 ± 1.7	29.0 [28.0, 30.0]	28.0 ± 1.9	29.0 [27.0, 29.0]	<0.001
≤23, n (%)	1 (0.4)		6 (1.6)		3 (4.6)		
24–27, n (%)	33 (13.9)		76 (20.0)		17 (26.2)		0.009
≥28, n (%)	203 (85.7)		298 (78.4)		45 (69.2)		
Depression, n (%)	30 (12.7)		95 (25.0)		(28) [43.1]		<0.001
Oral functions							
Present teeth, n	26.1 ± 2.6	26.0 [24.0, 28.0]	20.5 ± 8.1	23.0 [16.0, 27.0]	11.4 ± 8.2	13.0 [4.0, 18.0]	—
Masticatory performance	23.8 ± 3.0	24.2 [21.9, 26.0]	21.9 ± 4.3	22.6 [19.2, 25.1]	15.4 ± 7.4	16.8 [10.2, 21.6]	—
Tongue pressure, kPa	35.3 ± 5.8	34.1 [31.1, 38.3]	32.3 ± 7.7	32.1 [26.6, 37.6)	28.5 ± 9.1	26.2 [21.4, 36.1]	—
ODK, times/s	6.6 ± 0.6	6.6 [6.2, 7.0]	6.4 ± 0.7	6.4 [6.0, 6.8]	5.9 ± 1.0	6.2 [5.2, 6.6]	—
Subjective difficulty in eating	0 (0.0)		92 (24.2)		55 (84.6)		—

Subjective difficulty in swallowing	0	(0.0)	144	(37.9)	38	(58.5)	—
Medical history							
Hypertension, n (%)	92	(38.8)	160	(42.1)	30	(46.2)	0.513
Heart disease, n (%)	31	(13.1)	63	(16.6)	15	(23.1)	0.134
Diabetes mellitus, n (%)	21	(8.9)	43	(11.3)	10	(15.4)	0.296
Hyperlipidemia, n (%)	87	(36.7)	145	(38.2)	24	(36.9)	0.931
Osteoporosis, n (%)	26	(11.0)	74	(19.5)	13	(20.0)	0.016
Chronic obstructive pulmonary disease, n (%)	0	(0.0)	2	(0.5)	1	(1.5)	0.234
Osteoarthritis, n (%)	30	(12.7)	61	(16.1)	7	(10.8)	0.346
Spinal stenosis, n (%)	22	(9.3)	41	(10.8)	5	(7.7)	0.675

Malignant neoplasm, n (%)	22	(9.3)	70	(18.4)	6	(9.2)	0.003
Anemia, n (%)	5	(2.1)	10	(2.6)	5	(7.7)	0.053
Stroke, n (%)	8	(3.4)	21	(5.5)	11	(16.9)	<0.001
Chronic kidney diseases, n (%)	1	(0.4)	1	(0.3)	1	(1.5)	0.356
Fracture, n (%)	35	(14.8)	71	(18.7)	16	(24.6)	0.154
Medications $\geq 5$ , n (%)	36	(15.2)	111	(29.2)	27	(41.5)	<0.001
Social frailty							
Robust, n (%)	118	(49.8)	155	(40.8)	14	(21.5)	
Prefrailty, n (%)	84	(35.4)	131	(34.5)	22	(33.8)	<0.001
Frailty, n (%)	35	(14.8)	94	(24.7)	29	(44.6)	
Physical frailty							
Robust, n (%)	151	(63.7)	178	(46.8)	17	(26.2)	
Prefrailty, n (%)	82	(34.6)	188	(49.5)	42	(64.6)	<0.001

Frailty, n (%)	4 (1.7)	14 (3.7)	6 (9.2)
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Categorical variables are shown as the number (percentage) and were analyzed using the chi-square test. A *P*-value < 0.05 was considered statistically significant. Continuous variables were analyzed with the Bonferroni-corrected Jonckheere-Terpstra test. A *P*-value < 0.006 was considered statistically significant. The Jonckheere-Terpstra test was not used because it was clear that oral functions decreased with OF. The number of subjects taking more than five medications was not documented; Therefore, the number of subjects on polypharmacy are shown as a proportion. BMI, body mass index; JST-IC, Japan Science and Technology Agency Index of Competence; MMSE, Mini-Mental State Examination; MNA-SF, Mini Nutritional Assessment-Short Form; ODK, oral diadochokinesis; Q1, first quartile; Q3, third quartile; SD, standard deviation; SMI, skeletal muscle mass index.

