Archives of Gerontology and Geriatrics 129 (2025) 105670

Contents lists available at ScienceDirect

Archives of Gerontology and Geriatrics

journal homepage: www.elsevier.com/locate/archger

Association of the 25-question Geriatric Locomotive Function Scale with all-cause mortality in older adults: The Nagahama study

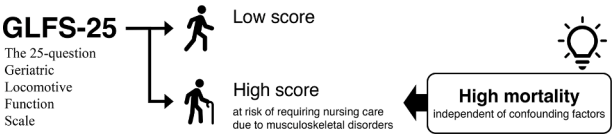
Yasuharu Tabara [a,b,*], Tome Ikezoe [c], Kazuya Setoh [a], Takahisa Kawaguchi [b], Fumihiko Matsuda [b]

[a] Graduate School of Public Health, Shizuoka Graduate University of Public Health, Aoi-ku, Shizuoka, 420-0881, Japan
[b] Center for Genomic Medicine, Kyoto University Graduate School of Medicine, Sakyo-ku, Kyoto, 606-8507, Japan
[c] Faculty of Rehabilitation, Kansai Medical University, Hirakata, Osaka, 573-1136, Japan

HIGHLIGHTS

- The GLFS-25 is a questionnaire to determine the severity of locomotive syndrome.
- The GLFS-25 was associated with all-cause mortality independently of sarcopenia.
- The GLFS-25 could be useful for the identification of individuals at risk.

GRAPHICAL ABSTRACT



ARTICLE INFO

Keywords:
Locomotive syndrome
Sarcopenia
All-cause mortality
General population
Longitudinal studies

ABSTRACT

Backgrounds: Locomotive syndrome is a condition in which a person is at risk of requiring nursing care due to musculoskeletal disorders. The 25-question Geriatric Locomotive Function Scale (GLFS-25) was developed to determine the severity of locomotive syndrome. In this study, we aimed to determine the prognostic significance of the GLFS-25 for all-cause mortality.

Methods: The study participants consisted of 3,447 community residents aged ≥65 years. All-cause mortality was determined using residential registry records. Skeletal muscle mass assessed via bioimpedance methods was considered in the analysis as a confounding factor.

Results: During a mean follow-up period of 3,236 days (30,566 person–years), 288 cases of all-cause mortality occurred. When participants were categorized by the GLFS-25 score [grade 1: <7 points (n = 1,948); grade 2: ≥7 to <16 points (n = 894); grade 3: ≥16 points (n = 605)], their survival probability decreased linearly with increasing grade (log-rank test P = 0.014). In a Cox proportional hazards model adjusted for confounding factors, including low skeletal muscle mass, GLFS-25 grade 3 was identified as an independent risk factor for all-cause mortality (hazard ratio: 1.60; P = 0.007) in the subpopulation aged ≥70 years but not in the overall population (P = 0.062). The hazard ratio for all-cause mortality with GLFS-25 grade 3 and low skeletal muscle mass combined was 2.66 (P < 0.001).

Conclusion: The GLFS-25 is independently associated with all-cause mortality in older adults. Using this questionnaire to assess locomotive syndrome could be useful for identifying individuals at risk.

* Coresponding author at: Graduate School of Public Health, Shizuoka Graduate University of Public Health, Kita-ando 4-27-2, Aoi-ku, Shizuoka, 420-0881, Japan.
E-mail address: tabara@s-sph.ac.jp (Y. Tabara).

https://doi.org/10.1016/j.archger.2024.105670
Received 22 August 2024; Received in revised form 11 October 2024; Accepted 22 October 2024
Available online 22 October 2024

1. Introduction

Locomotive syndrome is a concept proposed by the Japanese Orthopaedic Association to indicate a condition in which a person is at risk of requiring nursing care because of disorders of the bones, joints, muscles, and nerves (Nakamura, 2008). The 25-question Geriatric Locomotive Function Scale (GLFS-25) has generally been used as a screening tool to assess the degree of locomotive syndrome in older (≥65 years) adults (Seichi et al., 2012). Several longitudinal studies reported that the GLFS-25 score was associated with the incidence of locomotive syndrome (Yoshimura et al., 2022) and the need for long-term care (Ide et al., 2021; Niwa et al., 2021). Although one study (Niwa et al., 2021) reported a significant association with the composite outcome of care requirement and death, no study has investigated the prognostic significance of the GLFS-25 score for all-cause mortality.

Sarcopenia is a phenotype characterized by reduced skeletal muscle mass, weak muscle strength, and reduced physical activity (Chen et al., 2020), which partially overlaps with the features of locomotive syndrome. Indeed, significant correlations between locomotive syndrome and each component of sarcopenia have been noted in several observational studies (Kobayashi et al., 2023). We previously reported that a low skeletal muscle mass index (SMI) calculated from bioimpedance measures of skeletal muscles was independently associated with all-cause mortality (Tabara, Setoh, Kawaguchi & Matsuda, 2022). We also reported that a low body mass index (BMI), a representative measure of malnutrition, was associated with all-cause mortality (Tabara, Nakatani & Miyachi, 2021) through partial mediation by a low SMI (Tabara et al., 2022). Given that background, the practical use of the GLFS-25 in care prevention settings requires clarification about whether locomotive syndrome as assessed by the GLFS-25 predicts all-cause mortality independently of a low SMI and a low BMI.

In this longitudinal study in a general population, we aimed to clarify the prognostic significance of the GLFS-25 for all-cause mortality in older adults, with consideration of the possible involvement of sarcopenia in the relationship.

2. Methods

2.1. Study participants

Our analysis used data from the Nagahama study, a longitudinal cohort study of community residents living in Nagahama City, a suburban city in Shiga prefecture in central Japan (Tabara et al., 2024; Takeshita et al., 2023). The baseline survey in the Nagahama study was conducted between 2008 and 2010. Nagahama City residents aged 30–74 years who were living independently were eligible to participate. The Nagahama study design required a clinical survey to be conducted every 5 years after the baseline survey. For the present study, we analyzed data obtained at the second survey (conducted between 2012 and 2016), when locomotive syndrome was assessed using the GFLS-25. Of 9840 Nagahama study participants, 3447 were included in the analysis after the exclusion of individuals aged <65 years ($n = 6264$), having an implanted pacemaker ($n = 10$), receiving hemodialysis therapy ($n = 4$), lacking a GLFS-25 score obtained between 2013 and 2016 ($n = 99$), and lacking clinical values required for the analysis ($n = 16$).

All procedures in the Nagahama study were approved by the ethics committee of the Kyoto University Graduate School of Medicine and the Nagahama Municipal Review Board. Written informed consent was obtained from all participants before enrolment.

2.2. All-cause mortality

All-cause mortality was identified by reviewing residential registry records managed by the Nagahama City Office. Participants who had relocated out of Nagahama City were censored. The follow-up period was calculated from participation in the follow-up (second) survey to the date of relocation or death or to the study end date (March 31, 2024).

Table 1
The 25-question Geriatric Locomotive Function Scale.

1	Did you have any pain (including numbness) in your neck or upper limbs (shoulder, arm, or hand)?
2	Did you have any pain in your back, lower back, or buttocks?
3	Did you have any pain (including numbness) in your lower limbs (hip, thigh, knee, calf, shin, ankle, or foot)?
4	To what extent has it been painful to move your body in daily life?
5	To what extent has it been difficult to get up from a bed or lie down?
6	To what extent has it been difficult to stand up from a chair?
7	To what extent has it been difficult to walk inside the house?
8	To what extent bas it been difficult to wear and take off shirts?
9	To what extent has it been difficult to wear and take off trousers and pants?
10	To what extent has it been difficult to use the toilet?
11	To what extent has it been difficult to wash your body in the bath?
12	To what extent has it been difficult to go up and down stairs?
13	To what extent has it been difficult to walk briskly?
14	To what extent has it been difficult to keep yourself neat?
15	How far can you keep walking without rest?
16	To what extent has it been difficult to go out to visit neighbors?
17	To what extent has it been difficult to carry objects weighing approximately 2 kg?
18	To what extent has it been difficult to go out using public transportation?
19	To what extent have simple tasks and housework (preparing meals, cleaning up, etc.) been difficult?
20	To what extent have load-bearing tasks and housework (cleaning the yard, carrying heavy bedding, etc.) been difficult?
21	To what extent has it been difficult to perform sports activity (jogging, swimming, gate ball, dancing, etc.)?
22	Have you been restricted from meeting your friends?
23	Have you been restricted from joining social activities (meeting friends, playing sports, engaging in activities and hobbies, etc.)?
24	Have you ever felt anxious about falls in your house?
25	Have you ever felt anxious about being unable to walk in the future?

2.3. GLFS-25

The GLFS-25 is a self-administered questionnaire consisting of 25 questions relating to pain in various body parts, activities of daily living, social activities, and concerns about physical impairment (Table 1) (Seichi et al., 2012). Participants were asked to rate the 25 questions on a five-point scale from no impairment (0 points) to severe impairment (4 points). The points total was used as an index of locomotive syndrome, with higher scores indicating worsening locomotive function.

2.4. Skeletal muscle mass

Appendicular lean mass was estimated using a bioelectrical impedance analysis device (InBody 430: InBody Co. Ltd., Seoul, ROK). The device can estimate lean mass from the resistance and reactance of arms, trunk, and legs at three different frequencies (5, 50, and 250 kHz) of an alternating 250-A current. The SMI was calculated by dividing the appendicular lean mass by body height in meters squared (Chen et al., 2020). Low SMI was defined as less than 7.0 kg/m^2 in men and less than 5.7 kg/m^2 in women based on criteria published by the Asian Working Group for Sarcopenia (Chen et al., 2020).

2.5. Clinical parameters

Clinical parameters analyzed in this study were obtained at the follow-up (second) survey in the Nagahama study. Given the findings in our previous study (Tabara et al., 2021), which clarified a U-shaped association between BMI and all-cause mortality in Japanese individuals, we considered low BMI (<20 kg/m^2) to be a risk factor for all-cause mortality. Data on smoking and drinking habits, history of cardiovascular diseases including stroke and myocardial infarction, and medications were obtained using a self-reported structured questionnaire. Depressive symptom was assessed using the Center for

Table 2
Clinical characteristics of study participants.

	Overall	≥70 Years
	3447	1979
Age, years	71.2 ± 4.1	74.2 ± 2.8
Sex, men%	40.2	43.5
Body mass index, kg/m^2	22.5 ± 3.0	22.5 ± 3.0
Low body mass index, %	20.4	20.2
Skeletal muscle mass index, kg/m^2	6.6 ± 0.9	6.6 ± 0.9
Low skeletal muscle index, %	25.9	29.7
Smoking, never/past/current%	68.0/25.0/7.0	67.1/27.0/5.9
Alcohol consumption, Go/week	3.6 ± 7.2	3.7 ± 6.9
History of cardiovascular diseases, %	8.6	9.9
Systolic blood pressure, mmHg	133 ± 17	134 ± 17
Diastolic blood pressure, mmHg	72 ± 10	72 ± 10
Hemoglobin A1c, %	5.7 ± 0.5	5.7 ± 0.5
High-density lipoprotein cholesterol, mg/dL	65 ± 17	64 ± 17
Low-density lipoprotein cholesterol, mg/dL	117 ± 28	114 ± 27
Albumin, g/dL	4.2 ± 0.2	4.2 ± 0.2
Estimated glomerular filtration rate, ml/min/1.73m^2	70.3 ± 13.4	68.7 ± 13.5
CES-D score, points	13 ± 7	13 ± 7
GLFS-25 score, points	9 ± 11	11 ± 13

Values are frequencies or means with standard deviation. Low body mass index was defined as <20.0 kg/m^2. Low skeletal muscle mass index was defined <7.0 kg/m^2 in men and 5.7 kg/m^2 in women. Go is the traditional Japanese liquor unit, where 1 Go corresponds to 22 g ethanol. Cardiovascular diseases include stroke and myocardial infarction. eGFR, estimated glomerular filtration rate; CES-D, Center for Epidemiologic Studies Depression Scale; GLFS-25, 25-question Geriatric Locomotive Function Scale.

Epidemiologic Studies Depression Scale. The 25 questions of the GLFS and 20 questions of the depression scale were included in that questionnaire.

2.6. Statistical analysis

Data are presented as frequencies or means with standard deviation. The log-rank test was used to assess group differences from Kaplan–Meier curves. The proportional hazards assumption was assessed using the Schoenfeld residual test. A Cox proportional hazards model was used to identify factors associated with all-cause mortality. Statistical analyses were performed using the JMP Pro software application (version 17.2.0: SAS Institute, Cary, NC, USA) and the STATA software application (version 18.0: Stata Corp LLC, College Station, TX, USA). P Values less than 0.05 were considered indicative of statistical significance.

3. Results

Table 2 presents the clinical characteristics of the study participants. Because the mean GLFS-25 score increased after 70 years of age in both sexes (Fig. 1), an association analysis was also performed for the subpopulation aged ≥70 years (Table 2).

During the mean 3236 days of follow-up (30,566 person–years), 288 all-cause deaths occurred in the overall population, whereas 217 deaths occurred in the subpopulation 70 years of age and older (17,351 person–years). Fig. 2 presents the related Kaplan–Meier curves for all-cause mortality. When participants were categorized into groups according to GLFS-25 scores (grade 1: <7 points; grade 2: ≥7 to <16 points; grade 3: ≥16 points) (Seichi et al., 2012), a significant linear association between the grade of the GLFS-25 score and survival probability was evident. The Cox proportional hazards model analysis (Table 3) demonstrated a significant association between the highest GLFS-25 grade and all-cause mortality in the older subpopulation, but not in the overall population even after adjustment for possible confounding factors including a low SMI and a low BMI. The association in the older population remained significant even after excluding early death cases (within 1 year of follow-up) and after further adjustment of the CES-D score in the model (GLFS-25 score grade 3, hazard ratio = 1.50, $P = 0.028$).

In the Cox proportional hazards models analyzing participants aged ≥70 years, a low BMI was identified as a significant determinant when a low SMI was not included in the model (hazard ratio: 1.52; $P = 0.014$), indicating that a low SMI was an intermediate factor in the relationship between a low BMI and mortality. Even in the analysis excluding a low SMI from the model, the highest GLFS-25 grade was also significantly associated with all-cause mortality (hazard ratio: 1.64; $P = 0.004$).

Fig. 3 presents the hazard ratio for all-cause mortality based on the combination of GLFS-25 grade 3 and a low SMI, which was 2.66 ($P < 0.001$), whereas the hazard ratios for a low SMI or GLFS-25 grade 3 alone did not show a significant association with all-cause mortality.

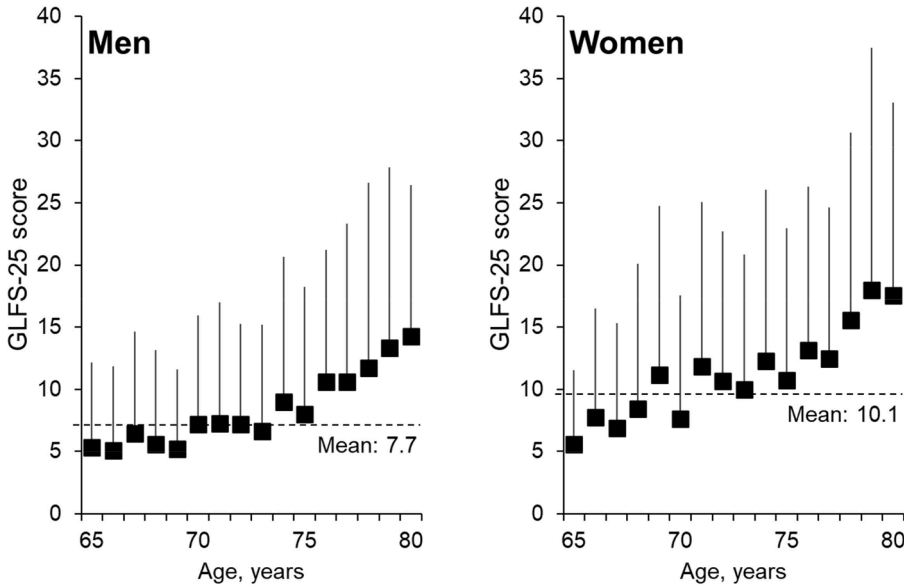


Fig. 1. Age differences for scores on the 25-question Geriatric Locomotive Function Scale.
Values are means with standard deviation. The horizontal lines indicate the mean for the study population.

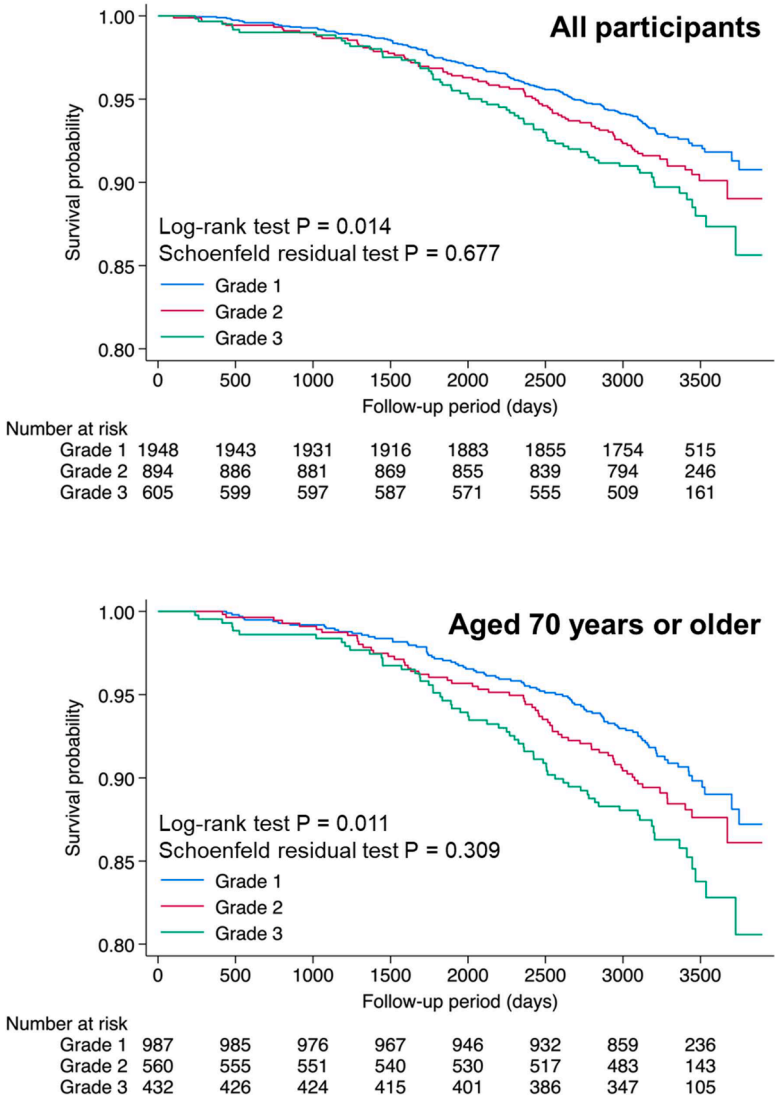


Fig. 2. Kaplan–Meier curves for all-cause mortality by score on the 25-question Geriatric Locomotive Function Scale (GLFS-25).
Participants were divided by GLFS-25 score as < 7, grade 1; ≥7–<16, grade 2; ≥16, grade 3. The proportional hazards assumption was assessed using the Schoenfeld residual test. Group differences in the Kaplan–Meier curves were assessed using the log-rank test.

Table 3
Cox proportional hazards model for all-cause mortality.

	Total participants		Participants aged ≥70 years			
					Excluding early death cases	
	HR (95 % CI)	P	HR (95 % CI)	P	HR (95 % CI)	P
Age, years	1.10 (1.07–1.14)	<0.001	1.12 (1.06–1.17)	<0.001	1.11 (1.06–1.17)	<0.001
Sex, women	0.51 (0.36–0.72)	<0.001	0.54 (0.36–0.81)	0.003	0.53 (0.36–0.80)	0.003
Smoking	1.50 (1.08–2.07)	0.015	1.69 (1.17–2.48)	0.005	1.67 (1.16–2.46)	0.006
Low body mass index	0.99 (0.71–1.39)	0.969	1.18 (0.81–1.71)	0.380	1.21 (0.83–1.75)	0.325
Low skeletal muscle mass index	1.61 (1.22–2.12)	0.001	1.60 (1.16–2.18)	0.004	1.58 (1.15–2.16)	0.006
GLFS-25 score						
Grade 1	reference		reference		reference	
Grade 2	1.21 (0.92–1.60)	0.179	1.29 (0.93–1.78)	0.124	1.30 (0.94–1.79)	0.118
Grade 3	1.34 (0.99–1.82)	0.062	1.60 (1.14–2.22)	0.007	1.56 (1.11–2.18)	0.011

Adjusted factors were history of cardiovascular diseases, systolic blood pressure, serum albumin levels, high-density lipoprotein cholesterol levels, and estimated glomerular filtration rate. Early deaths were deaths occurring within 1 year from the start of follow-up. HR, hazard ratio; CI, confidence interval; GLFS-25, 25-question Geriatric Locomotive Function Scale.

4. Discussion

In this longitudinal study of a general population, we observed that the GLFS-25 score was significantly associated with all-cause mortality in the population 70 years of age and older. That association was independent of possible confounding factors including physical factors (a

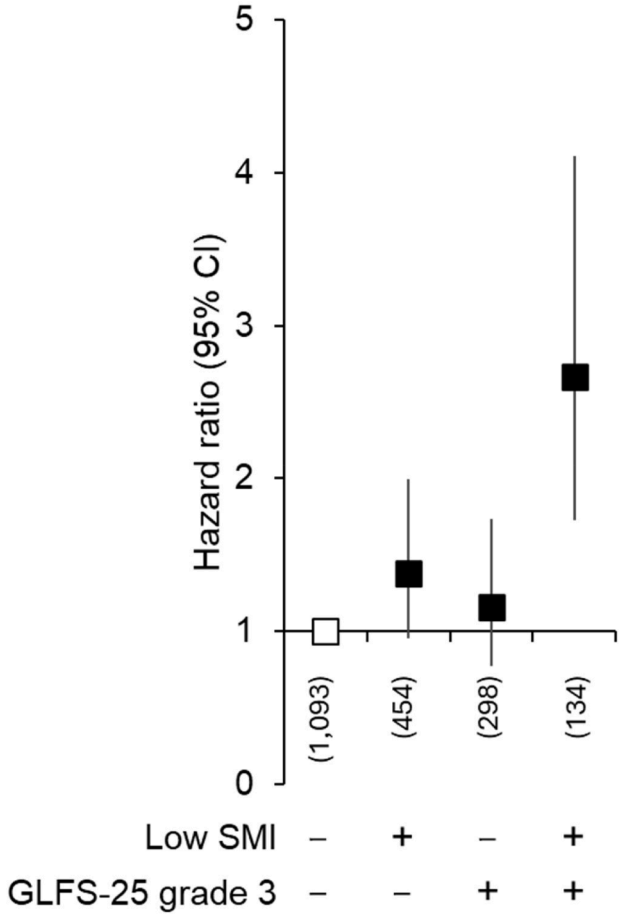


Fig. 3. Hazard ratios for all-cause mortality by the combination of a grade 3 score on the 25-question Geriatric Locomotive Function Scale (GLFS-25) and a low skeletal muscle mass index (SMI) in the population aged ≥70 years.
Hazard ratios with 95 % confidence intervals are shown. The number of participants in each group is shown in parentheses. A low SMI was defined as <7.0 kg/m^2 in men and <5.7 kg/m^2 in women. The highest GLFS-25 grade (grade 3) was defined as a score of ≥16 points. Adjustments were applied for age, sex, history of cardiovascular diseases, smoking, systolic blood pressure, serum albumin levels, high-density lipoprotein cholesterol levels, and estimated glomerular filtration rate.

low SMI and a low BMI), phycological factors (CES-D score), and history of cardiovascular diseases, which were known to be associated with mortality in older adults. Furthermore, the association remained significant even with the exclusion of early deaths from the analysis, indicating that reverse causation could be excluded from the association between the GLFS-25 score and mortality.