1 3.2 Ordinal logistic regression analysis

2 The results of the ordinal logistic regression analysis, which was performed to investigate the factors  
 3 associated with OF, are shown in Table 3. There were significant associations with age (odds ratio [OR]  
 4 1.075, 95% confidence interval [CI] 1.045 – 1.104), MNA-SF score (OR 0.837, 95% CI 0.735 – 0.953),  
 5 stroke (OR 2.423, 95% CI 1.197 – 4.899), number of medications used (OR 1.127, 95% CI 1.010 – 1.259),  
 6 SF (OR 1.680, 95% CI 1.080 – 2.612), and prePF (OR 1.726, 95% CI 0.202 – 2.479).

7

8 **Table 3.** Ordinal logistic regression analyses

Variable	OR	95% CI	P-value
Age	1.075	1.045 – 1.104	< 0.001
Sex (0: men, 1: women)	0.797	0.555 – 1.145	0.219
Education	0.948	0.892 – 1.007	0.082
MNA-SF scores	0.837	0.735 – 0.953	0.007
MMSE scores	0.987	0.888 – 1.097	0.810
Depression (0: no, 1: yes)	1.508	0.970 – 2.347	0.068
Hypertension (0: no, 1: yes)	0.780	0.539 – 1.129	0.188
Heart disease (0: no, 1: yes)	1.021	0.653 – 1.597	0.927
Diabetes mellitus (0: no, 1: yes)	1.213	0.716 – 2.054	0.474
Hyperlipidemia (0: no, 1: yes)	0.868	0.614 – 1.228	0.425
Osteoporosis (0: no, 1: yes)	0.929	0.581 – 1.486	0.758
Osteoarthritis (0: no, 1: yes)	0.976	0.617 – 1.543	0.918
Spinal stenosis (0: no, 1: yes)	0.929	0.542 – 1.590	0.788
Malignant neoplasm (0: no, 1: yes)	1.408	0.899 – 2.208	0.136
Anemia (0: no, 1: yes)	1.451	0.572 – 3.680	0.433

Stroke (0: no, 1: yes)		2.423	1.197 – 4.899	0.014
Fracture (0: no, 1: yes)		1.010	0.662 – 1.540	0.963
Number of medications		1.127	1.010 – 1.259	0.033
SF	Robust	1.000 (Reference)		
	preSF	1.138	0.790 – 1.639	0.488
	SF	1.680	1.080 – 2.612	0.021
PF	Robust	1.000 (Reference)		
	prePF	1.726	1.202 – 2.479	0.003
	PF	1.347	0.546 – 3.327	0.519

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### 3.3 Path analysis

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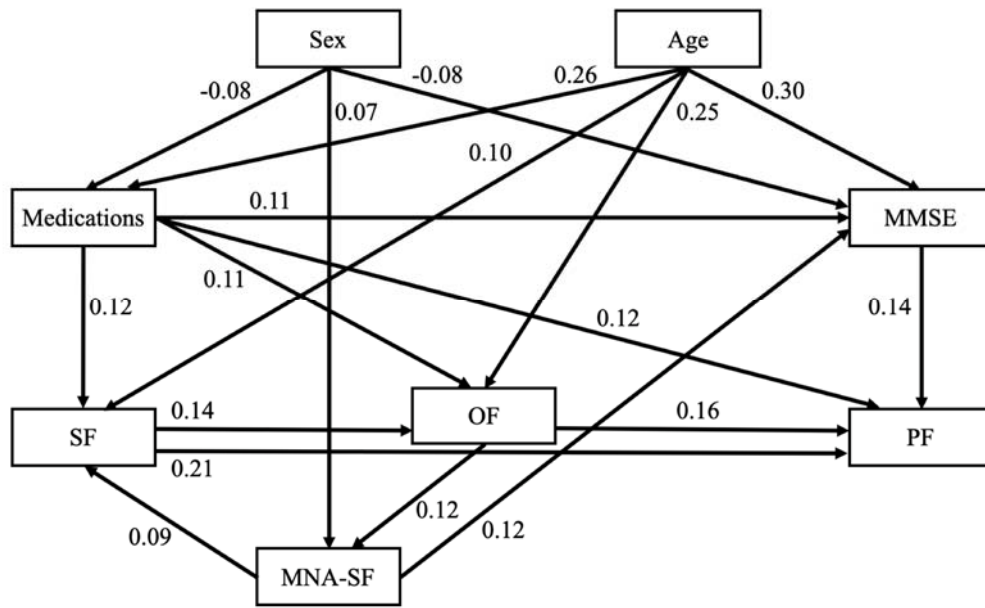
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MNA-SF and MMSE were analyzed as continuous variables. Age, MNA-SF, stroke, number of medications, SF, and prePF were significantly associated with OF. CI, confidence interval; MMSE, Mini-Mental State Examination; MNA-SF, Mini Nutritional Assessment-Short Form; OF, oral frailty; OR, odds ratio; PF, physical frailty; SF, social frailty

Path analysis is a statistical method used to analyze relationships between multiple factors. Figure 2 shows the path diagram derived by path analysis in this study. The best fit was selected among the path diagrams created by referring to the results of the ordinal logistic regression analysis. The pathway shows that the starting factor affected the stabbing factor. The diagram also shows that SF was directly related to OF and that the path coefficient from SF to OF was 0.141. Furthermore, both OF and SF were directly related to PF. The path coefficient from OF to PF was 0.155 and that from SF to PF was 0.206. All pathways were statistically significant. The GFI was 0.982, the NFI was 0.961, and the RMSEA was 0.026.



1  
 2 **Figure 2.** A pathway diagram demonstrating the relationship between OF and SF. MNA-SF (Mini  
 3 Nutritional Assessment-Short Form), MMSE (Mini-Mental State Examination), OF (oral frailty), SF (social  
 4 frailty), PF (physical frailty), and number of medications used were analyzed as categorical variables. Sex  
 5 (0, male; 1, female), medications (0,  $\leq 4$ ; 1,  $\geq 5$ ), OF, SF, PF (0, robust; 1, prefrailty; 2, frailty), MNA-SF  
 6 (0,  $\geq 12$ ; 1,  $\leq 11$ ), MMSE (0,  $\geq 28$ ; 1, 24 – 27; 2,  $\leq 23$ ). OF was directly related to PF, and SF was in the  
 7 background of OF. SF was directly associated with PF, and SF was associated with PF via OF.

8

9 **4. Discussion**

10 Longitudinal studies have shown that OF, an indicator of decline in oral function, and SF, an indicator of  
 11 decline in social function, are both predictors of dependency (Makizako et al., 2015b; Tanaka et al., 2018).  
 12 A decline in oral and social function appears connected to the deterioration of an individual’s general health  
 13 status. However, previous studies have not clearly defined the relationships between OF, SF, and PF. If a  
 14 relationship between the three frailties could be clarified, a more multifaceted and effective method for  
 15 preventing dependency could be established. The results of the present study suggest that SF directly relates  
 16 to OF and that both, OF and SF are directly related to PF.

17

18 The rate of PF in this study was 3.5%, which was lower than the prevalence of 7.4% reported by a meta-  
 19 analysis of Japanese community-dwelling older adults aged 65 years or older (Kojima et al., 2017). In the  
 20 present study, the mean JST-IC score for IADL was  $12.1 \pm 2.8$ , which is higher than the mean value of 9.5  
 21 previously reported for individuals aged 65 years or older (mean,  $74.0 \pm 2.8$  years) in other regions of Japan  
 22 (Iwasa et al., 2018). This study found that the ability to perform IADL was maintained; therefore, it is  
 23 reasonable to assume that the subjects in this study maintained good physical function and that the rate of



1 PF was low. Furthermore, this study found that deterioration from robust oral function to OF tended to be  
2 more common in subjects who were older, less educated, had poor nutritional status, had poorer physical  
3 and cognitive function, tended to be depressed, and were on polypharmacy. These findings are similar to  
4 those reported by Tanaka et al. (2018).

5  
6 In accordance with previous studies, this investigation defined three stages of OF, SF, and PF, comprising  
7 robust (no functional decline), prefrailty (mild functional decline), and frailty (accumulation of several types  
8 of functional decline) (Makizako et al., 2015a; Makizako et al., 2015b; Tanaka et al., 2018). These definitions  
9 reflect the association of a more severe stage with a greater risk of dependency.

10 Ordinal logistic regression analysis using the factors associated with PF as independent variables identified  
11 the factors associated with OF. Using path analysis, we examined how the factors associated with OF in the  
12 ordinal logistic regression analysis were associated with OF, SF, PF, and cognitive decline (Feng et al., 2017),  
13 which is an indicator of the psychological aspects of frailty. This study included a path analysis that could  
14 infer relationships between different types of frailty and clarify the factors associated with OF.