The GLFS-25 had been suggested for use in adults aged ≥65 years (Seichi et al., 2012). Although we did not investigate associations of the GLFS-25 score with the incidence of long-term care requirements, our findings indicated that this score might be even more appropriate for older individuals. In the present study, the GLFS-25 score demonstrated a linear increase with age in the population aged ≥70 years. Similar age-related changes were reported in another observational study (Yamada et al., 2020), supporting our suggestion regarding the age group to which the score is applicable.

The association between the GLFS-25 and all-cause mortality was independent of a low SMI. A previous cross-sectional study involving older adults (Inanaga et al., 2023) reported that the GLFS-25 score and the score of each component of the GLFS-25 (body pain, movement difficulty, usual care, activities of daily life, social activities, and cognition) were not significantly associated with the SMI. The lack of such an association was also reported in a meta-analysis of cross-sectional studies that investigated associations of various physical factors with the GLFS-25 score (Kobayashi et al., 2023). Given those results, the GLFS-25 might be associated with all-cause mortality as a reflection of conditions other than a low SMI. Unfortunately, we did not analyze physical factors such as grip strength and gait speed, which have been reported to be associated with the GLFS-25 score (Kobayashi et al., 2023) in the overall study population. Further investigation into whether the GLFS-25 is prognostic for mortality independent of those physical performance factors is warranted.

The highest hazard ratio for all-cause mortality was observed for the combination of GLFS-25 grade 3 and a low SMI, whereas the hazard ratio for either factor alone did not reach statistical significance. That observation indicates that in the Cox proportional hazards model, the participants with both GLFS-25 grade 3 and a low SMI helped increase the hazard ratio for each group when the combination of GLFS-25 and a low SMI was not included in the model as an independent variable. Measurement of the SMI might therefore be useful for discriminating individuals at higher risk from among the population with GLFS-25 grade 3.

A combination of the two-step and stand-up tests with the GLFS-25 score has been suggested as another method for assessing locomotive syndrome (Yoshimura et al., 2022). Unfortunately, data for those physical tests were not available for the entire study population; thus, we could not assess the prognostic significance of that composite score. Although no clear results have been reported concerning the association of the two-step and stand-up tests with mortality, the composite score was reported to be associated with the new onset of locomotive syndrome (Yoshimura et al., 2022). Further investigation into whether the addition of these physical tests to the GLFS-25 score improves the prognostic value of the GLFS-25 score alone is warranted.

To the best of our knowledge, this study is the first to show the prognostic significance of the GLFS-25 for all-cause mortality. Certain limitations should be noted while interpreting our findings. First, the study population consisted of physically independent community residents. Compared to the overall community residents, the study population might be health-biased. Second, because body size of East Asians including Japanese is smaller than that of European populations (Di Angelantonio & Bhupathiraju, 2016), further studies in various population is needed to extrapolate these findings in other population with different ethnic backgrounds. Third, because of a lack of data, individuals who might have had a history of fractures of the lower extremity were not excluded from the analysis. A history of fracture might have had a confounding effect on the association between the GLFS-25 score and mortality.

In conclusion, the GLFS-25 was independently associated with all-cause mortality. In addition to skeletal muscle decline, using the GLFS-25 in an assessment of locomotive syndrome could be useful for the identification of individuals at risk.

Financial support

The study was supported by a university grant, The Center of Innovation Program, The Global University Project, and a Grant-in-Aid for Scientific Research (25293141, 26670313, 26293198, 17H04182, 17H04126, 21H04850) from the Ministry of Education, Culture, Sports, Science and Technology of Japan; the Practical Research Project for Rare/Intractable Diseases (ek0109070, ek0109283, ek0109196, ek0109348), the Comprehensive Research on Aging and Health Science Research Grants for Dementia R&D (dk0207006, dk0207027), the Program for an Integrated Database of Clinical and Genomic Information (kk0205008), the Practical Research Project for Lifestyle-related Diseases including Cardiovascular Diseases and Diabetes Mellitus (ek0210066, ek0210096, ek0210116), the Research Program for Health Behavior Modification by Utilizing IoT (le0110005), and the Research and Development Grants for Longevity Science (dk0110040) from the Japan Agency for Medical Research and Development (AMED); the

Health Labour Sciences Research Grant (24AF1005) from the Ministry of Health, Labor and Welfare of Japan; the Takeda Medical Research Foundation, Daiwa Securities Health Foundation, Sumitomo Foundation, and the Mitsubishi Foundation.

CRediT authorship contribution statement

Yasuharu Tabara: Writing – review & editing, Writing – original draft, Funding acquisition, Formal analysis, Conceptualization. **Tome Ikezoe:** Investigation, Data curation. **Kazuya Setoh:** Investigation, Data curation. **Takahisa Kawaguchi:** Investigation, Data curation. **Fumihiko Matsuda:** Supervision, Project administration, Funding acquisition.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgment

We are extremely grateful to the Nagahama City Office and the nonprofit organization Zeroji Club for their assistance in conducting the Nagahama study. We also thank the editors of Crimson Interactive Pvt. Ltd. for their help with English language editing.

References

Chen, L. K., Woo, J., Assantachai, P., Auyeung, T. W., Chou, M. Y., Iijima, K., Jang, H. C., Kang, L., Kim, M., Kim, S., Kojima, T., Kuzuya, M., Lee, J. S. W., Lee, S. Y., Lee, W. J., Lee, Y., Liang, C. K., Lim, J. Y., Lim, W. S., Peng, L. N., Sugimoto, K., Tanaka, T., Won, C. W., Yamada, M., Zhang, T., Akishita, M., & Arai, H. (2020). Asian Working Group for Sarcopenia: 2019 Consensus update on sarcopenia diagnosis and treatment. *Journal of the American Medical Directors Association, 21*, 300–307.e2. https://doi.org/10.1016/j.jamda.2019.12.012

Global BMI Mortality Collaboration, Di Angelantonio, E., Bhupathiraju, ShN, et al. (2016). Body-mass index and all-cause mortality: Individual-participant-data meta-analysis of 239 prospective studies in four continents. *Lancet (London, England), 388*, 776–786. https://doi.org/10.1016/S0140-6736(16)30175-1

Ide, K., Yamato, Y., Hasegawa, T., Yoshida, G., Yasuda, T., Banno, T., Arima, H., Oe, S., Mihara, Y., Ushirozako, H., Yamada, T., Watanabe, Y., Nakai, K., Hoshino, H., Niwa, H., Togawa, D., & Matsuyama, Y. (2021). Prospective nursing care certification using the 25-question geriatric locomotive function scale. *Geriatrics & Gerontology International, 21*, 492–497. https://doi.org/10.1111/ggi.14169

Inanaga, S., Hasegawa, M., Kosuge, M., Ichimura, S., Morii, T., & Hosogane, N. (2023). Relationship between the 25-question Geriatric Locomotive Function Scale and physical function in the elderly people. *Journal of Bone and Mineral Metabolism, 41*, 550–556. https://doi.org/10.1007/s00774-023-01427-w

Kobayashi, T., Morimoto, T., Shimanoe, C., Ono, R., Otani, K., & Mawatari, M. (2023). Clinical characteristics of locomotive syndrome categorised by the 25-question Geriatric Locomotive Function Scale: A systematic review. *BMJ Open, 13*, Article E068645. https://doi.org/10.1136/bmjopen-2022-068645

Nakamura, K. (2008). A "super-aged" society and the "locomotive syndrome". *Journal of Orthopaedic Science : Official Journal of the Japanese Orthopaedic Association, 13*, 1–2. https://doi.org/10.1007/s00776-007-1202-6

Niwa, H., Ojima, T., Watanabe, Y., Ide, K., Yamato, Y., Hoshino, H., & Matsuyama, Y. (2021). Association between the 25-question Geriatric Locomotive Function Scale score and the incidence of certified need of care in the long-term care insurance system: The TOEI study. *Journal of Orthopaedic Science : Official Journal of the Japanese Orthopaedic Association, 26*, 672–677. https://doi.org/10.1016/j.jos.2020.05.004

Seichi, A., Hoshino, Y., Doi, T., Akai, M., Tobimatsu, Y., & Iwaya, T. (2012). Development of a screening tool for risk of locomotive syndrome in the elderly: The 25-question geriatric locomotive function scale. *Journal of Orthopaedic Science : Official Journal of the Japanese Orthopaedic Association, 17*, 163–172. https://doi.org/10.1007/s00776-011-0193-5

Tabara, Y., Matsumoto, T., Murase, K., Setoh, K., Kawaguchi, T., Wakamura, T., Hirai, T., Chin, K., & Matsuda, F. (2024). Sleep blood pressure measured using a home blood pressure monitor was independently associated with cardiovascular disease incidence: The Nagahama study. *Journal of Hypertension*. https://doi.org/10.1097/HJH.0000000000003781. In press.

Tabara, Y., Nakatani, E., & Miyachi, Y. (2021). Body mass index, functional disability and all-cause mortality in 330 000 older adults: The Shizuoka study. *Geriatrics & Gerontology International, 21*, 1040–1046. https://doi.org/10.1111/ggi.14286

Tabara, Y., Setoh, K., Kawaguchi, T., & Matsuda, F. (2022). Skeletal muscle mass index is independently associated with all-cause mortality in men: The Nagahama study. *Geriatrics & Gerontology International, 22*, 956–960. https://doi.org/10.1111/ggi.14491

Takeshita, M., Tabara, Y., Setoh, K., Nagao, K., Imaizumi, A., Kageyama, Y., Matsuda, F., & Nagahama study group. (2023). Development of a plasma-free amino acid-based risk score for the incidence of cardiovascular diseases in a general population: The Nagahama study. *Clinical Nutrition (Edinburgh, Scotland), 42*, 2512–2519. https://doi.org/10.1016/j.clnu.2023.10.024

Yamada, K., Ito, Y. M., Akagi, M., Chosa, E., Fuji, T., Hirano, K., Ikeda, S., Ishibashi, H., Ishibashi, Y., Ishijima, M., Itoi, E., Iwasaki, N., Izumida, R., Kadoya, K., Kamimura, M., Kanaji, A., Kato, H., Kishida, S., Mashima, N., Matsuda, S., Matsui, Y., Matsunaga, T., Miyakoshi, N., Mizuta, H., Nakamura, Y., Nakata, K., Omori, G., Osuka, K., Uchio, Y., Ryu, K., Sasaki, N., Sato, K., Senda, M., Sudo, A., Takahira, N., Tsumura, H., Yamaguchi, S., Yamamoto, N., Nakamura, K., & Ohe, T. (2020). Reference values for the locomotive syndrome risk test quantifying mobility of 8681 adults aged 20-89 years: A cross-sectional nationwide study in Japan. *Journal of Orthopaedic Science : Official Journal of the Japanese Orthopaedic Association, 25*, 1084–1092. https://doi.org/10.1016/j.jos.2020.01.011

Yoshimura, N., Iidaka, T., Horii, C., Mure, K., Muraki, S., Oka, H., Kawaguchi, H., Akune, T., Ishibashi, H., Ohe, T., Hashizume, H., Yamada, H., Yoshida, M., Nakamura, K., & Tanaka, S. (2022). Epidemiology of locomotive syndrome using updated clinical decision limits: 6-year follow-ups of the ROAD study. *Journal of Bone and Mineral Metabolism, 40*, 623–635. https://doi.org/10.1007/s00774-022-01324-8

Geriatrics Gerontology International

DOI: 10.1111/ggi.15078

ORIGINAL ARTICLE

EPIDEMIOLOGY CLINICAL PRACTICE AND HEALTH

Prognostic significance of the Questionnaire for Medical Checkup of Old-Old for the incidence of functional disability: The Shizuoka Kokuho Database study

Yasuharu Tabara,[1,2] Aya Shoji-Asahina,[1] Hiroshi Akasaka,[3,4] Ken Sugimoto[5] and Yoko Sato[1]

[1]Graduate School of Public Health, Shizuoka Graduate University of Public Health, Shizuoka, Japan
[2]Center for Genomic Medicine, Kyoto University Graduate School of Medicine, Kyoto, Japan
[3]Department of Hygiene and Preventive Medicine, School of Medicine, Iwate Medical University, Iwate, Japan
[4]Department of Geriatric and General Medicine, Osaka University Graduate School of Medicine, Osaka, Japan
[5]Department of General and Geriatric Medicine, Kawasaki Medical School, Okayama, Japan

Correspondence
Yasuharu Tabara, PhD, Graduate School of Public Health, Shizuoka Graduate University of Public Health, Kita-ando 4-27-2, Aoi-ku, Shizuoka 420-0881, Japan.
Email: tabara@s-sph.ac.jp

Received: 18 July 2024
Revised: 7 November 2024
Accepted: 3 January 2025

Aim: In the Japanese health checkup system for older adults aged ≥75 years, the Questionnaire for Medical Checkup of Old-Old (QMCOO) was adopted after 2020. However, the prognostic significance of this questionnaire for the incidence of functional disability is uncertain. The current study aimed to validate the prognostic significance of the QMCOO, and to develop a simple risk score for functional disability by analyzing health insurance claims data including annual health checkup data.

Methods: This study included 111 282 older adults aged 75–90 years who did not receive long-term care services at baseline. The study period was between the earliest day of participation in the health checkup after April 2020 and September 2022. The participants who were certified as care level 2 and higher during this period were considered as incident cases of functional disability.

Results: Within a mean follow-up duration of 1.7 years (191 085 person-years), 4578 functional disability cases were identified. In addition to the basic covariates, among the 15 items in the QMCOO, nine were identified as independent determinants. The probability of developing functional disability that was calculated using the model was associated with older age, male sex, underweight and poor responses to the QMCOO items. According to the weighted score based on the model, the participants was classified as functional disability probability of <1% to >45%.

Conclusions: The nine items in the QMCOO were associated with the incidence of functional disability. The weighted scoring system could be helpful for the use of the QMCOO. **Geriatr Gerontol Int 2025; 25: 260–266**.

Keywords: functional disability, health checkup, older adults, QMCOO, screening.

Introduction

The extension of life expectancy[1] has resulted in a rapid increase in the older adult population in Japan.[2] Avoiding the need for long-term care is the most important issue among older people to maintain their independence and quality of life. It has been estimated that the total additional medical and long-term care costs generated by functional limitations were US$72.7 billion, and the long-term care costs accounted for a large part of the total costs particularly in older people aged ≥85 years,[3] showing the importance of maintaining physical independence to reduce the health burden on the individual, but also the economic burden on society.

In Japan, older adults aged ≥75 years are required to enroll in the Latter-Stage Elderly Medical Care System, a health insurance system that partially covers the medical expenditure of insured people. In addition, municipalities, the insurer of this health insurance system, are obligated to provide annual health checkups (*Kouki Koureisha Kenshin*) to insured individuals. In addition to evaluating clinical factors associated with cardiovascular diseases, this health checkup includes a questionnaire survey to assess the potential risk of health issues that cannot be assessed through clinical examination alone. Until recently, a similar structured questionnaire for individuals aged <75 years was used in the health checkup for older adults. However, the Questionnaire for Medical Checkup of Old-Old (QMCOO) was adopted after 2020 to assess health issues specific to older adults, because the main cause of disability in those aged ≥75 years is geriatric syndromes, including frailty, fall and fractures, and dementia.[4] The QMCOO consists of 15 items from the following 10 domains: health

condition, mental health, eating behavior, oral function, bodyweight loss, physical function and falls, cognitive function, smoking, social participation and social support.[4] Several cross-sectional studies have reported a close correlation between the QMCOO score and score of the Kihon Checklist,[5,6] a frailty score developed in Japan to assess for care requirement in older adults, and a frailty score of the Cardiovascular Health Study.[7] Recently, Tanaka *et al.*[8] reported that a simply summed score of 15 items on the QMCOO was independently associated with incidence of functional disability in a general population. Validating the prognostic significance of this questionnaire with further consideration of weighting of each item could provide a basis for its use in identifying individuals who are at risk. Furthermore, given the possibility of internal correlation between items, it was uncertain whether all 15 items were needed for the calculation of the total score. Considering basic clinical factors assessed in the annual health checkup together with the responses to the selected items of QMCOO might further improve the accuracy of identifying individuals at-risk.

Given these backgrounds, the present study aimed to investigate the prognostic significance of the QMCOO for functional disability by analyzing data from the Shizuoka Prefecture-wide Kokuho Database, which includes health and care insurance claims data, and the annual health checkup data for older adults, and to develop a risk score consisting of weighted scores of selected QMCOO items and basic clinical factors assessed in the annual health checkup to facilitate identification of older adults at-risk for functional disability.

Methods

Data source

This study analyzed data from the Shizuoka Kokuho Database (SKDB ver. 2024.1 with the analysis data generation system ver. 4.0),[9,10] which comprises the Shizuoka Prefecture-wide individual-level data on the medical insurance claims and health checkup of enrollees in the National Health Insurance or the Latter-Stage Elderly Medical Care System. The current version of the SKDB covers the period from April 2012 to September 2022.

The National Health Insurance partially covers the medical expenditure of insured people. This insurance system is designed for individuals aged <75 years who are not eligible to be members of any employee-based health insurance. The Latter-Stage Elderly Medical Care System is a health insurance system for individuals aged >75 years and people aged 65–74 years who are physically handicapped. Older individuals aged ≥75 years, except those who have an occupation, are required to enroll in this insurance system. Enrollees for these insurance systems have the opportunity to receive a medical checkup (*Tokuei Kenshin*, *Kouki Koureisha Kenshin*) once a year.

Furthermore, the SKDB includes data on the Long-Term Care Insurance System, a care insurance system that covers daily care expenses for older people. Insured individuals who require long-term care are eligible for in-home or facility-based services according to their certified care level. The long-term care approval board in each municipality determines the certified care level by assigning a support level (levels 1–2) or a care level (levels 1–5) based on the applicant's mental and physical condition, and the opinion of their primary doctor. The care requirement certification is designed to be applied uniformly on a nationwide basis.

Study setting

This was a longitudinal observational study comprising residents aged ≥75 years in the Shizuoka Prefecture who participated in the Latter-Stage Elderly Medical Care System. The longitudinal analysis was carried out using the earliest day of participation after 2020 in the annual health checkup as the index day, with 12 months before the index day as the baseline period (Fig. S1). The follow-up duration was calculated as the number of days from the index day to the end of the follow-up period. Withdrawal cases from the insurance were treated as a censored case.

Using the earlier version of the SKDB, re-admission cases were provided with the same insurance ID as continuous enrollees by disregarding the intermediate period during which they were unsubscribed. However, the method of calculating the follow-up period was changed to exclude the intermediate unsubscribed period by setting the baseline to fall within the consecutive insurance enrollment period.

Study population

Of the 2 654 305 residents in the Shizuoka Prefecture who were included in the current version of the SKDB, those who participated in the health checkup after April 2020 ($n = 401\,854$) were extracted. Individuals aged ≥90 years ($n = 10\,691$) and <75 years ($n = 265\,388$), those who had been certified as care levels 2–5 ($n = 3817$) at the index day, those whose data on the clinical parameters required for this study were not available or widely deviated from its distribution ($n = 8141$), and those whose responses to the QMCOO had missing value ($n = 2535$) were excluded from the study. Finally, 111 282 older adults were ultimately included in this analysis.

The ethics committee of the Shizuoka Graduate University of Public Health (SGUPH_2021_001) approved the study procedure involving the SKDB analysis. Approval from the review board of each municipality for using their insurance data in medical studies was also obtained before receiving the data. Before the receipt of the SKDB data, all personal details were anonymized by the Shizuoka Federation of National Health Insurance Organizations. To ensure that the participants can refuse the use of their data, information related to this study was disclosed on the websites of the Shizuoka Prefectural Government Office and Shizuoka Graduate University of Public Health.

Outcome definition

To meet the conditions with the criteria of healthy life expectancy, which were determined by the Ministry of Health, Labor and Welfare, the participants who were certified as care level 2 and higher were considered to have functional disability. Furthermore, the associations between the QMCOO and all-cause mortality were investigated to validate items differently associated with functional disability and all-cause mortality. All-cause mortality was identified based on the withdrawal reason described in the health insurance data.

Clinical parameters

Clinical information and responses to the QMCOO were obtained from the annual health checkup records. During the baseline period, information on the participants' latest certified care level based on the data on the Long-Term Care Insurance System was collected. The Charlson Comorbidity Index[11] was calculated using the health insurance claims requested during the baseline period and was used as an index of severe comorbidity.

Statistical analysis

Values are expressed as the mean ± standard deviation or frequency. The Cox proportional hazards model was used to investigate factors associated with functional disability and all-cause mortality. The proportional hazards assumption was verified with a Schoenfeld residual test. The Cox proportional hazards model was also used to calculate the probability of developing functional disability according to the participants' baseline characteristics. A detailed description for the calculation of the probability can be found in a previous study.[12] The score sheet for functional disability (the SKDB functional disability score) was made based on the regression coefficient obtained from the final Cox proportional hazards model.[13]

Statistical analyses were carried out using JMP version 17.2.0 (SAS Institute, Cary, NC, USA). The Schoenfeld residual test and Harrell's C-index calculation were carried out using Stata version 18.0 (StataCorp, College Station, TX, USA). *P*-values of <0.05 were considered statistically significant.

Results

Table 1 shows the clinical characteristics of the study participants. Differences in clinical characteristics between participants who developed functional disability and who did not, and between participants who died or survived, are summarized in Tables S1 and S2, respectively. During a mean follow-up duration of 1.7 years (191 085 person-years), 4578 functional disability cases were recorded. Meanwhile, there were 3195 mortality cases during this period (194 593 person-years).