15  
16 The logistic regression analysis showed significant associations of OF with age, MNA-SF scores, history  
17 of stroke, number of medications used, SF, and prePF.

18 The findings of the present study regarding the association between multidimensional aspects of oral and  
19 social function are consistent with those in several previous reports (Mikami et al., 2019; Nagayoshi et al.,  
20 2017; Nakanishi et al., 1999; Takeuchi et al., 2013).

21 There were reports of an association between decline in oral function and decline in physical function  
22 (Tanaka et al., 2018; Watanabe et al., 2017). Although the present study found no association between OF  
23 and PF, there was an association between prePF and OF. It was inferred that the lack of association between  
24 OF and PF in this study was due to the low PF rate of 3.5% ( $n = 24$ ). A relationship between OF and the  
25 MNA-SF score was identified; this is consistent with the findings of previous studies on the association  
26 between a decline in oral function and decreased nutritional status (Kwon et al., 2017; Kwon, Suzuki,  
27 Kumagai, Shinkai, & Yukawa, 2006; Sura, Madhavan, Carnaby, & Crary, 2017).

28 Older adults often have multiple comorbidities and are likely to be on polypharmacy (Sirois et al., 2019).  
29 Xerostomia is one of the adverse effects of several medications commonly used in older adults and is  
30 associated with caries, deterioration of masticatory performance, and dysphagia (Barbe, 2018). The risk of  
31 hazardous events caused by an increase in the number of medications may be associated with a decline in  
32 oral function; however, this relationship is unclear, because no information regarding the adverse effects of  
33 medications was collected in this study. The mechanism of declining oral function and number of  
34 medications used or medication-related adverse events warrants further investigation in future studies.

35 Stroke has a variety of sequelae, including both, motor and sensory impairments (Winstein et al., 2016),  
36 and is responsible for considerable disability (Naruse, Sakai, Matsumoto, & Nagata, 2015). Patients  
37 requiring nursing care were excluded from this study, suggesting that the functional impairment attributable  
38 to stroke was mild. However, we demonstrated an association between stroke and OF; therefore, it may be

1 that various symptoms resulting from a history of stroke were related to a decline in oral function, even if  
2 they were mild.

3  
4 The results of path analysis showed that SF was directly related to OF. Kobayashi, Wardle, & von Wagner  
5 (2015) reported an association between decline in social function and decreased health literacy. Preservation  
6 of health literacy is useful for health maintenance in daily life; however, a decline in health literacy leads to  
7 worsening health care and ability to self-manage disease (Sørensen et al., 2012). Oral diseases, such as caries  
8 and periodontal disease, are associated with lifestyle habits, including diet and hygiene (Petersen, 2008).  
9 Therefore, a lowering of general health literacy, which stems from a decline in social function, seems to be  
10 connected with a lowering of oral health literacy. Decreased oral health literacy can lead to poor oral hygiene,  
11 tooth loss, and even a decline in oral function. Furthermore, the opportunities for conversation are likely to  
12 decrease alongside a decline in social function. Decreased speaking may lead to reduced tongue pressure as  
13 a result of a decrease in the tongue movements involved in speech intelligibility. Furthermore, tongue  
14 pressure is associated with masticatory performance and speed of tongue movement (Kugimiya et al., 2019;  
15 Sagawa et al., 2019). These reports suggest that decreased opportunities for conversation lead to decreased  
16 tongue pressure, decreased masticatory performance, and slowing of tongue movement. Therefore, the  
17 results of this path analysis, which demonstrate the possibility of SF in the background of OF, seem to be  
18 appropriate. This study found that SF was directly associated with PF, which is in line with previous research  
19 (Makizako et al., 2019). Shimada et al. (2010) reported that loss of social roles and difficulty in responding  
20 to environmental changes reduces the frequency of activity by narrowing the range of behaviors in older  
21 adults. Narrowing of the range and frequency of activity decreases the amount of physical activity, and this  
22 is linked to PF. This study found that SF was not only directly related to PF, but also indirectly via OF.  
23 Moreover, a decline in oral function was identified to be one of the factors through which a decline in social  
24 function was connected to a decline in physical function. The process by which this occurs may involve not  
25 only a decrease in physical activity, but also a decline in oral function due to a reduction in the amount of  
26 interaction with others and decreased opportunities for conversation. The decline in social function may lead  
27 to a lowering of oral health literacy via a weakening of relationships with others, and in turn, cause a decline  
28 in oral function. Therefore, strategies to prevent or manage a decline in oral function should also focus on  
29 maintaining and improving social function. This will involve securing opportunities to engage with others,  
30 with the aim of maintaining oral health literacy.