Table 1 Clinical characteristics of the study participants

Age (years)	81.1 ± 4.0
Male sex (%)	25.7
Body mass index (kg/m^2)	22.5 ± 3.4
Rate of hospitalization (%)	9.7
Certified care level at baseline (%)	
Support level 1	1.4
Support level 2	1.9
Care level 1	3.3
Charlson comorbidity index	2.7 ± 2.3
Systolic blood pressure (mmHg)	135 ± 17
Diastolic blood pressure (mmHg)	73 ± 11
Hypertension (%)	35.3
HDL cholesterol (mg/dL)	64 ± 16
Low HDL cholesterol (%)	4.7
LDL cholesterol (mg/dL)	117 ± 29
High LDL cholesterol (%)	20.4
Hemoglobin A1c (%)	5.8 ± 0.6
High hemoglobin A1c (%)	61.6
Creatinine (mg/dL)	0.8 ± 0.3
High creatinine (%)	14.8
Alanine aminotransferase (U/L)	18 ± 11
High alanine aminotransferase (%)	10.3
Urinary glucose, −/±/+/≥2/≥3 (%)	95.2/1.1/1.1/0.8/1.8
Urinary protein, −/±/+/≥2/≥3 (%)	81.2/10.2/6.0/2.0/0.7

Total participants $n = 111\,282$.Values are presented as the mean ± standard deviation or frequency. History of hospitalization was obtained retrospectively from the care insurance data up to 12 months before the index date. The certification of support requirement was determined using the long-term care approval board. Hypertension: systolic blood pressure ≥140 mmHg or diastolic blood pressure ≥90 mmHg irrespective of antihypertensive drug use; low high-density lipoprotein (HDL) cholesterol: <40 mg/dL; high low-density lipoprotein (LDL) cholesterol: ≥140 mg/dL; high hemoglobin A1c: ≥5.6%; high creatinine: ≥1.0 mg/dL; high alanine aminotransferase: ≥42 U/L (men) or ≥ 23 U/L (women).

Table S3 summarizes the frequency of responses for each item in the QMCOO. Table S4 presents the differences in terms of responses between individuals who developed functional disability and those who did not. If the hazard ratio of each item for functional disability was calculated separately with adjustment for age, sex and body mass index, all items showed a significant association (Fig. 1). Similar results were observed in the analysis of all-cause mortality (Fig. 1).

Table S5 presents the results of the Cox proportional hazards model analysis including all items of the QMCOO for the incidence of functional disability. This analysis showed that 10 items of the QMCOO were significant determinants. Furthermore, similar results were observed in the following sensitivity analyses: further adjustment of the Charlson Comorbidity Index (Table S6), excluding incident cases of functional disability within 180 days of follow up (Table S7), age-separated analysis at 80 years-of-age (Tables S8 and S9) and sex-separated analysis (Tables S10 and S11). The factors associated with the incidence of functional disability did not change, even when all-cause mortality was considered as a competing risk factor (Table S12).

Among the 10 QMCOO items independently associated with the incidence of functional disability, Q05 (Have you choked on your tea or soup recently?) showed an opposite association in the basic factor-adjusted analysis (Fig. 1) and in the fully adjusted analysis (Table S5), even after further adjustment of the Charlson Comorbidity Index (Table S6). Figure 2 shows changes in the hazard ratio of Q05 after adding clinical markers and other items from the questionnaire into the Cox proportional hazards model. Considering the instability of the association, Q05 was ultimately excluded from the model. Similar results were obtained in the analysis for all-cause mortality (Fig. S2).

Table 2 shows the summary results of the final Cox proportional hazards model for functional disability. In this final model, given the similar hazard ratios of urinary protein ± and + or higher groups (Table S5), we included urinary protein as two groups to simplify the model. Although several factors did not meet proportional hazard assumption tested by Schoenfeld's residuals (Table S13), we did not exclude these factors from the model given the rho value. The Harrell's C-index of the final model was 0.818, whereas that of the model without the QMCOO was 0.784.

The 2-year event-free probability for the means of risk factors was approximately 0.9705. Based on these results, a score sheet for the incidence of functional disability, the SKDB functional disability score, was developed (Table 3). Furthermore, the predicted probability within 2 years was calculated (Table 3). Figure S3 shows the number of participants with a 2-year probability of ≥10% or ≥5% and <10%. The frequency of individuals with a probability of ≥5% or increased linearly with increasing age. Table S14 shows the clinical characteristics and response rates for the selected items among the subgroups divided by the probability. Participants with a higher probability were more likely to be men, underweight and certified as support level or care level at baseline. Participants with a higher probability had a greater frequency of poor responses for each item.

Discussion

The present longitudinal study that used prefecture-wide data of older adults showed that nine items in the QMCOO were

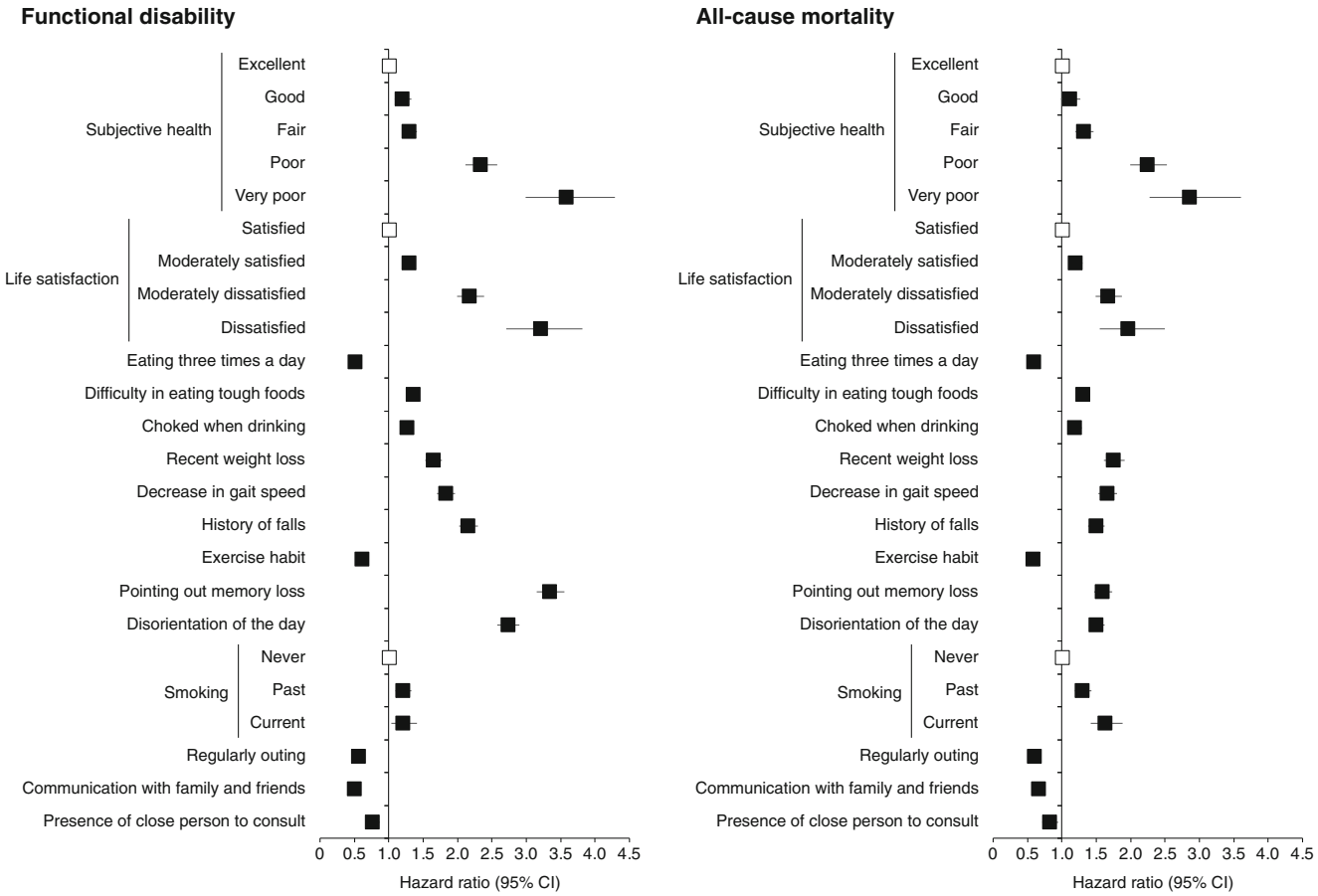


Figure 1 Hazard ratios of functional disability and all-cause mortality for each item in the Questionnaire for Medical Checkup of Old-Old. The adjusted hazard ratio and 95% confidence interval of age, sex and body mass index were calculated. The hazard ratios of each item were calculated using the Cox proportional hazards model. Open squares indicate references in the calculation of the hazard ratio.

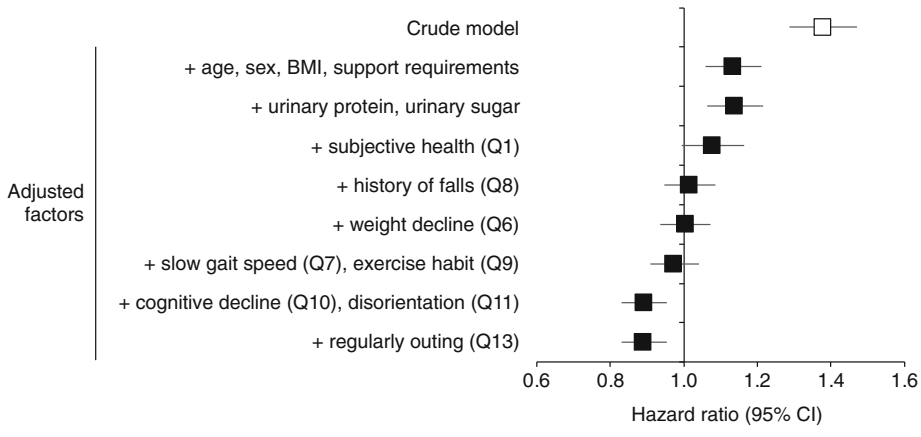


Figure 2 Changes in the hazard ratio of Q05 (choked when drinking) for functional disability through a stepwise adjustment of factors associated with functional disability. Values are presented as hazard ratio and 95% confidence interval. Body mass index (BMI; <20 kg/m^2), urinary protein level (≥±), urinary glucose level (≥±) and subjective health (Q1, poor or extremely poor) were included in the model as a dichotomized value.

independent determinants of functional disability. A simple risk score consisting of the selected QMCOO items and basic clinical factors available for identifying individuals at risk for functional disability was developed.

Japanese individuals aged ≥75 years are required to enroll in the Latter-Stage Elderly Medical Care System. Hence, the proportion of participants in this insurance system was 98.6% at 2022.[14] However, only 28.1% of all insured individuals participated in the health checkup.[15] Hence, the study results might have a healthy bias, which can be particularly strong in the older adult population with a relatively lower participation rate in health checkups.[10] Therefore, the 2-year probability of functional disability calculated in this study

Table 2 Cox proportional hazards model for functional disability including the selected factors

		Coefficient	HR (95% CI)	*P*-value
Age (years)		0.102	1.11 (1.10–1.12)	<0.001
Sex (men)		0.299	1.35 (1.27–1.44)	<0.001
Body mass index (<20 kg/m^2)		0.229	1.26 (1.18–1.34)	<0.001
Certified care level at baseline	Support level 1	0.814	2.26 (1.93–2.64)	<0.001
	Support level 2	1.137	3.12 (2.76–3.52)	<0.001
	Care level 1	1.619	5.05 (4.67–5.46)	<0.001
Urinary glucose (≥±)		0.250	1.28 (1.15–1.43)	<0.001
Urinary protein (≥±)		0.362	1.44 (1.35–1.53)	<0.001
Q01: How is your health condition? (Poor or very poor)		0.240	1.27 (1.18–1.37)	<0.001
Q03: Do you eat three times a day? (No)		0.234	1.26 (1.14–1.41)	<0.001
Q06: Have you lost 2 kg or more in the past 6 months? (Yes)		0.158	1.17 (1.08–1.26)	<0.001
Q07: Do you think you walk slower than before? (Yes)		0.248	1.28 (1.19–1.38)	<0.001
Q08: Have you experienced a fall in the past year? (Yes)		0.345	1.41 (1.32–1.51)	<0.001
Q09: Do you go for a walk for your health at least once a week? (No)		0.217	1.24 (1.17–1.32)	<0.001
Q10: Do your family or friends point out your memory loss? (Yes)		0.559	1.75 (1.63–1.87)	<0.001
Q11: Do you find yourself not knowing today's date? (Yes)		0.452	1.57 (1.47–1.68)	<0.001
Q13: Do you go out at least once a week? (No)		0.341	1.41 (1.31–1.52)	<0.001

Responses to Q03, Q09 and Q13 were flipped and then included in the regression model. CI, confidence interval; HR, hazard ratio.

Table 3 The Shizuoka Kokuho database score for functional disability

Score sheet			Predicted probability	
Items		Points	Total score	Probability (%)
Age	75–79 years	3	≤3	0.8
	80–84 years	8	4–9	1.2
	85–89 years	13	10–14	2.0
Sex (men)		3	15–19	3.2
Body mass index (<20 kg/m^2)		2	20–24	5.4
Certified care level at baseline	Support level 1	8	25–29	8.5
	Support level 2	11	30–34	13.6
	Care level 1	16	35–39	21.4
Urinary glucose (≥±)		2	≥40	≥45.6
Urinary protein (≥±)		4		
Q01: How is your health condition? (Poor or very poor)		4		
Q03: Do you eat three times a day? (No)		2		
Q06: Have you lost 2 kg or more in the past 6 months? (Yes)		2		
Q07: Do you think you walk slower than before? (Yes)		2		
Q08: Have you experienced a fall in the past year? (Yes)		3		
Q09: Do you go for a walk for your health at least once a week? (No)		2		
Q10: Do your family or friends point out your memory loss? (Yes)		6		
Q11: Do you find yourself not knowing today's date? (Yes)		5		
Q13: Do you go out at least once a week? (No)		3		

Responses to Q09 and Q13 were flipped. The points of age groups were calculated by subtracting 75 points (points for individuals aged 74 years) from the crude points of each group (75–79 years: 78 points, 80–84 years: 83 points, 85–89 years: 88 points).

might be lower than the actual value for the whole older adult population. The results of the current study should be interpretated with caution that it was useful in identifying individuals at-risk for functional disability among older individuals who participated in the annual health checkups.

Among the 15 items in the QMCOO, 10 items were significantly associated with the incidence of functional disability. Among them, nine items, except for Q05, were included in the final assessment model. After reducing the number of items, the QMCOO became easy to use as a risk assessment tool. Among the five items, which were not identified as significant determinants, "keeping communication with family and friends" (Q14) and "having close persons to consult" (Q15) had large bias (≥95%) in the frequency of responses, which could have contributed to the lack of association with the incidence of functional disability. "Satisfaction in daily life" (Q02) is a concept that represents not only physical conditions, but also socioeconomic status and other social factors.[16] Thus, it might not be suitable for the risk assessment of functional impairment.

It was challenging to consider the reason why "difficulty in eating tough foods" (Q04) was not associated with the outcomes. The conditions assessed in this question might overlap with conditions that were assessed by other questions. A previous cross-sectional study investigating the association between QMCOO

and frailty[17] also did not identify this item as a significant determinant.

Smoking is an established risk factor of cardiovascular diseases. However, there was no marked difference in the frequency of smoking habit at the baseline between a population who developed functional disability and those who did not, supporting the notion that "current smoking" (Q12) was not directly associated with the development of functional disability.

The hazard ratio of Q05 (Have you choked on your tea or soup recently?) was reduced to <1.0 after adjusting for other factors associated with the development of functional disability. This question was used in the QMCOO to assess frailty of oral function.[18] In the simple adjusted model, this question was positively associated with functional disability, probably reflecting the deterioration of oral function. The precise reason why the association was inverted in the full adjusted model was uncertain. However, a possible explanation was that laryngeal cough reflex is a normal defense response in preventing aspiration pneumonia.[19] Therefore, in the model adjusted for frailty status by other factors, it might be that those who are able to show a normal protective response to aspiration should be interpreted as being less likely to develop functional disability. It was reported that individuals with dysphagia do not always have a cough reflex.[20] A previous longitudinal study of the Japanese older population also showed a gradual decrease in the hazard ratio of this question for all-cause mortality, though the hazard ratio remained significant in the fully adjusted model.[21] Given that the previous study included a population aged ≥65 years, the prognostic significance of this question might be interpreted differently for different age groups. Another possibility was reduced reliability of responses to the questions due to cognitive decline. Because dementia was the most frequent cause of functional disability in participants aged ≥75 years,[22] it is possible that participants likely to progress to functional disability did not answer the question accurately. However, the results did not change in the analysis of participants further adjusted for severe comorbidities, including dementia. Furthermore, it was unlikely that the effects of cognitive decline would affect only Q05. The effects of cognitive decline, if any, might not be substantial to change the present findings.

The final Cox proportional hazards model included nine QMCOO items and a limited number of clinical parameters, which were consistently associated with functional disability in any conditional analysis. The final model was extremely simple and only comprised factors that could be obtained from annual health checkup data, thereby increasing the usefulness of this model in the risk assessment of older individuals in municipal health practice activities. Individuals certified as support level or care level 1 at baseline were not excluded from the analysis to ensure the availability of this risk assessment model to different individuals who participated in the annual health checkups. If individuals who are at the support level or care level 1 were excluded from the analysis, the use of this risk assessment model is limited to individuals who are physically independent. Due to the same reason, individuals who have histories of hospitalization within 12 months before the health checkup day for any reasons were not excluded from the analysis. However, hospitalization history was not consequently identified as a significant determinant. Several participants had comorbidities assessed using the Charlson Comorbidity Index. Although Tanaka *et al.*[8] reported that the hazard ratio for functional disability was higher for the combination of QMCOO and Charlson Comorbidity Index than for either alone, the baseline comorbidities were also not considered in the analysis, because information on comorbidities cannot be easily assessed during health checkups. However, further adjustment of the Charlson Comorbidity Index in the Cox proportional hazards model did not significantly change the results. Hence, disregarding comorbidities in the risk assessment did not lead to major bias.

To facilitate the use of this risk assessment model in preventing functional disability, the SKDB functional disability score was developed based on the results of the Cox proportional hazards model. Although this risk score had some errors in the calculation of the probability due to the use of an integer value than the actual regression coefficient, we believe that this score, combined with the frequency chart of high-risk populations, might help determine which individuals require intervention.

In addition to the abovementioned strengths and limitations, the present study had several limitations that should be noted. First, this study used KDB in Shizuoka Prefecture residents. The rate of care certification differs between prefectures.[23] Hence, studies using nationwide data could improve predictive performance. Second, the follow-up period was short, because the QMCOO was used after 2020. The risk assessment score developed in this study might be useful to identify individuals who will need long-term care within a few years. Third, the causes of functional disability could not be identified. The results of individual analyses based on primary diseases for functional disability, which include dementia, cerebrovascular diseases, frailty and musculoskeletal diseases, might further facilitate the classification of individuals at-risk. Fourth, although lower education attainment has been reported to be independently associated with the incidence of functional disability,[24] we did not consider socioeconomic status, because the current Japanese health checkup system for older adults is not designed to assess socioeconomic status.

In conclusion, nine items in the QMCOO were independent determinants of the incidence of functional disability. The present findings, along with the SKDB functional disability score, could help identify older individuals who require preventive interventions against functional disability.

Acknowledgements

We thank the Shizuoka Prefectural Government, 35 city and town offices in the Shizuoka prefecture, and the Shizuoka Federation of National Health Insurance Organizations for their help in constructing the SKDB dataset. We also thank the editors of Crimson Interactive for their help in the preparation of this manuscript. This study did not receive financial support.

Disclosure statement

The authors declare no conflict of interest.

Data availability statement

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

References

1 Ikeda N, Saito E, Kondo N *et al*. What has made the population of Japan healthy? *Lancet* 2011; **378**: 1094–1105. https://doi.org/10.1016/S0140-6736(11)61055-6.
2 Ishibashi H. Locomotive syndrome in Japan. *Osteoporos Sarcopenia* 2018; **4**: 86–94. https://doi.org/10.1016/j.afos.2018.09.004.
3 Okamoto S, Sakamoto H, Kamimura K, Komamura K, Kobayashi E, Liang J. Economic effects of healthy ageing: functional limitation,

forgone wages, and medical and long-term care costs. *Health Econ Rev* 2023; **13**: 28. https://doi.org/10.1186/s13561-023-00442-x.
4 Satake S, Arai H. Questionnaire for medical checkup of old-old (QMCOO). *Geriatr Gerontol Int* 2020; **20**: 991–992. https://doi.org/10.1111/ggi.14004.
5 Yakabe M, Shibasaki K, Hosoi T *et al*. Validation of the questionnaire for medical checkup of old-old (QMCOO) score cutoff to diagnose frailty. *BMC Geriatr* 2023; **23**: 157. https://doi.org/10.1186/s12877-023-03885-3.
6 Deguchi N, Osuka Y, Kojima N *et al*. Questionnaire for medical checkup of old-old is non-inferior to the Kihon checklist in screening frailty among independent older adults aged 75 years and older: the Itabashi longitudinal study on aging. *Geriatr Gerontol Int* 2024; **24**: 176–181. https://doi.org/10.1111/ggi.14759.
7 Li J, Yasuoka M, Kinoshita K *et al*. Validity of the questionnaire for medical checkup of old-old (QMCOO) in screening for physical frailty in Japanese older outpatients. *Geriatr Gerontol Int* 2022; **22**: 902–903. https://doi.org/10.1111/ggi.14472.
8 Tanaka T, Yoshizawa Y, Sugaya K *et al*. Predictive validity of the questionnaire for medical checkup of old-old for functional disability: using the National Health Insurance Database System. *Geriatr Gerontol Int* 2023; **23**: 124–130. https://doi.org/10.1111/ggi.14533.
9 Nakatani E, Tabara Y, Sato Y, Tsuchiya A, Miyachi Y. Data resource profile of Shizuoka Kokuho database (SKDB) using integrated health- and care-insurance claims and health checkups: the Shizuoka study. *J Epidemiol* 2022; **32**: 391–400. https://doi.org/10.2188/jea.JE20200480.
10 Tabara Y, Nakatani E, Miyachi Y. Body mass index, functional disability and all-cause mortality in 330 000 older adults: the Shizuoka study. *Geriatr Gerontol Int* 2021; **21**: 1040–1046. https://doi.org/10.1111/ggi.14286.
11 Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis* 1987; **40**: 373–383. https://doi.org/10.1016/0021-9681(87)90171-8.
12 NIPPON DATA80 Research Group. Risk assessment chart for death from cardiovascular disease based on a 19-year follow-up study of a Japanese representative population. *Circ J* 2006; **70**: 1249–1255. https://doi.org/10.1253/circj.70.1249.
13 Nishimura K, Okamura T, Watanabe M *et al*. Predicting coronary heart disease using risk factor categories for a Japanese urban population, and comparison with the framingham risk score: the suita study. *J Atheroscler Thromb* 2014; **21**: 784–798. https://doi.org/10.5551/jat.19356.
14 Ministry of Health, Labour and Welfare in Japan. Survey of insured persons in the Latter-stage Elderly Medical Care System, https://www.mhlw.go.jp/stf/seisakunitsuite/bunya/iryouhoken/database/seido/kouki_jittai.html. Accessed 9 June, 2024.
15 Ministry of Health, Labour and Welfare in Japan. Health services for the elderly, https://www.mhlw.go.jp/stf/seisakunitsuite/bunya/kenkou_iryou/iryouhoken/hokenjigyou/index_00003.html. Accessed 9 June, 2024.
16 Borg C, Hallberg IR, Blomqvist K. Life satisfaction among older people (65+) with reduced self-care capacity: the relationship to social, health and financial aspects. *J Clin Nurs* 2006; **15**: 607–618. https://doi.org/10.1111/j.1365-2702.2006.01375.x.
17 Yakabe M, Shibasaki K, Hosoi T *et al*. Effectiveness of the questionnaire for medical checkup of old-old (QMCOO) to diagnose frailty in community-dwelling older adults. *Geriatr Gerontol Int* 2022; **22**: 127–131. https://doi.org/10.1111/ggi.14328.
18 Ishizaki T, Masui Y, Nakagawa T *et al*. Construct validity of a new health assessment questionnaire for the National Screening Program of older adults in Japan: the SONIC study. *Int J Environ Res Public Health* 2022; **19**: 10330. https://doi.org/10.3390/ijerph191610330.
19 Irwin RS, Boulet LP, Cloutier MM *et al*. Managing cough as a defense mechanism and as a symptom. A consensus panel report of the American College of Chest Physicians. *Chest* 1998; **114**: 133S–181S. https://doi.org/10.1378/chest.114.2_supplement.133s.
20 Nishida T, Yamabe K, Ide Y, Honda S. Utility of the eating assessment Tool-10 (EAT-10) in evaluating self-reported dysphagia associated with Oral frailty in Japanese community-dwelling older people. *J Nutr Health Aging* 2020; **24**: 3–8. https://doi.org/10.1007/s12603-019-1256-0.
21 Yamamoto T, Aida J, Shinozaki T *et al*. Cohort study on laryngeal gough reflex, respiratory disease, and death: a mediation analysis. *J Am Med Dir Assoc* 2019; **20**: 971–976. https://doi.org/10.1016/j.jamda.2019.01.155.
22 Yoshida D, Ninomiya T, Doi Y *et al*. Prevalence and causes of functional disability in an elderly general population of Japanese: the Hisayama study. *J Epidemiol* 2012; **22**: 222–229. https://doi.org/10.2188/jea.je20110083.
23 Ministry of Health, Labour and Welfare in Japan. Report on the status of long-term care insurance, https://www.mhlw.go.jp/topics/kaigo/toukei/joukyou.html#link01. Accessed 9 June, 2024.
24 Nurrika D, Zhang S, Tomata Y, Sugawara Y, Tanji F, Tsuji I. Education level and incident functional disability in elderly Japanese: the Ohsaki cohort 2006 study. *PLoS One* 2019; **14**: e0213386. https://doi.org/10.1371/journal.pone.0213386.