31 Tanaka et al. (2018) reported that age and polypharmacy were directly related to OF. Barbe (2018) also  
32 reported an association of medication-induced xerostomia with caries, deterioration of masticatory  
33 performance, and dysphagia. Comorbidity and the long-term morbidity associated with several chronic  
34 diseases are also associated with frailty (Castrejón-Pérez, Gutiérrez-Robledo, Cesari, & Pérez-Zepeda, 2017).  
35 An accumulation of adverse events associated with chronic disease and polypharmacy and may be related  
36 to not only deterioration of general health status but also a decline in oral function.

37 This study also found a direct association between the MNA-SF score and OF. There are reports of an  
38 association between masticatory performance and vitamin and mineral deficiency (Kwon et al., 2017),

1 deterioration in subjective masticatory performance with a decline in diversity in the diet (Kwon et al., 2006),  
2 and dysphagia with malnutrition (Sura et al., 2017). A decline in oral function, such as masticatory  
3 performance and swallowing, may negatively impact the intake of nutrients. The results of this study are  
4 consistent with these reports. It is clear that the risk of malnutrition was associated with a transition from  
5 robust oral function to OF. Therefore, management of OF may prevent undernutrition.

6 The factors found to be directly related to OF in this study support the findings of previous reports.  
7 Furthermore, MNA-SF was directly associated with SF, suggesting that OF may lead to SF via malnutrition.  
8 The interaction between decreased social function and oral function may indeed be bidirectional, and should  
9 be investigated in future longitudinal and interventional studies.

10 Age, the MNA-SF score, and polypharmacy were directly related to SF. Makizako et al. (2015b) reported  
11 an association between age and SF and Tani et al. (2015) identified an association between unhealthy dietary  
12 behaviors and eating or living alone. Furthermore, given that use of five or more medications was identified  
13 as a risk factor for falls (Kojima et al., 2012) and that falls are associated with social isolation (Pohl, Cochrane,  
14 Schepp, & Woods, 2018), the relationship between polypharmacy and SF is likely to be consistent. The  
15 relationship between SF and its background factors is in line with previous reports, and the results in this  
16 regard also support the validity of this study.

17 Polypharmacy and the MMSE score were directly related to PF in this investigation; this is consistent with  
18 previous investigations that identified associations between polypharmacy and PF (Saum et al., 2017) and  
19 between cognitive decline and PF (Feng et al., 2017). Furthermore, the factors identified to be in the  
20 background of PF in this study are consistent with previous reports. Age, the MNA-SF score, and  
21 polypharmacy were directly related to the MMSE score, supporting previous reports, which identified an  
22 association between cognitive decline and aging (Sakuma et al., 2017), malnutrition (Ozawa et al., 2013),  
23 and polypharmacy (Niikawa et al., 2017). This study also identified that aging was directly related to  
24 polypharmacy, an association that has also been reported before (Saum et al., 2017).

25 The path model used in this investigation had a high level of fit, and all pathways showed a relationship  
26 between OF, SF, and PF, as in previous research. The congruence between these results and those in previous  
27 reports confirm the generalizability of these findings.

28  
29 There are several limitations to this study. First, the associations between decline in oral function and  
30 cognitive decline (Kugimiya et al., 2019; Watanabe et al., 2018), social relationships and risk of dementia  
31 (Kuiper et al., 2015), and dietary patterns and risk of dementia (Ozawa et al., 2013) have already been  
32 reported. Although the path analysis showed a relationship between the MNA-SF and MMSE scores, there  
33 was no significant pathway between OF or SF and the MMSE score. The path analysis also indicated a  
34 circular relationship between OF, SF, and the MNA-SF score, suggesting that a deterioration in nutritional  
35 status was involved in the process which decreased oral and social function lead to cognitive decline. OF,  
36 SF, malnutrition, and cognitive decline are associated with PF and dependency (Feng et al., 2017; Makizako  
37 et al., 2015b; Soysal et al., 2019; Tanaka et al., 2018). The fact that the relationships between these four  
38 factors could be inferred in this study is one of the important grounds for investigating effective measures