Supporting Information

Additional supporting information may be found in the online version of this article at the publisher's website:

Data S1. Supporting Information.

How to cite this article: Tabara Y, Shoji-Asahina A, Akasaka H, Sugimoto K, Sato Y. Prognostic significance of the Questionnaire for Medical Checkup of Old-Old for the incidence of functional disability: The Shizuoka Kokuho Database study. Geriatr. Gerontol. Int. 2025;25:260–266. https://doi.org/10.1111/ggi.15078

diseases

MDPI

Article

Is Oral Function Associated with the Development of Sarcopenic Obesity and Sarcopenia in Older Adults? A Prospective Cohort Study

Sho Shirotori [1,†], Yoko Hasegawa [1,2,*,†], Koutatsu Nagai [3], Hiroshi Kusunoki [4,5], Shogo Yoshimura [1], Kana Tokumoto [2], Hirokazu Hattori [2], Kayoko Tamaki [5], Kazuhiro Hori [1], Hiromitsu Kishimoto [2] and Ken Shinmura [5]

[1] Department of Comprehensive Prosthodontics, Graduate School of Medical and Dental Sciences, Niigata University, 2-5274 Gakkocho-dori, Chuo-ku, Niigata City 951-8514, Japan
[2] Department of Oral and Maxillofacial Surgery, Hyogo Medical University, Nishinomiya City 663-8501, Japan
[3] Department of Physical Therapy, School of Rehabilitation, Hyogo Medical University, Kobe City 650-8530, Japan; nagai-k@hyo-med.ac.jp
[4] Department of Internal Medicine, Osaka Dental University, Osaka City 540-0008, Japan
[5] Department of General Internal Medicine, Hyogo Medical University, Nishinomiya City 663-8501, Japan; kayoko_tamaki@hotmail.com (K.T.); ke-shimmura@hyo-med.ac.jp (K.S.)
* Correspondence: cem17150@dent.niigata-u.ac.jp; Tel.: +81-025-227-2891; Fax: +81-025-229-3454
† These authors contributed equally to this work.

Abstract: Background: Sarcopenic obesity, defined as the concurrent loss of muscle mass and adipose tissue accumulation, is associated with reduced physical function and poor health status in older adults. Although oral function can impact the overall health of older adults, its role in the development of sarcopenic obesity remains unclear. Herein, we aimed to examine the association between oral function and the incidence of sarcopenic obesity. Methods: This longitudinal cohort study included 597 independent older adults (aged ≥65 years) from Tamba-Sasayama, a rural region of Japan, who participated in academic studies between June 2016 and December 2023. Participants underwent surveys at least twice, with a minimum two-year interval. The participants were divided into four groups (robust, obese, sarcopenic, and sarcopenic obese) according to their health condition. Sarcopenic obesity was diagnosed based on the guidelines of the Japanese Working Group on Sarcopenic Obesity. The oral function was evaluated by assessing the number of remaining teeth, tongue pressure, occlusal force, masticatory performance, and oral diadochokinesis. Cox proportional hazards regression analysis evaluated the association between oral function and the incidence of sarcopenic obesity after adjusting for relevant confounders. Results: The sarcopenic obesity group was older, had lower skeletal muscle mass, and inferior physical function. This cohort also had the highest prevalence of hypertension and significantly fewer remaining teeth. The proportion of individuals with sarcopenic obesity was 1.7% of the total population, with 2.8% in the obesity group at baseline, and 8.0% of those were diagnosed with sarcopenia progressing to sarcopenic obesity. The Cox regression model revealed that reduced tongue pressure was significantly associated with an increased risk of sarcopenic obesity, with a hazard ratio of 0.906 (95% confidence interval: 0.829–0.990; $p = 0.028$), independent of other variables related to sarcopenia and obesity. Conclusions: Our findings suggest that oral function is associated with the incidence of sarcopenic obesity but not with that of sarcopenia or obesity alone.

Keywords: sarcopenic obesity; obesity; tongue pressure; oral function; hypertension

Academic Editor: Julio Plaza-Díaz

Received: 27 February 2025
Revised: 26 March 2025
Accepted: 3 April 2025
Published: 5 April 2025

Citation: Shirotori, S.; Hasegawa, Y.; Nagai, K.; Kusunoki, H.; Yoshimura, S.; Tokumoto, K.; Hattori, H.; Tamaki, K.; Hori, K.; Kishimoto, H.; et al. Is Oral Function Associated with the Development of Sarcopenic Obesity and Sarcopenia in Older Adults? A Prospective Cohort Study. *Diseases* **2025**, *13*, 109. https://doi.org/10.3390/diseases13040109

1. Introduction

Sarcopenia and obesity are two major health concerns impacting the older population and have substantial implications for their overall health and quality of life. Sarcopenia is characterized by the age-related loss of muscle mass, strength, and physical performance [1,2]. In older adults, obesity is associated with an elevated risk of falls, reduced functionality, diminished quality of life, and increased mortality. It also increases the risk of cardiovascular diseases, metabolic disorders, cognitive impairment, and arthritis [3,4].

The interplay between obesity and skeletal muscles in the aging population is complex, with evidence suggesting both protective and deleterious effects. Although obesity is associated with impaired physical function and resistance to anabolic stimuli, it may also lead to greater muscle mass in weight-bearing muscles than in older, lean individuals [5,6].

The coexistence of sarcopenia and obesity leads to sarcopenic obesity, a condition that has garnered increasing attention owing to its profound effects on health outcomes [6–8]. Sarcopenic obesity is characterized by muscle weakness due to sarcopenia combined with the metabolic complications of obesity. These conditions exhibit a synergistic relationship, each exacerbating the progression [8]. Sarcopenic obesity is associated with a higher risk of cardiovascular disease, diabetes, and impaired physical function than either condition alone. Sarcopenic obesity involves a vicious cycle of cross-talk between adipose and muscle tissue, and increased white adipose tissue and local muscle fat infiltration leading to inflammatory adipokine secretion, inhibiting protein synthesis and inducing catabolism. Cytokine secretion by fat mass affects muscle tissue and other organs, such as the liver and white adipose tissue, inhibiting insulin signaling and increasing the risk of insulin resistance [9,10]. Additionally, peri-muscular fat plays a critical role in different phenotypes of sarcopenic obesity, influencing inflammatory pathways and metabolic dysfunction. Furthermore, hormone-related responses vary across phenotypes, which may contribute to the secretion of inflammatory adipokines and the modulation of cytokine effects [11]. The interaction between reduced muscle quality and enhanced adiposity increases health risks, particularly in older populations [12–16].

The impact of sarcopenia and obesity on oral health is mediated via distinct pathways. A notable association exists between sarcopenia and oral function, primarily attributed to the interaction between muscle mass and masticatory abilities [17,18]. Sarcopenia typically results in reduced masticatory muscle strength, leading to compromised food intake and nutritional deficiencies. Moreover, older individuals with sarcopenia exhibit an increased susceptibility to oral health complications, including periodontal disease and dental caries, owing to difficulties in maintaining adequate oral hygiene [19].

Obesity is strongly associated with chronic systemic inflammation, exacerbating the progression of periodontal disease [20,21]. In addition, individuals with obesity have a higher propensity for recurrent and severe periodontal diseases. This phenomenon is partially attributed to decreased salivary production [22], which compromises the natural cleansing mechanisms of the oral cavity and increases the risk of dental caries [23,24].

Although the individual effects of sarcopenia and obesity on oral health have been previously studied, the combined impact of sarcopenic obesity on oral health remains elusive. Given the established associations among sarcopenia, obesity, and oral health, examining the long-term implications of sarcopenic obesity on oral health outcomes is critical. However, longitudinal studies of sarcopenic obesity, its progression over time, and its relationship with oral health are limited. Considering that both sarcopenia and obesity contribute to physical limitations and adverse health outcomes that can affect oral well-being, it is reasonable to expect that the progression of sarcopenic obesity, which combines these two conditions, is linked to oral health deterioration.

In the cohort study, we aimed to investigate the longitudinal association between sarcopenic obesity and oral health. We hypothesized that oral function is independently associated with physical condition and function, contributing to the development of sarcopenic obesity.

2. Material and Methods

This study encompassed independent older adults (aged ≥65 years) from Sasayama, rural Tamba-Sasayama City, Hyogo Prefecture, Japan, who participated in academic studies between June 2016 and December 2023. This cohort was designated the Frail Elderly in the Tamba-Sasayama Area (FESTA) study. The study was conducted in accordance with the ethical standards established by the Ethics Committees of both Hyogo Medical University (approval number: Rinhi-0342) and Niigata University (Approval number: G2021-0027).

The recruitment process was executed by placing newspaper advertisements and posters at the Sasayama Medical Center and Hyogo Medical University, resulting in the voluntary participation of study subjects. To be eligible for participation, individuals were required to meet the following criteria: they had to be independent older adults aged ≥65 years, residing in the Tamba-Sasayama region of Hyogo Prefecture, capable of traveling to the Sasayama Medical Center via public transportation or private vehicle, and without cognitive impairment (MMSE score >22). From among 1016 participants, 597 surveyed at least twice at a minimum interval of two years were included in the analysis. Individuals who could not ambulate independently (except those using a cane) were excluded. Participants were provided with comprehensive information regarding the objectives and methodology of the study, and written informed consent was obtained before their participation.

2.1. Evaluation Items

Participants were required to provide information regarding their medical and smoking histories via a questionnaire. Blood pressure was measured using a fully automatic calibrated oscillator (BP-203 RVII, Colin Co., Kyoto City, Japan).

Body composition was assessed via bioelectrical impedance analysis (BIA) using an InBody 770 device (InBody Japan, Inc., Koto Ward, Tokyo, 136-0071, Japan). Body mass index (BMI), limb skeletal muscle mass (LBM), and percent body were determined using BIA (InBody Co., Seoul, Republic of Korea).

2.2. Diagnosis of Sarcopenic Obesity

The participants were categorized into four groups based on their health status: robust, obese, sarcopenic, and sarcopenic obese. The classification method follows the flowchart depicted in Figure 1.

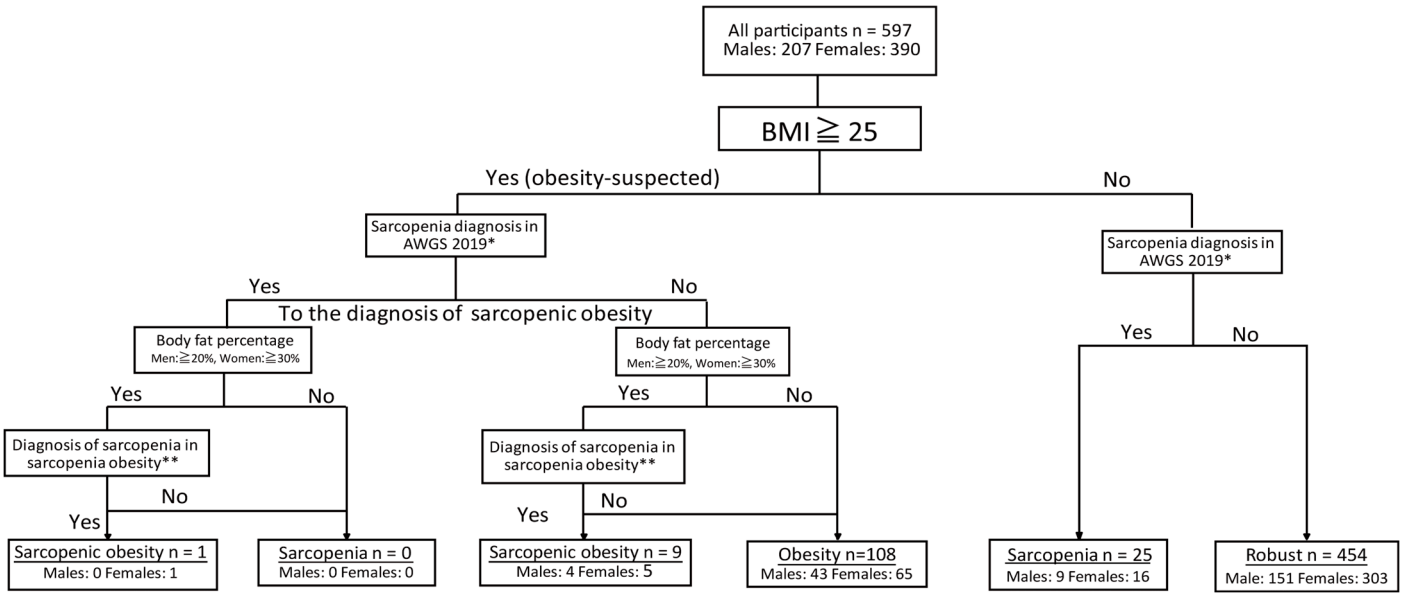


Figure 1. Classification of participants with sarcopenic obesity. *: Low skeletal muscle mass (kg/m^2) + low muscle strength or/and low physical function (diagnosis of sarcopenia [25]). **: Low skeletal muscle mass (kg/BMI) + low muscle strength or low physical function (diagnosis of sarcopenia obesity [26].

First, obesity screening was conducted according to the criteria established by the Japan Society for the Study of Obesity [26]. Individuals with a BMI of ≥25 kg/m^2 were classified as "obesity-suspected". Sarcopenic obesity was diagnosed based on the criteria established by the Japanese Society of Gerontology [26], in which obesity was determined by body fat percentage with thresholds set at >20% for males and >30% for females.

Sarcopenia was defined using the same diagnostic criteria as for sarcopenia alone, incorporating skeletal muscle mass, grip strength, and five-times-sit-to-stand-test (FTSST) performance. However, in the case of sarcopenic obesity, muscle mass was adjusted for BMI, and values of <0.789 for males and <0.512 for females were deemed to indicate low muscle mass [26]. Sarcopenic obesity was diagnosed when an individual met the criteria for both obesity and sarcopenia, as described above.

Sarcopenia was diagnosed based on the criteria set by the Asian Working Group for Sarcopenia (AWGS) [25], incorporating assessments of muscle strength (grip strength), physical function (FTSST performance), and muscle mass (height-adjusted appendicular skeletal muscle mass in kg/m^2). Sarcopenia was identified in individuals who exhibited both reduced muscle strength and physical function, as well as low muscle mass. Muscle weakness was defined as grip strength of <28 kg in males and <18 kg in females, while a decline in physical function was indicated by an FTSST completion time exceeding 12 s [25]. Muscle mass was assessed using the skeletal muscle mass index (SMI), with values below 7.0 kg/m^2 in males and 5.7 kg/m^2 in females classified as having low muscle mass [25].

Based on these criteria, individuals with low muscle mass, reduced muscle strength, and physical function were diagnosed with severe sarcopenia. Those with low muscle mass and either reduced muscle strength or reduced physical function were diagnosed with "sarcopenia". Both groups were jointly categorized as the sarcopenia group. Participants who did not meet the criteria for either obesity-suspected or sarcopenia were classified as the robust group.

In addition, sarcopenic obesity was further categorized into two distinct stages based on the disease severity. Stage I sarcopenic obesity was characterized by low muscle strength, reduced physical function, low muscle mass, and obesity. Stage II sarcopenic obesity was

defined by a further decline in muscle strength and physical function, low muscle mass, obesity, and the presence of comorbidities. Comorbidities were defined as the presence of at least one chronic disease in individuals aged ≥70 years, including metabolic disorders, liver disease, kidney disease, heart disease, respiratory disease, gastric ulcer, osteoporosis, rheumatoid arthritis, thyroid disease, collagen diseases, or stroke, which are all associated with an increased likelihood of sarcopenic obesity [7,26].

2.3. Evaluation of Oral Function

The oral function was objectively evaluated by assessing the number of remaining teeth, tongue pressure, occlusal force, masticatory performance, and oral diadochokinesis (ODK). A comprehensive oral health assessment was performed by dental professionals who had received more than two hours of training and calibration prior to the survey. The examination was conducted under optimal lighting conditions, with the subject seated in a reclining chair. Participants who routinely wore dentures were assessed while wearing the dentures.

The number of remaining teeth was defined by third molars and roots, and implants, bridges, and dentures were excluded. Tongue pressure was measured twice using a JMS Tongue Pressure Measuring Device (JMS Co., Ltd., Hiroshima, Japan), and the highest value was recorded [27]. The occlusal force was quantified using an Occlusal Force Meter (GM10, Nagano Keiki, Tokyo, Japan) [28,29]. The maximum occlusal forces on the left and right sides were measured, and their sum was used in subsequent analysis [30,31]. Masticatory performance was evaluated using a standardized masticatory performance evaluation method (scoring method) using gummy jelly [31]. The participants chewed gummy jelly (UHA Mikakuto, Osaka, Japan) 30 times, followed by a visual evaluation of the expectorated fragments using a 10-level scale ranging from 0 to 9 [32]. Tongue motor function was evaluated using ODK. The articulatory velocity of /ta/ was measured using ODK measurement equipment (KENKOU-KUN Handy; Takei Scientific Instruments Co., Ltd., Niigata, Japan) [30].

2.4. Data Analysis

Data are presented as mean ± standard error (SE) for continuous variables. Differences between the two groups were assessed using the Student's *t*-test. Comparisons among three or more groups were performed using one-way analysis of variance (ANOVA), followed by post hoc multiple comparisons. The Bonferroni correction was applied to adjust the *p*-values for multiple comparisons.

Categorical variables are presented as absolute numbers (*n*) and relative frequencies (%). Differences between categorical variables were analyzed using the chi-square or Fisher's exact test, as appropriate, based on the expected cell counts.

We conducted Cox regression analysis using the incidence of sarcopenic obesity as the event and the time from baseline to follow-up as the time variable to determine whether oral function was an independent factor contributing to the development of sarcopenic obesity. The independent variable was the onset of sarcopenic obesity, and the explanatory variables were those showing a statistically significant difference between the health status groups in the cross-sectional analysis at baseline. The adjusted variables were sex, age, and health status at baseline (divided into four groups). Those with sarcopenic obesity at baseline were excluded from the analysis. We checked for multicollinearity between the explanatory variables and selected the variable with the highest significance level in cases of overlap. The final model was determined using a stepwise method (variable reduction Wald test) and multiple imputations. The criteria for adding and deleting variables were set at $p < 0.05$ and $p < 0.10$, respectively, with a maximum of 20 iterations.

For subgroup analyses, we conducted Cox regression analyses with sarcopenia onset as the event, targeting participants assigned to the robust or obese group at baseline, and examined factors contributing to the onset of sarcopenia. We also conducted a Cox regression analysis with obesity onset as the event, targeting participants in the robust or sarcopenia groups at baseline, and examined factors contributing to the onset of obesity. The subgroup analyses excluded participants with sarcopenic obesity at baseline or follow-up. Cox regression analysis of the subgroups was based on analysis of the onset of sarcopenic obesity.

Statistical significance was defined as a *p*-value of 0.05. All the statistical analyses were performed using SPSS, version 25.0.0 (IBM Corp., Armonk, NY, USA).

3. Results

Table 1 presents the participants' characteristics.

Table 1. Baseline and follow-up characteristics of participants.

A Summary of Participant in Baseline											
		Overall (*n* = 597)			**Males (*n* = 207)**			**Females (*n* = 390)**			***p*-Value**
Age (yr) *		72.8	±	0.2	73.7	±	0.4	72.3	±	0.3	0.003
Duration (day)		947.8	±	15.2	936.3	±	26.5	954.0	±	18.5	0.579
Smoking history *		177 (29.6%)			152 (73.4%)			25 (6.4%)			<0.001
Obesity											
BMI (kg/m^2) *		22.6	±	0.1	23.2	±	0.2	22.2	±	0.1	<0.001
Body fat (%) *		27.3	±	0.3	23.1	±	0.4	29.6	±	0.3	<0.001
	High body weight	118 (19.8%)			47 (22.7%)			71 (18.2%)			0.189
	High body fat *	339 (56.8%)			149 (72.0%)			190 (48.7%)			<0.001
Sarcopenia											
Skeletal muscle mass index (kg/BMI) *		0.708	±	0.006	0.868	±	0.008	0.623	±	0.005	<0.001
Low skeletal muscle mass *		92 (15.4%)			51 (24.6%)			41 (10.5%)			<0.001
Skeletal muscle mass index (kg/m^2) *		6.45	±	0.04	7.40	±	0.05	5.98	±	0.03	<0.001
Low skeletal muscle mass		185 (31.0%)			60 (29.0%)			125 (32.1%)			0.441
Grip strength (kg) *		28.2	±	0.5	35.4	±	0.4	24.4	±	0.7	<0.001
Low muscle strength		46 (7.7%)			18 (8.7%)			28 (7.2%)			0.509
Five times sit-to-stand test (s) *		7.2	±	0.1	7.6	±	0.1	7.0	±	0.1	0.002
Low physical function		20 (3.4%)			9 (4.3%)			11 (2.8%)			0.324
Comorbidities											
Metabolic diseases											
	Diabetes mellitus *	61 (10.2%)			34 (16.4%)			27 (6.9%)			<0.001
	Hypertension *	253 (42.2%)			100 (48.3%)			152 (39.0%)			0.028
	Hyperlipemia	140 (23.5%)			40 (19.3%)			100 (25.6%)			0.083
	Cardiovascular *	40 (6.7%)			21 (10.1%)			19 (4.9%)			0.014
Asthma		14 (2.3%)			4 (1.9%)			10 (2.6%)			0.627
Tuberculosis		5 (0.8%)			2 (1.0%)			3 (0.8%)			
Pneumonia		10 (1.7%)			5 (2.4%)			5 (1.3%)			0.304
Blood pressure											
SBP (mmHg) *		139.0	±	0.7	136.7	±	1.2	140.2	±	0.8	0.013
DBP (mmHg) *		80.3	±	0.4	79.1	±	0.7	81.0	±	0.5	0.039
Diagnosis of sarcopenia obesity											
Robust		454 (76.0%)			151 (72.9%)			303 (77.7%)			0.835
Obesity		108 (18.1%)			43 (20.8%)			65 (16.7%)			
Sarcopenia											
Sarcopenia		23 (3.9%)			8 (3.9%)			15 (3.8%)			
Severe sarcopenia		2 (0.3%)			1 (0.5%)			1 (0.5%)			
Sarcopenic obesity											
Stage I		2 (0.3%)			1 (0.5%)			1 (0.3%)			
Stage II		8 (1.3%)			3 (1.4%)			5 (1.3%)			
Oral function											
	Remaining teeth	20.9	±	0.3	20.7	±	0.6	21.0	±	0.4	0.713
	Occlusal force (kg) *	59.5	±	1.4	66.4	±	2.8	55.9	±	1.6	<0.001
	Tongue pressure (kg)	33.5	±	0.3	34.0	±	0.6	33.2	±	0.4	0.295
	Oral diadochokinesis *	30.5	±	0.2	29.2	±	0.5	31.1	±	0.3	<0.001
Kihon checklist											
Masticatory function		105 (17.6%)			29 (14.0%)			76 (19.5%)			0.094
Swallowing function		146 (24.5%)			51 (24.6%)			95 (24.4%)			0.940
Dry mouth		178 (29.8%)			56 (27.1%)			122 (31.3%)			0.282

Table 1. *Cont.*

A summary of participant in follow-up											
		Overall (*n* = 597)			**Males (*n* = 207)**			**Females (*n* = 390)**			***p*-Value**
Age *		75.3	±	0.2	76.2	±	0.4	74.9	±	0.3	0.006
Smoking history *		177 (29.6%)			152 (73.4%)			25 (6.4%)			<0.001
Obesity											
BMI (kg/m^2) *		22.5	±	0.1	23.1	±	0.2	22.2	±	0.1	0.001
Body fat (%) *		27.3	±	0.3	23.2	±	0.4	29.6	±	0.4	<0.001
	High body weight	118 (19.8%)			43 (20.8%)			75 (19.2%)			0.652
	High body fat *	330 (55.3%)			143 (69.1%)			187 (47.9%)			<0.001
Sarcopenia											
Skeletal muscle mass index (kg/BMI) *		0.697	±	0.006	0.857	±	0.008	0.612	±	0.005	<0.001
	Low skeletal muscle mass *	110 (18.4%)			54 (26.1%)			56 (14.4%)			<0.001
Skeletal muscle mass index (kg/m^2) *		6.38	±	0.04	7.30	±	0.05	5.90	±	0.03	<0.001
	Low skeletal muscle mass *	113 (18.9%)			68 (32.9%)			45 (11.5%)			<0.001
Grip strength (kg) *		26.8	±	0.3	34.0	±	0.4	22.9	±	0.2	<0.001
	Low Muscle strength *	62 (10.4%)			29 (14.0%)			33 (8.5%)			0.034
Five times sit-to-stand test (s) *		7.3	±	0.1	7.6	±	0.2	7.2	±	0.1	0.038
	Low Physical function	19 (3.2%)			10 (4.8%)			9 (2.3%)			0.095
Comorbidities											
Metabolic diseases											
	Diabetes mellitus *	71 (11.9%)			35 (16.9%)			36 (9.2%)			0.006
	Hypertension *	261 (43.7%)			102 (49.3%)			159 (40.8%)			0.046
	Hyperlipemia	154 (25.8%)			46 (22.2%)			108 (27.7%)			0.146
	Cardiovascular *	52 (8.7%)			25 (12.1%)			27 (6.9%)			0.034
Asthma		14 (2.3%)			4 (1.9%)			10 (2.3%)			0.627
Tuberculosis		7 (1.2%)			2 (1.0%)			5 (1.3%)			0.733
Pneumonia		15 (2.5%)			8 (3.9%)			7 (1.8%)			0.124
Blood pressure											
SBP (mmHg) *		139.6	±	0.7	137.5	±	1.1	140.7	±	0.9	0.034
DBP (mmHg)		79.6	±	0.5	78.4	±	0.7	80.2	±	0.6	0.064
Diagnosis of sarcopenia obesity *											
Robust		440 (73.7%)			146 (70.5%)			294 (75.4%)			0.046
Obesity		108 (18.1%)			37 (17.9%)			71 (18.2%)			
Sarcopenia											
Sarcopenia		36 (6.0%)			15 (7.2%)			21 (5.4%)			
Severe sarcopenia		3 (0.5%)			3 (1.4%)			0 (0.0%)			
Sarcopenia obesity											
Stage I		0 (0.0%)			0 (0.0%)			0 (0.0%)			
Stage II		10 (1.7%)			6 (2.9%)			4 (1.0%)			
Oral function											
	Remaining teeth	20.1	±	0.3	19.9	±	0.6	20.2	±	0.4	0.619
	Occlusal force (kg)	48.9	±	1.4	51.6	±	2.6	47.4	±	1.7	0.153
	Tongue pressure (kg) *	33.0	±	0.4	34.1	±	0.6	32.3	±	0.4	0.015
	Oral diadochokinesis *	30.4	±	0.2	29.4	±	0.4	30.9	±	0.2	0.001
Kihon checklist											
Masticatory function		115 (20.5%)			44 (22.6%)			71 (19.3%)			0.368
Swallowing function		148 (26.3%)			53 (27.2%)			95 (25.9%)			0.740
Dry mouth		176 (31.4%)			52 (26.8%)			124 (33.9%)			0.086

* Data are presented as mean ± SE. $p < 0.05$, calculated using Student's *t*-test, chi-squared test, or Fisher's exact test for sex differences. Definitions: duration, number of days from baseline to follow-up. The diagnostic criteria and classification methods for sarcopenic obesity, including BMI, skeletal muscle mass index, muscle strength, and physical function, have been detailed in the 'Diagnosis of Sarcopenic Obesity' section. Participants were grouped into robust, obese sarcopenia (sarcopenia and severe sarcopenia), and sarcopenia obesity (sarcopenic obesity stages I and II) groups. Abbreviations: SBP, mean systolic blood pressure; DBP, mean diastolic blood pressure. Oral diadochokinesis: Represented tongue motor function by the "ta" sound.

This study included 597 participants (207 males and 390 females). The mean age was 72.8 ± 0.2 years, with males being slightly older (73.7 ± 0.4 years) than females (72.3 ± 0.3 years) ($p = 0.003$). Regarding obesity indicators, males had a higher mean BMI (23.2 ± 0.2 kg/m^2) than females (22.2 ± 0.1 kg/m^2) ($p < 0.001$). However, females had a higher body fat percentage (29.6 ± 0.3%) than males (23.1 ± 0.4%) ($p < 0.001$). Interestingly, a higher proportion of males (72.0%) had high body fat levels than females (48.7%) ($p < 0.001$).

Regarding sarcopenia markers, males had a higher SMI (0.868 ± 0.008 kg/BMI) than females (0.623 ± 0.005 kg/BMI) ($p < 0.001$). Males also had higher grip strength (35.4 ± 0.4 kg) than females (24.4 ± 0.7 kg) ($p < 0.001$).

At baseline, the distribution of sarcopenia and obesity categories was similar between both sexes, with 76.0% classified as robust, 18.1% as obese, 4.2% as sarcopenic, and 1.6% as sarcopenic obesity.

At follow-up, the mean age increased to 75.3 ± 0.2 years. The prevalence of sarcopenia and sarcopenic obesity showed sex-based differences ($p = 0.046$). Among male participants, 8.6% were classified as sarcopenic (including severe sarcopenia) and 2.9% as sarcopenic obese, compared with 5.4% and 1.0% among female participants, respectively. However, the differences between male and female participants were non-significant.

Table 2 shows the relationships between health conditions (robustness, obesity, sarcopenia, and sarcopenic obesity) and related factors.

Significant age differences were detected between the groups ($p < 0.001$). Participants in the sarcopenia and sarcopenic obesity groups were older than those in the robust and obese groups. The mean age increased across all groups at follow-up, with the largest increase noted in the sarcopenia group (from 76.3 to 79.6 years). There were no significant sex differences between the groups at baseline or follow-up. Body composition metrics showed consistent patterns at baseline and follow-up. BMI and body fat percentage were significantly higher in the obese and sarcopenic obesity groups than in the robust and sarcopenia groups ($p < 0.001$). The SMI (kg/BMI) was the lowest in the sarcopenic obesity group at both the baseline and follow-up. Physical function measurements revealed notable differences. Grip strength was significantly lower in the sarcopenia group at baseline ($p = 0.012$) and follow-up ($p = 0.001$). The FTSST time was significantly longer in the sarcopenia and sarcopenic obesity groups at both baseline and follow-up ($p < 0.001$), with the gap widening at follow-up. The prevalence of hypertension was highest in the sarcopenic obesity group at baseline (70.0%) and follow-up (80.0%).

Table 2. The relationship between sarcopenic obesity and associated factors.

(a): Baseline		Robust (*n* = 454)	Obesity (*n* = 108)	Sarcopenia (*n* = 25)	Sarcopenic obesity (*n* = 10)	*p*-Value	
Age *		72.5 ± 0.3	72.6 ± 0.5	76.3 ± 1.5	78.3 ± 1.2	<0.001	B, C, D, E
Sex							
Male		151 (72.9%)	43 (20.8%)	9 (4.3%)	4 (1.9%)	0.614	
Female		303 (77.7%)	65 (16.7%)	16 (4.1%)	6 (1.5%)		
Smoking history		130 (28.6%)	37 (34.3%)	7 (28.0%)	3 (30.0%)	0.715	
Obesity							
BMI (kg/m^2) *		21.6 ± 0.1	26.5 ± 0.1	20.7 ± 0.4	28.8 ± 0.8	<0.001	A, C, D, E, F
Body fat (%) *		25.5 ± 0.3	33.8 ± 0.5	27.2 ± 1.3	39.2 ± 1.2	<0.001	A, C, D, F
Sarcopenia							
	Skeletal muscle mass index (kg/BMI) *	0.726 ± 0.007	0.663 ± 0.014	0.623 ± 0.028	0.546 ± 0.040	<0.001	A, B, C
	Skeletal muscle mass index (kg/m^2) *	6.33 ± 0.04	7.09 ± 0.08	5.56 ± 0.15	6.97 ± 0.32	<0.001	A, B, D, F
Grip strength (kg) *		28.5 ± 0.7	29.5 ± 0.9	20.8 ± 1.1	22.4 ± 2.9	0.012	B, D
	Five times sit-to-stand test (s) *	7.0 ± 0.1	7.4 ± 0.2	9.3 ± 0.7	9.4 ± 1.1	<0.001	B, C, D, E
Comorbidities							
Metabolic diseases							
Diabetes mellitus		45 (9.9%)	10 (9.3%)	3 (12.0%)	3 (30.0%)	0.212	
Hypertension *		179 (39.4%)	58 (53.7%)	8 (32.0%)	7 (70.0%)	0.009	
Hyperlipemia		112 (24.7%)	23 (21.3%)	5 (20.0%)	0 (0.0%)	0.274	
Cardiovascular diseases		29 (6.4%)	9 (8.3%)	2 (8.0%)	0 (0.0%)	0.725	
Respiratory diseases							
Asthma		11 (2.4%)	3 (2.8%)	0 (0.0%)	0 (0.0%)	0.816	
Tuberculosis		4 (0.9%)	0 (0.0%)	1 (4.0%)	0 (0.0%)	0.260	
Pneumonia		8 (1.8%)	1 (0.9%)	1 (4.0%)	0 (0.0%)	0.710	
Blood pressure							
SBP (mmHg) *		137.9 ± 0.8	142.3 ± 1.5	139.3 ± 3.6	151.3 ± 5.2	0.009	
DBP (mmHg) *		79.7 ± 0.5	83.1 ± 0.9	76.6 ± 2.4	87.2 ± 2.7	0.001	A, D, F
Oral function							
	Remaining teeth *	21.3 ± 0.4	20.2 ± 0.8	20.2 ± 1.9	10.8 ± 3.2	0.001	C, E, F
	Occlusal force (kg) *	60.3 ± 1.6	60.2 ± 3.8	54.4 ± 6.7	30.0 ± 6.0	0.042	C, E
	Tongue pressure (kg) *	33.0 ± 0.4	36.8 ± 0.8	29.2 ± 1.3	32.5 ± 3.6	<0.001	A, D
	Oral diadochokinesis *	30.9 ± 0.3	30.3 ± 0.5	28.2 ± 1.1	24.6 ± 2.0	0.001	C, E
Kihon checklist							
Masticatory function		78 (17.2%)	20 (18.5%)	6 (24.0%)	1 (10.0%)	0.748	
Swallowing function *		109 (24.0%)	21 (19.4%)	11 (44.0%)	5 (50.0%)	0.017	
Dry mouth		136 (30.0%)	30 (27.8%)	10 (40.0%)	2 (20.0%)	0.590	

Table 2. *Cont.*

(b): Follow-up	Robust (n = 440)	Obesity (n = 108)	Sarcopenia (n = 39)	Sarcopenic obesity (n = 10)	p-Value	
Age *	74.9 ± 0.3	75.1 ± 0.5	79.6 ± 1.1	80.3 ± 1.5	<0.001	B, C, D, E
Sex						
Male	146 (70.5%)	37 (17.9%)	18 (8.7%)	6 (2.9%)	0.136	
Female	294 (75.4%)	71 (18.2%)	21 (5.4%)	4 (1.0%)		
Smoking history	125 (28.4%)	34 (31.5%)	15 (38.5%)	3 (30.0%)	0.583	
Obesity						
BMI (kg/m^2) *	21.6 ± 0.1	26.7 ± 0.2	20.7 ± 0.4	27.0 ± 0.5	<0.001	A, B, C, D, F
Body fat (%) *	25.5 ± 0.3	35.0 ± 0.5	24.6 ± 1.1	37.0 ± 1.5	<0.001	A, C, D, F
Sarcopenia						
Skeletal muscle mass index (kg/BMI) *	0.718 ± 0.007	0.633 ± 0.013	0.671 ± 0.024	0.585 ± 0.042	<0.001	A, C
Skeletal muscle mass index (kg/m^2) *	6.28 ± 0.04	6.97 ± 0.09	5.82 ± 0.12	6.75 ± 0.34	<0.001	A, B, D, F
Grip strength (kg) *	27.1 ± 0.3	27.9 ± 0.8	20.3 ± 0.8	24.7 ± 2.7	<0.001	B, D
Five times sit-to-stand test (s) *	7.1 ± 0.1	7.2 ± 0.2	8.9 ± 0.6	11.9 ± 1.0	<0.001	B, C, D, E, F
Comorbidities						
Metabolic diseases						
Diabetes mellitus	53 (12.0%)	12 (11.1%)	4 (10.3%)	3 (30.0%)	0.355	
Hypertension *	184 (41.8%)	63 (58.3%)	16 (41.0%)	8 (80.0%)	0.002	
Hyperlipemia	117 (26.6%)	30 (27.8%)	8 (20.5%)	2 (20.0%)	0.797	
Cardiovascular diseases	44 (10.0%)	10 (9.3%)	2 (5.1%)	0 (0.0%)	0.559	
Respiratory diseases						
Asthma	10 (2.3%)	5 (4.6%)	1 (2.6%)	0 (0.0%)	0.546	
Tuberculosis	5 (1.1%)	0 (0.0%)	2 (5.1%)	0 (0.0%)	0.083	
Pneumonia	13 (3.0%)	2 (1.9%)	2 (5.1%)	0 (0.0%)	0.698	
Blood pressure						
SBP (mmHg)	138.3 ± 0.8	142.2 ± 1.4	145.1 ± 3.3	146.0 ± 4.5	0.015	
DBP (mmHg)	79.2 ± 0.5	81.0 ± 0.9	81.4 ± 2.3	75.0 ± 1.7	0.158	
Oral function						
Remaining teeth	20.5 ± 0.4	19.4 ± 0.8	18.8 ± 1.6	17.0 ± 3.1	0.290	
Occlusal force (kg)	49.3 ± 1.6	51.7 ± 3.6	41.2 ± 4.4	25.5 ± 4.0	0.079	
Tongue pressure max (kg) *	32.4 ± 0.4	36.2 ± 0.8	31.0 ± 1.5	29.1 ± 4.1	<0.001	A, D
Diadochokinesis	30.5 ± 0.2	30.2 ± 0.5	29.7 ± 0.9	26.8 ± 2.2	0.124	
Kihon checklist						
Masticatory function	85 (20.6%)	19 (18.4%)	10 (26.3%)	1 (11.1%)	0.671	
Swallowing function *	110 (26.7%)	19 (18.4%)	15 (39.5%)	4 (44.4%)	0.041	
Dry mouth *	134 (32.7%)	21 (20.4%)	19 (50.0%)	2 (22.2%)	0.006	

Table 2a shows the baseline, and 2b shows the follow-up. Data are presented as mean ± SE. * indicates a significant difference according to one-way analysis of variance, Pearson's chi-square test, or Fisher's exact test. The p-value was calculated using the one-way analysis of variance or Pearson's chi-square test/Fisher's Exact Test, or calculated using Pearson's chi-square and Mann-Whitney U tests, with Bonferroni correction applied for multiple comparisons. The significance level was set at 5%. Significant differences between groups are denoted as follows: A, a significant difference exists between the robust and obesity groups; B, a significant difference exists between the robust and sarcopenia groups; C, a significant difference exists between the robust and sarcopenic obesity groups; D, a significant difference exists between the obesity and sarcopenia groups; E, a significant difference exists between the obesity and sarcopenic obesity groups; F, a significant difference exists between the sarcopenia and sarcopenic obesity groups. The variable descriptions are the same as in Table 1.

Participants in the sarcopenic obesity group had significantly fewer remaining teeth at baseline (p = 0.001). However, this difference was non-significant at follow-up. The obesity group exhibited the highest tongue pressure at both time points (p = 0.001).

Table 3 shows changes in health status between baseline and follow-up across four health states: robust, obesity, sarcopenia, and sarcopenic obesity.

Most participants maintained their baseline health status during follow-up, particularly those classified as "robust" (89.9%) and "obesity" (76.9%). Some participants showed improvements; 18.5% of those with obesity at baseline were reclassified as robust at follow-up, 44.0% of participants with sarcopenia improved to robust, and 60.0% of participants with sarcopenic obesity were reclassified as obese.

Conversely, the health of some participants deteriorated; 4.2% of participants classified as robust became obese, 5.5% developed sarcopenia, and 1.9% of obese participants progressed to sarcopenia. Among participants with sarcopenic obesity at baseline, 10.0% improved and became robust, while 30.0% of participants remained sarcopenic obese at follow-up.

Table 3. Changes in health status between baseline and follow-up.

		Follow-Up			
		Robust (440)	**Obesity (108)**	**Sarcopenia (39)**	**Sarcopenic Obesity (10)**
Baseline	**Robust (454)**	408 (89.9%)	19 (4.2%) A	25 (5.5%) B	2 (0.4%) †
	Obesity (108)	20 (18.5%)	83 (76.9%)	2 (1.9%) B	3 (2.8%) †
	Sarcopenia (25)	11 (44.0%)	-	12 (48.0%)	2 (8.0%) †
	Sarcopenic obesity (10)	1 (10.0%) *	6 (60.0%) *	-	3 (30.0%) *

Percentages indicate the proportion of participants within each baseline or follow-up group. A: events in the Cox regression analysis of the onset of obesity. B: events in the Cox regression analysis of the onset of sarcopenia. †: group with onset of sarcopenic obesity (events in the Cox regression analysis of sarcopenic obesity). * excluded from all Cox regression analyses.

The McNemar–Bowker test (χ^2 = 10.803, df = 6, p = 0.095) indicated no statistically significant changes in the overall distribution of health states between baseline and follow-up. During the follow-up period, most "robust" participants (408, 89.9%) maintained their health status, while 46 participants (10.1%) experienced deterioration. Among those with altered health status at baseline, 32 (22.4%) showed improved robustness.

Table 4 shows the results of examining the factors contributing to the occurrence of sarcopenic obesity based on the results of the prospective longitudinal analysis. After Cox regression analysis, four risk factors remained for the development of sarcopenic obesity. Males had a significantly higher risk of developing sarcopenic obesity than females (hazard ratio [HR] = 20.191, 95% confidence interval [CI]: 3.151–129.366, p = 0.002). As BMI increased, the risk of developing sarcopenic obesity also increased significantly (HR = 2.118, 95% CI: 1.554–2.886, $p < 0.001$). Furthermore, an increase in skeletal muscle mass significantly decreased the risk of sarcopenic obesity (HR = 0.661, 95% CI: 0.510–0.857, p = 0.002). Among oral functions, elevated tongue pressure slightly reduced the risk of sarcopenic obesity (HR = 0.906, 95% CI: 0.829–0.990, p = 0.028). The goodness of fit of the model was significant (-2 log-likelihood = 57.618, $p < 0.001$), and four significant predictors were identified from among the nine original variables.

Following the subclass analysis, three variables remained in the final model as risk factors for sarcopenia development. Males had a significantly higher risk of developing sarcopenia than females (HR = 31.231, 95% CI: 9.660–100.974, $p < 0.001$). Individuals exhibiting declining physical function (decline in grip strength or extension of the time to stand from a chair) had a significantly lower risk of developing sarcopenia (hazard ratio [HR] = 0.188, 95% CI: 0.065–0.543, p = 0.002). Furthermore, enhanced skeletal muscle mass significantly reduced the risk of developing sarcopenia (HR = 0.571, 95% CI: 0.469–0.695, $p < 0.001$). The goodness of fit of the model was significant (-2 log-likelihood = 286.929, $p < 0.001$).

The final model retained the two variables as risk factors for developing obesity. Males tended to have a higher risk of developing obesity than females, although the difference was non-significant (HR = 2.702, 95% CI: 0.830–8.801, p = 0.099). Elevated body fat percentage significantly increased the risk of developing obesity (hazard ratio [HR] = 1.192, 95% CI: 1.095–1.297, $p < 0.001$). These results were obtained using a stepwise reduction of variables (Wald test). The goodness of fit of the model was significant (-2 log-likelihood = 187.068, $p < 0.001$). Oral function variables were non-significant explanatory variables in the development of sarcopenia or obesity.

Table 4. Factors contributing to the occurrence of sarcopenic obesity, sarcopenia, and obesity.