1 for the multifaceted concept of frailty in the future. These relationships could not be determined in this study  
2 because of its cross-sectional design; therefore, longitudinal and intervention studies are needed. Second,  
3 although Makizako et al. (2015a) have reported an association between age and PF, there was no significant  
4 pathway between these two variables in this study, possibly because the older subjects had already  
5 participated in previous health checkups and maintained their level of physical function over the course of  
6 the study. Third, although Soysal et al. (2019) reported an association between malnutrition and PF, we could  
7 not identify a significant pathway between the MNA-SF score and PF in this study. The MNA-SF score was  
8 indirectly associated with PF via SF, and the MMSE score but was not directly associated with PF. However,  
9 there seemed to be a connection between malnutrition and a decline in physical function via declines in  
10 social and cognitive function. Therefore, it will be necessary to consider decreased social function and  
11 cognition when the relationships between malnutrition and decline in physical function are examined in the  
12 future. Fourth, this study only included older individuals who were able to independently attend for  
13 assessment and excluded those with severe deterioration of physical and cognitive function; this could have  
14 introduced a degree of selection bias. Therefore, the results of this study cannot be generalized to persons  
15 with severe psychosomatic impairment. Finally, the cross-sectional nature of the study meant that no causal  
16 relationships could be identified; however, the path model used in the study had a high level of fit. All OF,  
17 SF, and PF pathways were significant, as in previous reports, and are generalizable to older independent  
18 adult populations. This study suggests that the relationship between OF, SF, and PF would lead to a general  
19 deterioration in health. This may provide an important perspective for future research on frailty.

20

21 The logistic regression analysis showed that the factors associated with OF were a decline in social function,  
22 a decline in physical function, decreased nutritional status, and an increased number of medications used.  
23 These are known frailty-related factors (Makizako et al., 2015b; Saum et al., 2017; Soysal et al., 2019). It is  
24 important to detect OF at an early stage and use a multifaceted approach to maintain general health. The  
25 results of the path analysis highlight the possibility that SF is connected to OF. Therefore, the development  
26 of comprehensive and effective methods to manage declines in oral function will also need to consider  
27 evaluation of social function and its role in the maintenance of oral health literacy.

## 28 **5. Conclusion**

29 In this study, OF, SF, and PF were found to be mutually related in community-dwelling older adults. SF  
30 was directly related to OF, and OF in turn was directly related to PF. A decline in social function may  
31 contribute to decreased oral and physical function. This implies that optimal management of OF will also  
32 require evaluation and management of SF. These associations will be important considerations when  
33 devising appropriate measures for management of OF.

34

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### 3 **Declarations of interest**

4 None.

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1 **Appendices**

2 **Table A1.** Correspondence rate for each item potentially associated with oral frailty

	Overall	Men	Women
Oral frailty	n (%)	n (%)	n (%)
Number of present teeth	190 (27.9)	64 (24.0)	126 (30.4)
Masticatory performance	27 (4.0)	7 (2.6)	20 (4.8)
Tongue pressure	141 (20.7)	62 (23.2)	79 (19.0)
ODK /ta/	39 (5.7)	9 (3.4)	30 (7.2)
Subjective difficulty in eating (yes)	147 (21.6)	42 (15.7)	105 (25.3)
Subjective difficulty in swallowing (yes)	182 (26.7)	67 (25.1)	115 (27.7)

3 ODK, oral diadochokinesis

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1 **Table A2.** Correspondence rate for each item potentially associated with social frailty

	Overall	Men	Women
Social frailty	n (%)	n (%)	n (%)
Living alone (yes)	185 (27.1)	42 (15.7)	143 (34.5)
Going out less frequently compared with last year (yes)	127 (18.6)	50 (18.7)	77 (18.6)
Visits friends sometimes (no)	211 (30.9)	108 (40.4)	103 (24.8)
Feels helpful to friends or family (no)	57 (8.4)	36 (13.5)	21 (5.1)
Talks with someone every day (no)	65 (9.5)	27 (10.1)	38 (9.2)

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1 **Table A3.** Correspondence rate for each item potentially associated with physical frailty

	Overall	Men	Women
Physical frailty	n (%)	n (%)	n (%)
Unintentional weight loss	83 (12.2)	47 (17.6)	36 (8.7)
Exhaustion	171 (25.1)	59 (22.1)	112 (27.0)
Low activity	102 (15.0)	39 (14.6)	63 (15.2)
Weakness	85 (12.5)	25 (9.4)	60 (14.5)
Slowness	47 (6.9)	17 (6.4)	30 (7.2)

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