	B	Standard Error of B	Wald	*p*-Value	Exp(B)	95.0% CI for Exp(B)	
						Lower	Upper
Model 1: Development of sarcopenic obesity							
Sex (Males = 1; Females = 0)	3.005	0.948	10.056	0.002	20.191	3.151	129.366
BMI	0.750	0.158	22.553	<0.001	2.118	1.554	2.886
Tongue pressure	−0.099	0.045	4.799	0.028	0.906	0.829	0.990
Limb skeletal muscle mass	−0.414	0.132	9.813	0.002	0.661	0.510	0.857
Model 2: Development of sarcopenia							
Sex (Males = 1; Females = 0)	3.441	0.599	33.041	<0.001	31.231	9.660	100.974
Either decreased grip strength or prolonged chair time	−1.672	0.542	9.521	0.002	0.188	0.065	0.543
Limb skeletal muscle mass	−0.561	0.100	31.275	<0.001	0.571	0.469	0.695
Model 3: Development of obesity							
Sex (Males = 1; Females = 0)	0.994	0.602	2.723	0.099	2.702	0.830	8.801
Body fat	0.176	0.043	16.546	<0.001	1.192	1.095	1.297

Cox regression analysis (stepwise variable reduction method (Wald)). The criteria for adding and removing variables were set at $p < 0.05$ and $p < 0.10$, respectively, with a maximum of 20 iterations. B: partial regression coefficient, Exp (B): hazard ratio. Events: incidence of sarcopenic obesity (model 1), sarcopenia (model 2), and obesity (model 3). Time variable: number of days from baseline to follow-up. The time from baseline to follow-up was used as a variable to determine whether oral function was an independent factor contributing to the development of sarcopenic obesity. Explanatory variables: model 1, age, sex, baseline health status (robust, obese, sarcopenic), body mass index (BMI), limb skeletal muscle mass, decreased grip strength or increased chair time, hypertension, oral diadochokinesis (ODK), and chewing performance; model 2, age, sex, baseline health status (robust, obese), BMI, limb skeletal muscle mass, loss of grip strength or prolonged chair time, hypertension, tongue pressure, and chewing performance; model 3, age, sex, baseline health status (robust or sarcopenic), BMI, limb skeletal muscle mass, body fat, hypertension, tongue pressure, and chewing performance.

4. Discussion

In the current study, we aimed to elucidate the longitudinal relationship between sarcopenic obesity and oral function in independent older adults. Sex, body composition, and muscle mass were the most consistent predictors across outcomes. Additionally, tongue pressure was associated with the risk of sarcopenic obesity but was not a significant predictor of sarcopenia or obesity.

4.1. Characteristics of Sarcopenic Obesity

We showed that individuals with sarcopenic obesity were significantly older, exhibited higher body fat, and had poorer muscle function (longer FTSST times) than their robust or obese counterparts. These findings reinforce the notion that sarcopenic obesity is a more severe phenotype resulting from the interplay between sarcopenia and obesity. Furthermore, the high prevalence of comorbid conditions in this group, such as diabetes and hypertension, aligns with previously reported findings [33,34], underscoring the systemic impact of sarcopenic obesity on metabolic and cardiovascular health.

Prospective analyses revealed that males have a substantially higher risk of developing sarcopenic obesity than females. This may be due to sex-based differences in body composition [35], hormonal changes [36], lifestyle factors [37], or oral health behaviors [37]. These findings highlight the need for sex-specific interventions to mitigate sarcopenic obesity and its associated health risks.

For gender differences in sarcopenic obesity, previous studies have shown that aging in men is associated with decreased testosterone secretion, which induces skeletal muscle loss [38]. Reduced testosterone levels are also linked to increased visceral fat accumulation, as decreased physical activity and energy imbalance result in unused energy being stored as visceral fat. Furthermore, gender differences in dietary habits may contribute to the higher risk of sarcopenic obesity in men. Visceral fat secretes inflammatory cytokines,

which may play a significant role in the development of sarcopenic obesity [6,21]. These sex-related differences may explain the higher hazard ratio observed for males in this study.

In addition, the prevalence of sarcopenic obesity revealed a slight decline over time, with some cases showing improvement or reclassification into obesity or robust categories, respectively. These trends suggest that targeted interventions focusing on weight management, physical activity, and oral health could reverse or stabilize the progression of sarcopenic obesity in older adults. Exercise interventions, such as resistance training and aerobic exercise, can effectively improve sarcopenic obesity [39]. Furthermore, while the relationship between sarcopenia, malnutrition, and oral frailty has been reported [40,41], reports have also suggested that declining masticatory function can hinder the consumption of meat and other foods high in protein, leading to a decrease in muscle mass [42]; hence, maintaining oral function may be effective in improving sarcopenic obesity.

4.2. Associations Between the Incidence of Sarcopenic Obesity and Oral Health

In this study, we confirmed the association between sarcopenic obesity and its development and oral function indices, such as tongue pressure and skeletal muscle mass. Accordingly, a decline in oral function may be associated with the development of sarcopenic obesity; however, the direction of causality remains unclear.

Inadequate nutrition could cause further muscle loss and metabolic abnormalities [43,44]. Specifically, subjects with sarcopenic obesity exhibited the lowest occlusal force and tongue pressure, which are important for chewing and overall oral health, and it was clear that occlusal force had some effect on the progression of sarcopenic obesity. Reduced tongue pressure observed in individuals with sarcopenic obesity may be attributed to several factors. Sarcopenia is associated with lower muscle quality, which can extend to the muscles involved in oral function, potentially reducing tongue pressure [45]. Chronic low-grade inflammation associated with obesity may affect muscle function, including mastication [46]. The loss of muscle mass, a well-known characteristic of sarcopenia, combined with increased fat mass in obesity, may negatively impact the strength of oral muscles [47].

The fact that tongue pressure contributes significantly to nutritional intake through its role in swallowing function and its relationship to systemic skeletal muscle strength makes it a more specific indicator than other oral function measures. Sarcopenic obesity in the elderly is characterized by the accumulation of visceral fat due to age-related loss of muscle mass and reduced physical activity. Previous cross-sectional studies have demonstrated a positive correlation between tongue pressure and total body skeletal muscle mass [48,49]. Furthermore, the tongue plays a critical role in transporting food masses during the feeding and swallowing process [50]. Considering that adequate tongue pressure supports normal nutrient intake and is positively associated with general skeletal muscle function and strength, it may be a specific factor in reducing the risk of developing sarcopenic obesity. Additionally, tongue pressure tends to be associated with sarcopenia more strongly than other oral function indicators, such as the number of teeth or swallowing ability [51]. This suggests that interventions focused solely on dental restoration or prosthetics may be insufficient. Instead, enhancing eating and swallowing functions, along with nutritional support, may be necessary to effectively prevent or manage sarcopenic obesity [52,53].

The relationship between sarcopenic obesity and reduced tongue pressure is likely bidirectional. Lower tongue pressure may lead to difficulties in eating, potentially resulting in a reduced intake of protein-rich foods and contributing to further muscle loss [45]. Conversely, the systemic effects of sarcopenic obesity may lead to reduced muscle strength in the oral system [46].

It is important to note that while our study found a significant association between tongue pressure and sarcopenic obesity, other oral function indicators, such as occlusal force

and number of remaining teeth, were not identified as significant predictors in our final model. This finding suggests that the relationship between oral function and sarcopenic obesity may be complex and multifaceted, warranting further investigation [46].

4.3. Clinical Implications

Our findings suggest that promoting a balanced nutritional intake could potentially be a useful strategy for preventing or managing sarcopenic obesity. However, our study did not include direct nutritional interventions, and this approach remains a potential avenue for future research. It may be valuable in preventing sarcopenic obesity in older adults without reducing swallowing-related oral muscles while supporting the maintenance of skeletal muscle and physical functions and managing obesity. Additionally, continuously evaluating tongue pressure and monitoring longitudinal changes may be beneficial in delaying or reversing the progression of sarcopenic obesity.

4.4. Study Limitations

This study has several limitations. A potential limitation is the relatively small number of participants diagnosed with sarcopenic obesity at baseline (n = 10), which may reduce statistical power and affect generalizability. Additionally, the small sample size may increase the risk of false positives and false negatives, making it difficult to detect significant associations. Future studies with larger sample sizes and more diverse populations are warranted to confirm our results and provide a more comprehensive understanding of the relationship between oral function and sarcopenic obesity.

Furthermore, the study cohort was derived from a specific rural region in Japan, which may limit its generalizability to other populations with different lifestyles or healthcare access. The relatively short follow-up period may also hinder the detection of long-term associations between oral function and sarcopenic obesity. However, previous studies have shown that even shorter periods (3–6 months) can detect changes in body composition related to sarcopenic obesity, suggesting that our follow-up period of over two years is sufficient for this purpose [6].

Additionally, while we attempted to adjust for some potential confounding factors, such as age, sex, and health status, in our statistical models, residual confounding factors may still be present. Factors such as nutritional intake, medication use, and exercise habits could influence both oral function and the development of sarcopenic obesity. Since this study was conducted in Japan, the findings may not be fully applicable to Western populations or other Asian countries with different dietary patterns, exercise habits, and diagnostic criteria for sarcopenic obesity. To better understand these relationships and enhance generalizability, future research should incorporate detailed dietary assessments, such as food frequency questionnaires or dietary recalls, while also focusing on larger, more diverse populations with extended follow-up periods to address potential confounders and explore causative mechanisms. Furthermore, this study did not assess comprehensive oral health, particularly periodontal status. Severe periodontitis can cause systemic inflammation and exacerbate muscle deterioration associated with sarcopenic obesity. Future studies should include periodontal assessments to clarify the role of inflammation in this relationship.

5. Conclusions

Our study showed that sarcopenic obesity was independently associated with oral function, particularly tongue pressure. Although we did not detect a direct link between sarcopenia/obesity alone and oral function, the combination of sarcopenia and obesity appeared to be strongly associated with oral health. These findings suggest that preserving and enhancing tongue muscles, which are crucial for swallowing and other oral functions,

could potentially play a role in delaying the development of sarcopenic obesity. However, further research is required to establish causality and explore the complex relationships between oral function, sarcopenia, and obesity.

Furthermore, our findings demonstrated that reduced tongue pressure was significantly associated with a decreased risk of developing sarcopenic obesity (HR = 0.906, 95% CI: 0.829–0.990, $p = 0.028$). These results suggest that tongue pressure assessment could be a valuable tool in routine geriatric evaluations, particularly for identifying individuals at risk of sarcopenic obesity. However, further research is needed to determine its validity as a definitive screening tool.

Future studies should explore intervention approaches combining nutritional guidance, resistance exercise, and tongue pressure training to improve muscle function. Additionally, developing a staging system for early sarcopenia detection and integrating oral health assessments into geriatric care may enhance diagnostic accuracy and health management.

Author Contributions: Conceptualization, Y.H. and K.S.; formal analysis, S.S. and S.Y.; data curation, S.S., Y.H. and K.T. (Kayoko Tamaki); data acquisition, S.S., S.Y., K.T. (Kana Tokumoto), H.H., H.K. (Hiromitsu Kishimoto), H.K. (Hiroshi Kusunoki), K.N., K.T. (Kayoko Tamaki) and K.H.; writing (original draft), S.S.; writing (review and editing), Y.H. and H.K. (Hiromitsu Kishimoto); supervision, H.K. (Hiromitsu Kishimoto) and K.S.; project administration, Y.H.; and funding acquisition, Y.H. All authors have read and agreed to the published version of the manuscript.

Funding: This study was supported in part by JSPS KAKENHI (grant number: 22K19496) (2022–2024), the National Center for Geriatrics and Gerontology (Choujyu 20-1, 21-18) (2022–2023), and Health Labour Sciences Research Grant (24FA1005) (2024) (Shinmura).

Institutional Review Board Statement: The study was conducted in accordance with the Declaration of Helsinki and approved by the ethics committee of Hyogo College of Medicine (approval no. Rinhi 0342, approval date: 23 May 2017) and Niigata University (Approval number: G2021-0027). All methods were carried out in accordance with the relevant guidelines and regulations.

Informed Consent Statement: Written informed consent has been obtained from all subjects involved in the study to publish this paper.

Data Availability Statement: Data supporting the findings of this study are available from the corresponding author upon reasonable request. However, the data are not publicly available due to privacy and ethical restrictions.

Acknowledgments: We would like to express our sincere gratitude to all the participants who took part in the FESTA study. We would also like to express our deep appreciation to the staff of the Department of Oral and Maxillofacial Surgery at Hyogo Medical University and the medical staff at Hyogo Medical University who cooperated with the FESTA study.

Conflicts of Interest: The authors declare no conflicts of interest. The funders had no role in the study design, data collection and analysis, manuscript preparation, or decision to publish this study.

References

1. Choi, K.M. Sarcopenia and sarcopenic obesity. *Korean J. Intern. Med.* **2016**, *31*, 1054–1060. [CrossRef]
2. Roh, E.; Choi, K.M. Health Consequences of Sarcopenic Obesity: A Narrative Review. *Front. Endocrinol.* **2020**, *11*, 332. [CrossRef]
3. Gill, L.E.; Bartels, S.J.; Batsis, J.A. Weight Management in Older Adults. *Curr. Obes. Rep.* **2015**, *4*, 379–388. [CrossRef]
4. van den Broek-Altenburg, E.; Atherly, A.; Holladay, E. Changes in healthcare spending attributable to obesity and overweight: Payer- and service-specific estimates. *BMC Public Health* **2022**, *22*, 962. [CrossRef]
5. Morgan, P.T.; Smeuninx, B.; Breen, L. Exploring the Impact of Obesity on Skeletal Muscle Function in Older Age. *Front. Nutr.* **2020**, *7*, 569904. [CrossRef] [PubMed]
6. Batsis, J.A.; Villareal, D.T. Sarcopenic obesity in older adults: Aetiology, epidemiology and treatment strategies. *Nat. Rev. Endocrinol.* **2018**, *14*, 513–537. [CrossRef] [PubMed]

7. Donini, L.M.; Busetto, L.; Bischoff, S.C.; Cederholm, T.; Ballesteros-Pomar, M.D.; Batsis, J.A.; Bauer, J.M.; Boirie, Y.; Cruz-Jentoft, A.J.; Dicker, D.; et al. Definition and Diagnostic Criteria for Sarcopenic Obesity: ESPEN and EASO Consensus Statement. *Obes. Facts* **2022**, *15*, 321–335. [CrossRef] [PubMed]
8. Liu, C.; Wong, P.Y.; Chung, Y.L.; Chow, S.K.; Cheung, W.H.; Law, S.W.; Chan, J.C.N.; Wong, R.M.Y. Deciphering the "obesity paradox" in the elderly: A systematic review and meta-analysis of sarcopenic obesity. *Obes. Rev.* **2023**, *24*, e13534. [CrossRef]
9. Unger, R.H. Longevity, lipotoxicity and leptin: The adipocyte defense against feasting and famine. *Biochimie* **2005**, *87*, 57–64. [CrossRef]
10. Lynch, G.M.; Murphy, C.H.; Castro, E.d.M.; Roche, H.M. Inflammation and metabolism: The role of adiposity in sarcopenic obesity. *Proc. Nutr. Soc.* **2020**, *79*, 435–447. [CrossRef]
11. Alalwan, T.A. Phenotypes of Sarcopenic Obesity: Exploring the Effects on Peri-Muscular Fat, the Obesity Paradox, Hormone-Related Responses and the Clinical Implications. *Geriatrics* **2020**, *5*, 8. [CrossRef] [PubMed]
12. Stephen, W.C.; Janssen, I. Sarcopenic-obesity and cardiovascular disease risk in the elderly. *J. Nutr. Health Aging* **2009**, *13*, 460–466. [CrossRef]
13. Park, S.H.; Park, J.H.; Song, P.S.; Kim, D.K.; Kim, K.H.; Seol, S.H.; Kim, H.K.; Jang, H.J.; Lee, J.G.; Park, H.Y.; et al. Sarcopenic obesity as an independent risk factor of hypertension. *J. Am. Soc. Hypertens. JASH* **2013**, *7*, 420–425. [CrossRef]
14. Baek, S.J.; Nam, G.E.; Han, K.D.; Choi, S.W.; Jung, S.W.; Bok, A.R.; Kim, Y.H.; Lee, K.S.; Han, B.D.; Kim, D.H. Sarcopenia and sarcopenic obesity and their association with dyslipidemia in Korean elderly men: The 2008-2010 Korea National Health and Nutrition Examination Survey. *J. Endocrinol. Investig.* **2014**, *37*, 247–260. [CrossRef]
15. Kera, T.; Kawai, H.; Hirano, H.; Kojima, M.; Fujiwara, Y.; Ihara, K.; Obuchi, S. Differences in body composition and physical function related to pure sarcopenia and sarcopenic obesity: A study of community-dwelling older adults in Japan. *Geriatr. Gerontol. Int.* **2017**, *17*, 2602–2609. [CrossRef]
16. Khadra, D.; Itani, L.; Tannir, H.; Kreidieh, D.; El Masri, D.; El Ghoch, M. Association between sarcopenic obesity and higher risk of type 2 diabetes in adults: A systematic review and meta-analysis. *World J. Diabetes* **2019**, *10*, 311–323. [CrossRef]
17. Hatta, K.; Ikebe, K. Association between oral health and sarcopenia: A literature review. *J. Prosthodont. Res.* **2021**, *65*, 131–136. [CrossRef]
18. Kugimiya, Y.; Iwasaki, M.; Ohara, Y.; Motokawa, K.; Edahiro, A.; Shirobe, M.; Watanabe, Y.; Taniguchi, Y.; Seino, S.; Abe, T.; et al. Association between sarcopenia and oral functions in community-dwelling older adults: A cross-sectional study. *J. Cachexia Sarcopenia Muscle* **2023**, *14*, 429–438. [CrossRef]
19. Abe, T.; Tominaga, K.; Ando, Y.; Toyama, Y.; Takeda, M.; Yamasaki, M.; Okuyama, K.; Hamano, T.; Isomura, M.; Nabika, T.; et al. Number of teeth and masticatory function are associated with sarcopenia and diabetes mellitus status among community-dwelling older adults: A Shimane CoHRE study. *PLoS ONE* **2021**, *16*, e0252625. [CrossRef] [PubMed]
20. Iwashita, M.; Hayashi, M.; Nishimura, Y.; Yamashita, A. The Link Between Periodontal Inflammation and Obesity. *Curr. Oral Health Rep.* **2021**, *8*, 76–83. [CrossRef] [PubMed]
21. Reytor-González, C.; Parise-Vasco, J.M.; González, N.; Simancas-Racines, A.; Zambrano-Villacres, R.; Zambrano, A.K.; Simancas-Racines, D. Obesity and periodontitis: A comprehensive review of their interconnected pathophysiology and clinical implications. *Front. Nutr.* **2024**, *11*, 1440216. [CrossRef] [PubMed]
22. Modéer, T.; Blomberg, C.C.; Wondimu, B.; Julihn, A.; Marcus, C. Association between obesity, flow rate of whole saliva, and dental caries in adolescents. *Obesity* **2010**, *18*, 2367–2373. [CrossRef] [PubMed]
23. Roa, I.; Del Sol, M. Obesity, salivary glands and oral pathology. *Colomb. Medica* **2018**, *49*, 280–287. [CrossRef]
24. Mohajeri, A.; Berg, G.; Watts, A.; Cheever, V.J.; Hung, M. Obesity and Dental Caries in School Children. *J. Clin. Med.* **2024**, *13*, 860. [CrossRef]
25. Chen, L.K.; Woo, J.; Assantachai, P.; Auyeung, T.W.; Chou, M.Y.; Iijima, K.; Jang, H.C.; Kang, L.; Kim, M.; Kim, S.; et al. Asian Working Group for Sarcopenia: 2019 Consensus Update on Sarcopenia Diagnosis and Treatment. *J. Am. Med. Dir. Assoc.* **2020**, *21*, 300–307.e2. [CrossRef]
26. Ishii, K.; Ogawa, W.; Kimura, Y.; Kusakabe, T.; Miyazaki, R.; Sanada, K.; Satoh-Asahara, N.; Someya, Y.; Tamura, Y.; Ueki, K.; et al. Diagnosis of sarcopenic obesity in Japan: Consensus statement of the Japanese Working Group on Sarcopenic Obesity. *Geriatr. Gerontol. Int.* **2024**, *24*, 997–1000. [CrossRef]
27. Utanohara, Y.; Hayashi, R.; Yoshikawa, M.; Yoshida, M.; Tsuga, K.; Akagawa, Y. Standard values of maximum tongue pressure taken using newly developed disposable tongue pressure measurement device. *Dysphagia* **2008**, *23*, 286–290. [CrossRef]
28. Hasegawa, Y.; Horii, N.; Sakuramoto-Sadakane, A.; Nagai, K.; Ono, T.; Sawada, T.; Shinmura, K.; Kishimoto, H. Is a History of Falling Related to Oral Function? A Cross-Sectional Survey of Elderly Subjects in Rural Japan. *Int. J. Environ. Res. Public Health* **2019**, *16*, 3843. [CrossRef]
29. Hasegawa, Y.; Sakuramoto, A.; Sugita, H.; Hasegawa, K.; Horii, N.; Sawada, T.; Shinmura, K.; Kishimoto, H. Relationship between oral environment and frailty among older adults dwelling in a rural Japanese community: A cross-sectional observational study. *BMC Oral Health* **2019**, *19*, 23. [CrossRef] [PubMed]

30. Thu Ya, M.; Hasegawa, Y.; Sta Maria, M.T.; Hattori, H.; Kusunoki, H.; Nagai, K.; Tamaki, K.; Hori, K.; Kishimoto, H.; Shinmura, K. Predicting cognitive function changes from oral health status: A longitudinal cohort study. *Sci. Rep.* **2024**, *14*, 24153. [CrossRef]
31. Marito, P.; Hasegawa, Y.; Tamaki, K.; Sta Maria, M.T.; Yoshimoto, T.; Kusunoki, H.; Tsuji, S.; Wada, Y.; Ono, T.; Sawada, T.; et al. The Association of Dietary Intake, Oral Health, and Blood Pressure in Older Adults: A Cross-Sectional Observational Study. *Nutrients* **2022**, *14*, 1279. [CrossRef] [PubMed]
32. Nokubi, T.; Yoshimuta, Y.; Nokubi, F.; Yasui, S.; Kusunoki, C.; Ono, T.; Maeda, Y.; Yokota, K. Validity and reliability of a visual scoring method for masticatory ability using test gummy jelly. *Gerodontology* **2013**, *30*, 76–82. [CrossRef]
33. Nojiri, S.; Itoh, H.; Kasai, T.; Fujibayashi, K.; Saito, T.; Hiratsuka, Y.; Okuzawa, A.; Naito, T.; Yokoyama, K.; Daida, H. Comorbidity status in hospitalized elderly in Japan: Analysis from National Database of Health Insurance Claims and Specific Health Checkups. *Sci. Rep.* **2019**, *9*, 20237. [CrossRef] [PubMed]
34. Aïdoud, A.; Gana, W.; Poitau, F.; Debacq, C.; Leroy, V.; Nkodo, J.A.; Poupin, P.; Angoulvant, D.; Fougère, B. High Prevalence of Geriatric Conditions Among Older Adults With Cardiovascular Disease. *J. Am. Heart Assoc.* **2023**, *12*, e026850. [CrossRef] [PubMed]
35. Hwang, J.; Park, S. Gender-Specific Prevalence and Risk Factors of Sarcopenic Obesity in the Korean Elderly Population: A Nationwide Cross-Sectional Study. *Int. J. Environ. Res. Public Health* **2023**, *20*, 1140. [CrossRef]
36. Du, Y.; Wang, X.; Xie, H.; Zheng, S.; Wu, X.; Zhu, X.; Zhang, X.; Xue, S.; Li, H.; Hong, W.; et al. Sex differences in the prevalence and adverse outcomes of sarcopenia and sarcopenic obesity in community dwelling elderly in East China using the AWGS criteria. *BMC Endocr. Disord.* **2019**, *19*, 109. [CrossRef]
37. Cao, W.; Zhu, A.; Chu, S.; Zhou, Q.; Zhou, Y.; Qu, X.; Tang, Q.; Zhang, Y. Correlation between nutrition, oral health, and different sarcopenia groups among elderly outpatients of community hospitals: A cross-sectional study of 1505 participants in China. *BMC Geriatr.* **2022**, *22*, 332. [CrossRef]
38. Rolland, Y.; Czerwinski, S.; Abellan Van Kan, G.; Morley, J.E.; Cesari, M.; Onder, G.; Woo, J.; Baumgartner, R.; Pillard, F.; Boirie, Y.; et al. Sarcopenia: Its assessment, etiology, pathogenesis, consequences and future perspectives. *J. Nutr. Health Aging* **2008**, *12*, 433–450. [CrossRef]
39. Reiter, L.; Bauer, S.; Traxler, M.; Schoufour, J.D.; Weijs, P.J.M.; Cruz-Jentoft, A.; Topinková, E.; Eglseer, D. Effects of Nutrition and Exercise Interventions on Persons with Sarcopenic Obesity: An Umbrella Review of Meta-Analyses of Randomised Controlled Trials. *Curr. Obes. Rep.* **2023**, *12*, 250–263. [CrossRef]
40. Tanaka, T.; Takahashi, K.; Hirano, H.; Kikutani, T.; Watanabe, Y.; Ohara, Y.; Furuya, H.; Tetsuo, T.; Akishita, M.; Iijima, K. Oral Frailty as a Risk Factor for Physical Frailty and Mortality in Community-Dwelling Elderly. *J. Gerontol. Ser. A Biol. Sci. Med. Sci.* **2018**, *73*, 1661–1667. [CrossRef]
41. Iwasaki, M.; Motokawa, K.; Watanabe, Y.; Shirobe, M.; Inagaki, H.; Edahiro, A.; Ohara, Y.; Hirano, H.; Shinkai, S.; Awata, S. Association between Oral Frailty and Nutritional Status Among Community-Dwelling Older Adults: The Takashimadaira Study. *J. Nutr. Health Aging* **2020**, *24*, 1003–1010. [CrossRef]
42. Takahara, M.; Shiraiwa, T.; Maeno, Y.; Yamamoto, K.; Shiraiwa, Y.; Yoshida, Y.; Nishioka, N.; Katakami, N.; Matsuoka, T.A.; Shimomura, I. Association of obesity, diabetes, and physical frailty with dental and tongue-lip motor dysfunctions in patients with metabolic disease. *Obes. Res. Clin. Pract.* **2021**, *15*, 243–248. [CrossRef] [PubMed]
43. McGlory, C.; van Vliet, S.; Stokes, T.; Mittendorfer, B.; Phillips, S.M. The impact of exercise and nutrition on the regulation of skeletal muscle mass. *J. Physiol.* **2019**, *597*, 1251–1258. [CrossRef]
44. Marshall, R.N.; Smeuninx, B.; Morgan, P.T.; Breen, L. Nutritional Strategies to Offset Disuse-Induced Skeletal Muscle Atrophy and Anabolic Resistance in Older Adults: From Whole-Foods to Isolated Ingredients. *Nutrients* **2020**, *12*, 1533. [CrossRef]
45. Moynihan, P.J.; Teo, J.L. Exploring Oral Function, Protein Intake, and Risk of Sarcopenia: A Scoping Review. *JDR Clin. Transl. Res.* **2024**, *9*, 4–20. [CrossRef]
46. Shirahase, R.; Watanabe, Y.; Saito, T.; Sunakawa, Y.; Matsushita, Y.; Tsugayasu, H.; Yamazaki, Y. A Cross-Sectional Study on the Relationship between Oral Function and Sarcopenia in Japanese Patients with Regular Dental Maintenance. *Int. J. Environ. Res. Public Health* **2022**, *19*, 5178. [CrossRef]
47. Nakazawa, Y.; Kikutani, T.; Igarashi, K.; Yajima, Y.; Tamura, F. Associations between tongue strength and skeletal muscle mass under dysphagia rehabilitation for geriatric out patients. *J. Prosthodont. Res.* **2020**, *64*, 188–192. [CrossRef]
48. Murakami, T.; Kamide, N.; Ando, M.; Hata, W.; Sakamoto, M. Association between tongue pressure and skeletal muscle mass and muscle function in community-dwelling older people without sarcopenia. *Eur. Geriatr. Med.* **2022**, *13*, 649–653. [CrossRef]
49. Hori, K.; Taniguchi, H.; Hayashi, H.; Magara, J.; Minagi, Y.; Li, Q.; Ono, T.; Inoue, M. Role of tongue pressure production in oropharyngeal swallow biomechanics. *Physiol. Rep.* **2013**, *1*, e00167. [CrossRef] [PubMed]
50. Chen, K.C.; Lee, T.M.; Wu, W.T.; Wang, T.G.; Han, D.S.; Chang, K.V. Assessment of Tongue Strength in Sarcopenia and Sarcopenic Dysphagia: A Systematic Review and Meta-Analysis. *Front. Nutr.* **2021**, *8*, 684840. [CrossRef]

51. Shimizu, A.; Fujishima, I.; Maeda, K.; Wakabayashi, H.; Nishioka, S.; Ohno, T.; Nomoto, A.; Kayashita, J.; Mori, N.; The Japanese Working Group on Sarcopenic Dysphagia. Nutritional Management Enhances the Recovery of Swallowing Ability in Older Patients with Sarcopenic Dysphagia. *Nutrients* **2021**, *13*, 596. [CrossRef] [PubMed]
52. Abe, S.; Kokura, Y.; Maeda, K.; Nishioka, S.; Momosaki, R.; Matsuoka, H.; Tomii, Y.; Sugita, S.; Shimizu, K.; Esashi, N.; et al. Effects of Undernutrition on Swallowing Function and Activities of Daily Living in Hospitalized Patients: Data from the Japanese Sarcopenic Dysphagia Database. *Nutrients* **2023**, *15*, 1291. [CrossRef] [PubMed]
53. Huang, S.W.; Ku, J.W.; Lin, L.F.; Liao, C.D.; Chou, L.C.; Liou, T.H. Body composition influenced by progressive elastic band resistance exercise of sarcopenic obesity elderly women: A pilot randomized controlled trial. *Eur. J. Phys. Rehabil. Med.* **2017**, *53*, 556–563. [CrossRef]

nutrients

MDPI

Article

Oral Frailty and Its Relationship with Physical Frailty in Older Adults: A Longitudinal Study Using the Oral Frailty Five-Item Checklist

Hiroshi Kusunoki [1,2,*], Yoko Hasegawa [3,4], Yasuyuki Nagasawa [1], Kensaku Shojima [1], Hiromitsu Yamazaki [1], Takara Mori [1,5], Shotaro Tsuji [6], Yosuke Wada [1], Kayoko Tamaki [1], Koutatsu Nagai [7], Ryota Matsuzawa [7], Hiromitsu Kishimoto [4], Hideo Shimizu [2] and Ken Shinmura [1]

1 Division of General Medicine, Department of Internal Medicine, Hyogo Medical University, Nishinomiya 663-8501, Hyogo, Japan
2 Department of Internal Medicine, Osaka Dental University, Hirakata 573-1121, Osaka, Japan
3 Division of Comprehensive Prosthodontics, Graduate School of Medical and Dental Sciences, Niigata University, Niigata 951-8514, Niigata, Japan
4 Department of Dentistry and Oral Surgery, Hyogo Medical University, Nishinomiya 663-8501, Hyogo, Japan
5 Amagasaki Medical COOP Honden Clinic, Amagasaki 660-0077, Hyogo, Japan
6 Department of Orthopedic Surgery, Hyogo Medical University, Nishinomiya 663-8501, Hyogo, Japan
7 School of Rehabilitation, Hyogo Medical University, Kobe 650-8530, Hyogo, Japan
* Correspondence: kusunoki1019@yahoo.co.jp

Abstract: Background/Objectives: Oral frailty, first identified in Japan in 2014, refers to a state between healthy oral function and severe decline, marked by minor issues, such as tooth loss and chewing difficulties. The oral frailty five-item checklist (OF-5) enables non-dental professionals to evaluate oral frailty using five key indicators: remaining teeth count, chewing difficulties, swallowing difficulties, dry mouth, and articulatory oral skills. Limited studies exist. Methods: This study examined the relationship between oral and physical frailties in older adults and assessed the prognosis of physical frailty using the OF-5. Participants aged ≥65 years were recruited from the frail elderly in the Sasayama–Tamba area, Hyogo, Japan, and their physical function was assessed in terms of grip strength, walking speed, and skeletal muscle mass. Blood markers, such as cystatin C, an indicator of renal function, were also analyzed. Results: A cross-sectional analysis indicated that oral frailty was correlated with reduced muscle mass, walking speed, and physical function. Women had lower hemoglobin and albumin levels and a greater prevalence of frailty than men. Longitudinal analysis revealed that initial OF-5 scores predicted increased physical frailty after 2–3 years, especially in those with higher baseline scores. The OF-5 was a significant factor for frailty progression in both sexes. Conclusions: These results suggest that early detection of oral frailty via the OF-5 may be useful in preventing the progression of overall frailty in older adults.

Keywords: oral frailty; physical frailty; oral frailty five-item checklist

Academic Editor: Mario Barbagallo

Received: 21 November 2024
Revised: 22 December 2024
Accepted: 23 December 2024
Published: 24 December 2024

Citation: Kusunoki, H.; Hasegawa, Y.; Nagasawa, Y.; Shojima, K.; Yamazaki, H.; Mori, T.; Tsuji, S.; Wada, Y.; Tamaki, K.; Nagai, K.; et al. Oral Frailty and Its Relationship with Physical Frailty in Older Adults: A Longitudinal Study Using the Oral Frailty Five-Item Checklist. *Nutrients* **2025**, *17*, 17. https://doi.org/10.3390/nu17010017

1. Introduction

Oral health is a critical component of overall health, life satisfaction, quality of life, and self-perception. Impairment of oral function is highly prevalent among older adults, and aging has been reported to interact indirectly with various domains of frailty through multiple pathways. A clear example of this relationship is age-related functional oral deterioration, characterized by poor dental hygiene, inadequate dental prostheses, and dietary deficiencies, which collectively contribute to an increased risk of nutritional frailty [1].

Oral frailty is defined as an age-related gradual decline in oral function, often accompanied by deteriorations in physical functions. This condition is associated with significant adverse health outcomes in older adults, including increased mortality, physical frailty, functional disabilities, reduced quality of life, and a higher risk of hospitalization and falls [2]. Poor oral health in the elderly is a major health concern due to its links to the pathogenesis of systemic frailty, suggesting that it is a multidimensional geriatric syndrome. As such, oral frailty may serve as a potential risk factor for systemic frailty [3]. Oral frailty was first proposed by the Japanese Geriatrics Society in 2014, and is described as an age-related decrease in oral function. Oral frailty is further defined as "the overlap of minor declines in dental or oral functions that may increase the risk of adverse health outcomes" [4,5].

This condition poses an increased risk of further decline in oral function; however, it remains reversible if early and appropriate interventions are implemented. Signs of oral frailty, including decreased tongue pressure, increased food spillage, slight chewing difficulties, and a dry mouth, are often subtle and easily overlooked. Recent studies have shown that oral frailty in older adults not only affects oral health but also has systemic implications, contributing to overall frailty and sarcopenia (age-related muscle loss) [4,6,7].

In 2023, a new diagnostic criterion for oral frailty, known as the oral frailty five-item checklist (OF-5), was proposed [4]. It comprises five items: fewer teeth, difficulty in chewing, difficulty in swallowing, dry mouth, and low articulatory oral motor skills. The OF-5 is designed to be implemented in various settings beyond dental care facilities, including non-dental healthcare facilities and community activities, and can be assessed by older individuals. The OF-5 has demonstrated robust predictive validity for physical frailty, physical impairment, and mortality among the older population in Japan [4]. Despite these advancements, the longitudinal impact of oral frailty on the progression of physical frailty, as assessed by the OF-5, remains poorly understood, particularly in rural populations.

On 1 April 2024, the Japanese Geriatrics Society, Japanese Geriatric Dentistry Society, and Japanese Society for Sarcopenia and Frailty introduced a joint statement on oral frailty diagnosed via the OF-5 [8]. The OF-5 facilitates early detection of oral frailty and promotes interdisciplinary collaboration in its management, particularly in the medical and dental fields.

In our epidemiological study conducted among community-dwelling older adults in Sasayama–Tamba, Hyogo Prefecture (the frail elderly in the Sasayama–Tamba area [FESTA] study), we focused on the relationship between oral function and physical frailty. The rural environment of Sasayama–Tamba, which is relatively close to a metropolitan area and maintains a stable population without extreme depopulation or aging, offers a unique context. It features a modern, healthy, elderly population centered on suburban agriculture, with low population turnover. This setting provides an important backdrop for studying the interaction between oral and physical frailty given its distinctive demographic and health characteristics. In our previous study, we found a significant correlation between tongue pressure and cystatin C levels, an indicator of kidney function in the FESTA study. Our findings also revealed a correlation between tongue pressure, an indicator of oral function, and physical parameters, such as grip strength, walking speed, and muscle mass [9].

The Oral Frailty Checklist/Oral Frailty Index-8 (OFI-8) was developed by the Japan Dental Association [10,11], and consists of eight items: (1) difficulties in chewing; (2) difficulties in swallowing; (3) denture use; (4) dry mouth; (5) going out less frequently; (6) feasibility of chewing hard food; (7) brushing teeth at least twice a day; and (8) regular attendance at a dental clinic. Items (1) to (3) were scored as 2, whereas the other items were scored as 1. The maximum possible score was 11: low risk, 0–2 points; moderate risk, 3 points; and high risk, >4 points. Oral frailty, as assessed using the OFI-8, was

independently associated with all-cause mortality, even after adjusting for physical and psychological frailty in older adults [12].

On the other hand, there are many reports on the associations of cystatin-C-related indices, including the creatinine-to-cystatin-C ratio (Cre/CysC ratio) and estimated glomerular filtration rate based on CysC (eGFRcys), with physical frailty and sarcopenia [13–20]. Our findings indicated that individuals at high risk for oral frailty, as assessed by the OFI-8, had lower levels of cystatin-C-related indices, grip strength, hemoglobin, and albumin, with a higher prevalence of oral frailty observed in women [21].

The OF-5 and OFI-8 share several common items, such as difficulties in chewing, difficulties in swallowing, and dry mouth. These three items are included in the Kihon checklist developed by the Japanese Ministry of Health, Labor, and Welfare, which consists of 25 questions in seven categories: physical strength, nutrition, eating, socialization, memory, mood, and lifestyle [22,23]. However, the OFI-5 differs from the OFI-8 in that it includes objective evaluations, such as the remaining teeth count and articulatory oral motor skills assessed by a dental specialist. The relationship between oral frailty and diagnosis using the OF-5, which includes objective measures based on dental examinations, grip strength, gait speed, and blood test indices, has not yet been examined. The comparative efficacy of the OF-5 in predicting physical frailty outcomes, especially in comparison to the OFI-8, has not been extensively explored, highlighting a vital area for investigation.

The longitudinal Kashiwa Study conducted by the University of Tokyo has also shown that oral frailty is a risk factor for physical frailty and is linked to life prognosis [3]. In the present study, we examined whether oral frailty, as diagnosed by the OF-5, predicts worsening physical frailty according to the Japanese Cardiovascular Health Study (J-CHS) criteria. Oral frailty, as assessed using the OF-5, has also been shown to be related to the development of physical disabilities and frailty [4].

This study aimed to assess, in a cross-sectional analysis, sex differences in physical and blood markers among individuals classified as having oral frailty by the OF-5. Additionally, using the OF-5, we aimed to investigate whether individuals classified as having suspected oral frailty (OF-5 score ≥ 2) exhibit differences in physical and biological markers, including height, weight, blood indices, and muscle strength, compared with those with lower OF-5 scores. We also explored whether these differences were associated with overall frailty. This study aimed to longitudinally assess the predictive value of the OF-5 checklist for physical frailty among older adults in Sasayama–Tamba by hypothesizing that higher OF-5 scores are significantly associated with an increased risk of physical frailty over time. Additionally, in a longitudinal analysis, we examined the association between OF-5 scores and the progression of physical frailty according to the J-CHS criteria. Finally, we evaluated the predictive value of OF-5 in comparison with other clinical markers over a follow-up period of 2–3 years.

2. Materials

2.1. Study Participants

This cross-sectional study within the FESTA study included individuals aged $\geq$65 years. Healthy community-dwelling older adults from the Sasayama–Tamba area, a rural region in Hyogo Prefecture, Japan, were recruited between 2017 and 2023. Body composition and blood sample analyses were performed as described previously [17,18]. Body composition was assessed using bioelectrical impedance analysis with an InBody 770 device (Inbody Japan Inc., Tokyo, Japan). Skeletal muscle mass index (SMI) was calculated as skeletal muscle mass divided by height squared (kg/m^2). Handgrip strength was measured according to previously established methods [17,18,24].

This cross-sectional study included 313 men and 621 women (934 in total). For the longitudinal study, 105 men and 224 women (329 in total) from the first cross-sectional survey who had no missing data in the second survey conducted 2–3 years later were included.

All procedures performed in this study, which involved human participants, adhered to the ethical standards of the institutional and/or national research committee where the studies were conducted (IRB approval number Rinhi 0342 at Hyogo Medical University) and the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

2.2. Evaluation of Physical Function

To assess gait speed, the participants were instructed to walk a 12 m walkway at their usual pace, and the time taken to walk 10 m was recorded. Maximum grip strength was measured via a grip strength tester (GRIP-A; Takei Ltd., Niigata, Japan) [25]. Knee extension strength (Nm) of the dominant leg was evaluated during isometric contraction of the knee extensor in a seated position, with the knee maintained at a 60° angle using a hand-held dynamometer (Sakai Medical Co., Ltd., Tokyo, Japan) [26].

2.3. Diagnosis of Frailty

Frailty phenotypes were assessed based on the five clinical features defined in the Cardiovascular Health Study (CHS): slow gait speed, weakness, exhaustion, low physical activity, and weight loss [27]. The frailty score was calculated using a modified version of the CHS (J-CHS) [28]. The number of applicable frailty phenotypes of the five was used to determine the J-CHS score. A score of 0 was defined as robust, 1 or 2 as pre-frail, and $\geq$3 as frail.

In a longitudinal study, during the second survey conducted 2–3 years after the first survey, the participants were categorized based on changes in their J-CHS frailty scores. Seventy-four participants (27 men and 47 women) whose scores had increased were defined as "worsened", 167 (51 men, 116 women) whose scores remained unchanged were categorized as "unchanged", and 88 (27 men, 61 women) whose scores had decreased were classified as "improved". Changes in the J-CHS frailty scores were used to classify the participants as improved, unchanged, or worsened, and comparisons were made across groups in terms of physical indices, blood markers, OF-5 scores, and the number of positive subjects for each item at the time of the first survey. Logistic regression analysis, including other indices, was used to determine whether the J-CHS scores worsened during the second survey.

2.4. Diagnosis of Sarcopenia

Sarcopenia was defined according to the criteria for the Asia Working Group for Sarcopenia (AWGS) 2019 [29]. Body composition was evaluated by bioelectrical impedance analysis (BIA) using an InBody 770® (InBody Japan Inc., Tokyo, Japan). The skeletal muscle mass index (SMI) was calculated as SMM/height^2 (kg/m^2). The handgrip power, the normal and maximal gait speed, five-time chair stand test (5CS), Timed Up and Go test (TUG), and Short Physical Performance Battery (SPPB) scores were evaluated as described previously [29]. Sarcopenia was considered if the participants had a low SMI (<7.0 kg/m^2 in men; <5.7 kg/m^2 in women) and weak handgrip strength (<28 kg in men; <18 kg in women) or low physical performance (normal gait speed < 1.0 m/s, 5CS $\geq$ 12 s or SPPB $\leq$ 9).

2.5. Evaluation of Oral Function

The participants were seated in reclinable nursing chairs and underwent oral examinations. The number of remaining teeth, occlusal force, and tongue pressure were assessed. Tongue pressure was measured twice using a JMS Tongue Pressure Measuring Device

(JMS Co., Ltd., Hiroshima, Japan), and the highest value was recorded [30]. To evaluate tongue motor function (oral diadochokinesis [ODK]), we used oral function measurement equipment (KENKOU-KUN Handy; Takei Scientific Instruments Co., Ltd., Niigata, Japan) to measure the articulatory velocity of /ta/ [31].

2.6. Calculation of eGFR

We calculated creatine-based eGFR (eGFRcre) and eGFRcys using equations provided by the Japanese Society of Nephrology [32,33].

2.7. Statistical Analysis

The results are expressed as the means ± standard deviations or percentages. For intergroup comparisons, Student's *t*-test was used for data analysis. Categorical variables are presented as absolute numbers (n) and relative frequencies (%), and were analyzed using the Fisher's exact test. Univariate and multivariate logistic regression analyses were performed to calculate the odds ratios and 95% confidence intervals. Data analysis was conducted using JMP version 17.1 software, with statistical significance set at $p < 0.05$.

3. Results

The characteristics of 313 men and 621 women (934 in total) are shown in Table 1. The prevalence of oral frailty was slightly >40% in both sexes, with no significant difference between the sexes. According to the J-CHS frailty criteria by sex, exhaustion tended to be greater in women than in men; however, there were no significant differences in the other four criteria. Muscle strength, muscle mass, and walking speed were generally greater in men than in women, although there were no sex differences in the Timed Up and Go (TUG) test or the five-time chair stand (5CS) test. Tongue pressure was greater in men, whereas ODK tended to be greater in women. However, no significant sex-related differences were observed in the number of teeth. Women also tended to be more prone to anemia, with higher total protein and albumin levels. Creatine, cystatin C, and Cre/CysC levels reflected muscle mass and tended to be higher in men than in women, whereas eGFR tended to be higher in women than in men.

Table 1. Baseline characteristics of participants according to sex.

	Total (n = 934)	**Men (n = 313)**	**Women (n = 621)**	***p***
Age (years)	74.0 ± 5.8	74.7 ± 5.9	73.6 ± 5.8	**<0.001**
Height (cm)	155.4 ± 8.3	163.9 ± 6.0	151.1 ± 5.5	**<0.001**
Body weight (kg)	55.0 ± 9.4	62.5 ± 8.8	51.2 ± 7.1	**<0.001**
Body mass index	22.7 ± 2.9	23.2 ± 2.8	22.4 ± 2.9	**<0.001**
Skeletal muscle mass (SMM) (kg)	15.7 ± 3.7	19.9 ± 2.8	13.6 ± 1.9	**<0.001**
Skeletal muscle mass index (SMI)	6.43 ± 0.93	7.37 ± 0.73	5.95 ± 0.59	**<0.001**
Body fat mass (kg)	15.3 ± 5.3	14.8 ± 5.3	15.6 ± 5.3	**0.035**
Percentage of BFM (%)	27.6 ± 7.3	23.2 ± 6.1	29.8 ± 6.9	**<0.001**
Grip power (kg)	26.7 ± 7.6	34.6 ± 6.5	22.7 ± 4.2	**<0.001**
Knee extension muscle strength (Nm)	336.5 ± 115.2	428.7 ± 114.2	290.0 ± 83.4	**<0.001**
Normal gait speed (m/s)	1.41 ± 0.24	1.38 ± 0.24	1.43 ± 0.24	**<0.001**
Maximal gait speed (m/s)	1.87 ± 0.32	1.94 ± 0.34	1.84 ± 0.30	**<0.001**
Timed Up and Go test (TUG)	6.33 ± 1.64	6.30 ± 1.93	6.35 ± 1.47	0.675
Five-time chair stand test (5CS)	7.53 ± 4.15	7.90 ± 4.77	7.34 ± 3.79	0.137

Table 1. *Cont.*

	Total (n = 934)	Men (n = 313)	Women (n = 621)	*p*
Cre (mg/dL)	0.75 ± 0.28	0.90 ± 0.19	0.68 ± 0.29	**<0.001**
CysC (mg/L)	0.95 ± 0.25	1.03 ± 0.23	0.91 ± 0.24	**<0.001**
Cre/CysC	0.80 ± 0.13	0.89 ± 0.12	0.75 ± 0.11	**<0.001**
eGFRcre (mL/min/1.73 m^2)	67.0 ± 14.1	66.2 ± 14.0	67.5 ± 14.1	**<0.001**
eGFRcys (mL/min/1.73 m^2)	73.3 ± 16.1	70.6 ± 16.5	74.7 ± 15.8	**<0.001**
eGFRcys/eGFRcre	1.10 ± 0.17	1.07 ± 0.17	1.12 ± 0.17	**<0.001**
Red blood cell (×104/μL)	439.5 ± 43.8	452.7 ± 48.5	432.9 ± 39.6	**<0.001**
Hemoglobin (g/dL)	13.5 ± 1.3	14.2 ± 1.5	13.2 ± 1.1	**<0.001**
Hematocrit (%)	40.8 ± 3.7	42.4 ± 4.0	40.1 ± 3.2	**<0.001**
Total protein (g/dL)	7.35 ± 0.47	7.33 ± 0.44	7.37 ± 0.39	**<0.001**
Albumin (g/dL)	4.32 ± 0.32	4.29 ± 0.31	4.34 ± 0.27	**<0.001**
Number of teeth, n	20.1 ± 8.8	19.6 ± 9.4	20.3 ± 8.5	0.357
Tongue pressure (kPa)	33.5 ± 8.6	34.3 ± 9.0	33.1 ± 8.3	**0.038**
Low articulatory oral motor skills (times/s)	6.05 ± 0.97	5.84 ± 1.12	6.16 ± 0.87	**<0.001**
Item of oral frailty				
Fewer teeth	316(33.8)	113(36.1)	203(32.7)	0.306
Difficulty in chewing	185(19.8)	51(16.3)	134(21.6)	0.056
Difficulty in swallowing	241(25.8)	65(20.8)	176(28.3)	**0.014**
Dry mouth	288(30.8)	73(23.2)	215(34.6)	**<0.001**
Low articulatory oral motor skills	336(36.0)	135(43.1)	201(32.4)	**0.002**
OF-5 score	1.46 ± 1.20	1.40 ± 1.11	1.50 ± 1.24	0.482
0, n(%)	227(24.3)	77(24.6)	150(24.2)	0.872
1, n(%)	296(31.7)	97(31.0)	199(32.0)	0.766
2, n(%)	234(25.0)	92(29.4)	142(22.9)	**0.031**
3, n(%)	117(12.6)	33(10.8)	84(13.5)	0.210
4, n(%)	49(5.2)	13(4.2)	36(5.8)	0.352
5, n(%)	11(1.2)	1(0.3)	10(1.6)	0.111
Oral frailty status				
Oral non-frailty, 0–1 OF-5 score, n(%)	523(56.0)	174(55.6)	349(56.2)	0.889
Oral frailty, ≥2 OF-5 score, n(%)	411(44.0)	139(44.4)	272(43.8)	
Item of frailty (J-CHS)				
Shrinking, n(%)	140(15.0)	47(15.0)	93(15.0)	1.000
Weakness (grip strength < 28 kg in men or 18 kg in women), n(%)	95(10.1)	25(8.0)	70(11.3)	0.136
Exhaustion, n(%)	223(23.9)	61(19.5)	162(26.0)	**0.028**
Slowness (gait speed < 1.0 m/s), n(%)	41(4.4)	14(4.5)	27(4.3)	1.000
Low activity, n(%)	261(27.9)	97(31.0)	164(26.4)	0.143
Frailty status (J-CHS criteria)				
Robust, n(%)	405(43.4)	138(44.1)	267(43.0)	0.780

Table 1. *Cont.*

	Total (n = 934)	Men (n = 313)	Women (n = 621)	*p*
Pre-frailty, n(%)	488(52.2)	165(52.7)	323(52.0)	0.890
Frailty, n(%)	41(4.4)	10(3.2)	31(5.0)	0.239
Sarcopenia status (AWGS criteria)				
Sarcopenia	67(7.2)	22(7.0)	45(7.2)	1.000
Non-sarcopenia	867(92.8)	291(93.0)	576(92.8)	

Cre, creatinine; CysC, cystatin C; eGFRcys, cystatin-based estimated glomerular filtration rate; eGFRcre, creatinine-based estimated glomerular filtration rate; OF-5, oral frailty five-item checklist; J-CHS, Japanese Cardiovascular Health Study criteria. The *p*-value represents the significant difference between women and men.

Using the J-CHS criteria for the diagnosis of physical frailty, more than half of the participants in both men and women were categorized as prefrail, while 4.4% of the overall population were diagnosed as frail (3.2% in men and 5.0% in women). A typical phenotype of physical frailty is age-related muscle loss, known as sarcopenia. Using the AWGS2019 diagnostic criteria for Asians, the prevalence of sarcopenia was estimated to be approximately 7% in both men and women, with no significant gender differences.

A score of ≥2 on the OF-5 indicates a diagnosis of oral frailty, which is associated with older age, shorter height, lower muscle mass and strength, and reduced physical functions, such as walking speed, TUG, and the 5CS test. Tongue pressure, number of teeth, and ODK were also reduced in individuals with oral frailty. The prevalence of sarcopenia was observed to be higher in both men and women with oral frailty. However, the difference was not statistically significant in men. Overall, the findings suggest that sarcopenia exhibits a similar trend to physical frailty (Table 2).

Table 2. Comparison of physical and oral function according to oral frailty status in men and women.

	Men (n = 313)			Women (n = 621)		
	Oral Non-Frailty, 0–1 OF-5 Score (n = 174)	**Oral Frailty, ≥2 OF-5 Score (n = 139)**	***p***	**Oral Non-Frailty, 0–1 OF-5 Score (n = 349)**	**Oral Frailty, ≥2 OF-5 Score (n = 272)**	***p***
Age (years)	73.7 ± 5.4	76.0 ± 6.2	**<0.001**	72.1 ± 5.3	75.5 ± 5.9	**<0.001**
Height (cm)	164.6 ± 5.9	163.1 ± 6.2	**0.018**	151.8 ± 5.3	150.2 ± 5.6	**<0.001**
Body weight (kg)	63.2 ± 8.6	61.6 ± 9.1	0.107	51.6 ± 7.4	50.6 ± 6.7	0.103
Body mass index	23.3 ± 2.6	23.2 ± 3.1	0.715	22.4 ± 2.9	22.5 ± 3.0	0.639
Skeletal muscle mass (SMM) (kg)	20.3 ± 2.8	19.3 ± 2.7	**0.001**	13.9 ± 1.9	13.3 ± 2.0	**<0.001**
Skeletal muscle mass index (SMI)	7.48 ± 0.71	7.24 ± 0.74	**0.005**	6.00 ± 0.58	5.88 ± 0.59	**0.014**
Body fat mass (kg)	14.6 ± 4.9	15.1 ± 5.7	0.453	15.7 ± 5.5	15.6 ± 5.1	0.894
Percentage of BFM (%)	22.7 ± 5.6	23.8 ± 6.6	0.095	29.6 ± 7.0	30.1 ± 6.8	0.339
Grip power (kg)	35.7 ± 6.3	33.2 ± 6.5	**<0.001**	23.5 ± 4.2	21.7 ± 4.1	**<0.001**
Knee extension muscle strength (Nm)	446.1 ± 110.9	406.9 ± 115.3	**0.002**	304.0 ± 74.1	271.7 ± 90.6	**<0.001**
Normal gait speed (m/s)	1.42 ± 0.24	1.35 ± 0.24	**0.007**	1.47 ± 0.23	1.38 ± 0.24	**<0.001**
Maximal gait speed (m/s)	2.00 ± 0.32	1.86 ± 0.34	**<0.001**	1.90 ± 0.28	1.76 ± 0.31	**<0.001**
Timed Up and Go test (TUG)	6.02 ± 1.64	6.65 ± 2.19	**0.004**	6.03 ± 1.21	6.75 ± 1.68	**<0.001**
Five-time chair stand test (5CS)	7.25 ± 2.49	8.71 ± 6.51	**0.007**	6.90 ± 3.36	7.91 ± 4.21	**<0.001**
Cre (mg/dL)	0.91 ± 0.21	0.88 ± 0.19	0.203	0.66 ± 0.13	0.68 ± 0.14	0.931
CysC (mg/L)	1.01 ± 0.23	1.04 ± 0.25	0.134	0.89 ± 0.28	0.93 ± 0.19	0.042
Cre/CysC	0.91 ± 0.12	0.86 ± 0.13	**<0.001**	0.76 ± 0.11	0.73 ± 0.10	**0.001**
eGFRcre (mL/min/1.73 m^2)	65.8 ± 14.5	66.7 ± 13.3	0.562	68.3 ± 13.9	66.3 ± 14.2	0.085

Table 2. *Cont.*

	Men (n = 313)			Women (n = 621)		
	Oral Non-Frailty, 0–1 OF-5 Score (n = 174)	**Oral Frailty, ≥2 OF-5 Score (n = 139)**	***p***	**Oral Non-Frailty, 0–1 OF-5 Score (n = 349)**	**Oral Frailty, ≥2 OF-5 Score (n = 272)**	***p***
eGFRcys (mL/min/1.73 m^2)	72.2 ± 16.5	68.5 ± 16.3	**0.049**	77.1 ± 15.6	71.7 ± 15.4	<0.001
eGFRcys/eGFRcre	1.11 ± 0.16	1.03 ± 0.18	**<0.001**	1.14 ± 0.17	1.09 ± 0.17	<0.001
Red blood cell (×10^4/μL)	453.3 ± 47.9	452.0 ± 49.4	0.823	436.2 ± 37.2	428.7 ± 42.1	0.020
Hemoglobin (g/dL)	14.2 ± 1.4	14.2 ± 1.6	0.826	13.3 ± 1.1	13.1 ± 1.1	0.012
Hematocrit (%)	42.4 ± 3.7	42.4 ± 4.3	0.968	40.3 ± 3.1	39.8 ± 3.3	**0.041**
Total protein (g/dL)	7.28 ± 0.43	7.36 ± 0.77	**0.029**	7.39 ± 0.39	7.35 ± 0.39	0.189
Albumin (g/dL)	4.28 ± 0.31	4.29 ± 0.48	0.286	4.36 ± 0.25	4.31 ± 0.29	**0.017**
Tongue pressure (kPa)	35.3 ± 8.4	33.1 ± 9.6	**0.032**	33.7 ± 7.5	32.4 ± 9.1	0.066
Number of teeth, n	23.0 ± 7.5	15.3 ± 10.0	**<0.001**	23.4 ± 6.5	16.4 ± 9.1	**<0.001**
Fewer teeth	27(15.8)	87(62.1)		48(13.8)	155(57.0)	
Low articulatory oral motor skills (times/s)	6.21 ± 0.88	5.37 ± 1.20	**<0.001**	6.22 ± 0.74	5.82 ± 0.92	**<0.001**
Low articulatory oral motor skills	37(21.6)	99(70.7)	**<0.001**	56(16.0)	145(53.3)	**<0.001**
Item of frailty (J-CHS criteria)						
Shrinking	23(13.2)	24(17.3)	0.342	40(11.4)	53(19.4)	**0.006**
Weakness (Grip strength < 28 kg in men or 18 kg in women), n(%)	9(5.2)	16(11.5)	0.057	24(6.9)	46(16.9)	**<0.001**
Exhaustion, n(%)	19(10.9)	42(30.2)	**<0.001**	64(18.3)	98(36.0)	**<0.001**
Slowness (Gait speed < 1.0 m/s), n(%)	6(3.4)	8(5.8)	0.412	11(3.2)	16(5.9)	0.114
Low activity, n(%)	47(27.0)	50(31.0)	0.110	64(18.3)	71(26.1)	**0.024**
Frailty status (J-CHS criteria)						
Robust, n(%)	92(52.9)	46(33.1)	**<0.001**	91(33.5)	176(50.4)	**<0.001**
Pre-frailty, n(%)	79(45.4)	86(61.9)	**0.004**	159(58.5)	164(47.0)	**<0.001**
Frailty, n(%)	3(1.7)	7(5.0)	0.115	22(8.0)	9(2.6)	0.097
Sarcopenia status (AWGS criteria)						
Sarcopenia, n(%)	6(3.4)	16(11.5)	0.120	17(4.9)	28(10.3)	**0.012**
Non-sarcopenia, n(%)	94(96.6)	123(88.5)		332(95.1)	244(89.7)	

Cre, creatinine; CysC, cystatin C; eGFRcys, cystatin-based estimated glomerular filtration rate; eGFRcre, creatinine-based estimated glomerular filtration rate; OF-5, oral frailty five-item checklist; J-CHS, Japanese Cardiovascular Health Study criteria.

Cystatin-C-related indices, including the Cre/CysC ratio and eGFRcys, which we have previously reported, were lower in individuals of both sexes with oral frailty [21]. Additionally, hemoglobin and albumin levels were lower in women with oral frailty. Both men and women with oral frailty were less robust and had more pre-frailty; however, owing to the small number of frail individuals, the difference was not significant in the amount of frailty.

A longitudinal study involving 329 participants (105 men and 224 women) revealed changes in oral function between the first and second follow-up surveys. Two to three years passed between the first and second follow-ups, during which no significant changes were observed in body size, grip strength, walking speed, SMI, or other parameters. However, cystatin-C-related indices (Cre/CysC, eGFRcys, and eGFRcys/eGFRcre) were significantly lower at the second follow-up in both men and women. In the second follow-up survey, albumin levels and tongue pressure did not significantly decrease in men but did show a significant decrease in women. According to the J-CHS frailty criteria, there was a tendency

for a decrease in pre-frailty among women during the second follow-up. Approximately half of the participants, both men and women, showed no changes in the relevant J-CHS items, whereas approximately a quarter showed either improvement or worsening (Table 3).

Table 3. Changes in physical and oral function from baseline to follow-up according to sex.

	Men (n = 105)			**Women (n = 224)**		
	First Survey	**Second Survey**	***p***	**First Survey**	**Second Survey**	***p***
Number of days to second survey	955.1 ± 351.7			985.5 ± 348.0		
Age (years)	73.6 ± 5.8	76.2 ± 5.9	**0.001**	72.1 ± 5.4	74.8 ± 5.4	**<0.001**
Height (cm)	164.1 ± 6.5	163.6 ± 6.6	0.566	151.4 ± 5.2	150.8 ± 5.3	0.252
Body weight (kg)	63.2 ± 8.5	62.3 ± 9.0	0.440	51.4 ± 6.6	51.1 ± 6.8	0.618
Body mass index	23.4 ± 2.6	23.2 ± 2.8	0.585	22.5 ± 2.8	22.5 ± 2.9	0.912
Skeletal muscle mass index (SMI)	7.44 ± 0.67	7.33 ± 0.70	0.242	5.93 ± 0.56	5.89 ± 0.58	0.397
Grip power (kg)	35.8 ± 7.1	34.2 ± 6.7	0.087	23.2 ± 4.2	22.8 ± 3.8	0.311
Normal gait speed (m/s)	1.39 ± 0.23	1.35 ± 0.25	0.249	1.44 ± 0.23	1.40 ± 0.23	0.117
Cre (mg/dL)	0.91 ± 0.19	0.92 ± 0.23	0.564	0.66 ± 0.14	0.69 ± 0.17	0.140
CysC (mg/L)	1.00 ± 0.22	1.09 ± 0.30	**0.017**	0.89 ± 0.17	0.95 ± 0.23	**0.001**
Cre/CysC	0.92 ± 0.13	0.86 ± 0.12	**0.001**	0.75 ± 0.10	0.72 ± 0.10	**0.005**
eGFRcre (mL/min/1.73 m^2)	65.8 ± 13.5	64.4 ± 13.5	0.453	68.6 ± 13.3	66.2 ± 13.4	0.052
eGFRcys (mL/min/1.73 m^2)	72.7 ± 15.6	66.2 ± 15.3	**0.003**	76.2 ± 14.6	70.3 ± 13.9	**<0.001**
eGFRcys/eGFRcre	1.12 ± 0.18	1.03 ± 0.16	**<0.001**	1.12 ± 0.17	1.07 ± 0.16	**0.002**
Hemoglobin (g/dL)	14.2 ± 1.4	14.0 ± 1.4	0.227	13.2 ± 1.0	13.1 ± 1.0	0.087
Albumin (g/dL)	4.3 ± 0.3	4.2 ± 0.3	0.128	4.4 ± 0.3	4.3 ± 0.3	**<0.001**
Number of teeth, n	20.7 ± 8.8	19.6 ± 8.8	0.380	21.1 ± 8.2	20.2 ± 8.3	0.271
Tongue pressure (kPa)	34.8 ± 8.8	34.4 ± 9.2	0.734	33.4 ± 8.5	31.8 ± 8.5	**0.040**
Low articulatory oral motor skills (times/s)	5.83 ± 1.12	5.98 ± 1.08	0.329	6.18 ± 0.80	6.13 ± 0.94	0.575
Item of oral frailty						
Fewer teeth, n(%)	36(34.3)	40(38.1)	0.667	67(29.9)	74(33.0)	0.542
Difficulty in chewing, n(%)	18(17.1)	26(24.8)	0.235	42(18.8)	47(21.0)	0.542
Difficulty in swallowing, n(%)	24(22.9)	29(27.6)	0.525	63(28.1)	61(27.2)	0.636
Dry mouth, n(%)	25(23.8)	30(28.6)	0.530	70(31.3)	73(32.7)	0.916
Low articulatory oral motor skills, n(%)	47(44.8)	35(33.3)	0.120	74(33.0)	76(33.9)	0.762
OF-5 score	1.43 ± 1.03	1.52 ± 1.13	0.523	1.41 ± 1.22	1.48 ± 1.20	0.559
0, n(%)	21(20.0)	21(20.0)	1.000	62(27.7)	50(22.3)	0.230
1, n(%)	36(34.3)	33(31.4)	0.663	69(30.8)	79(35.3)	0.318
2, n(%)	33(31.4)	32(30.5)	1.000	47(21.0)	50(22.3)	0.819
3, n(%)	12(11.4)	14(13.3)	0.835	33(14.7)	32(14.3)	1.000
4, n(%)	3(2.9)	4(3.8)	1.000	11(4.9)	9(4.0)	0.820
5, n(%)	0	1(1.0)	1.000	2(0.9)	4(1.8)	0.685
Oral frailty states						
Oral non-frailty, 0–1 OF-5 score, n(%)	57(54.9)	54(51.4)	0.782	131(58.7)	129(57.8)	0.849
Oral frailty, ≥2 OF-5 score, n(%)	48(45.7)	51(48.5)		92(41.3)	94(42.2)	
Item of frailty (J-CHS criteria)						
Shrinking	17(16.2)	17(16.2)	1.000	35(15.6)	33(14.7)	0.895
Weakness (grip strength < 28 kg in men or 18 kg in women)	7(6.7)	15(14.3)	0.113	16(7.2)	20(8.9)	0.603

Table 3. *Cont.*

	Men (n = 105)			Women (n = 224)		
	First Survey	**Second Survey**	***p***	**First Survey**	**Second Survey**	***p***
Exhaustion	18(17.1)	22(21.0)	0.598	49(21.9)	56(25.0)	0.504
Slowness (gait speed < 1.0 m/s)	4(3.8)	8(7.6)	0.373	6(2.7)	11(4.9)	0.323
Low activity	36(34.3)	23(21.9)	0.065	74(33.0)	41(18.3)	**<0.001**
J-CHS frailty status						
Robust, n(%)	43(41.0)	45(42.9)	0.889	92(41.1)	111(49.6)	0.088
Pre-frailty, n(%)	60(57.1)	58(55.2)	0.889	125(55.8)	99(44.2)	**0.014**
Frailty, n(%)	2(1.9)	2(1.9)	1.000	7(3.1)	14(6.2)	0.179
J-CHS change category						
Improved, n(%)	27(25.7)			61(27.2)		
Unchanged, n(%)	51(48.6)			116(51.8)		
Worsened, n(%)	27(25.7)			47(21.0)		

Cre, creatinine; CysC, cystatin C; eGFRcys, cystatin-based estimated glomerular filtration rate; eGFRcre, creatinine-based estimated glomerular filtration rate; OF-5, oral frailty five-item checklist; J-CHS, Japanese Cardiovascular Health Study criteria.

We also analyzed the baseline characteristics of the groups classified as improved/unchanged and worsened. In men, lower grip strength and fewer teeth at baseline were associated with disease worsening. In those who worsened, an OF-5 score of $\geq$2 at baseline was common, and many patients were assessed as having oral frailty at the first time point. Among women, swallowing and chewing problems were more frequently reported at baseline in the worsened group, although the only significant sex difference was observed in the total OF-5 scores. In summary, individuals with higher baseline OF-5 scores were more likely to experience worsening J-CHS scores at the second time point (Table 4).

Table 4. Baseline characteristics and oral frailty according to frailty progression status in men and women.

Results of First Survey	Men (n = 105)			Women (n = 224)		
	Improved or Unchanged (n = 78)	**Worsened (n = 27)**	***p***	**Improved or Unchanged (n = 177)**	**Worsened (n = 47)**	***p***
Age (years)	73.1 ± 5.7	75.1 ± 5.9	0.108	71.9 ± 5.4	73.2 ± 5.1	0.125
Height (cm)	164.3 ± 6.6	163.4 ± 6.2	0.544	151.5 ± 5.1	150.8 ± 5.6	0.426
Body weight (kg)	63.1 ± 8.3	63.6 ± 9.1	0.788	51.2 ± 6.5	52.4 ± 6.8	0.250
Body mass index	23.3 ± 2.5	23.8 ± 3.0	0.452	22.3 ± 2.8	23.0 ± 2.8	0.106
Skeletal muscle mass index (SMI)	7.48 ± 0.65	7.32 ± 0.70	0.276	5.93 ± 0.54	5.95 ± 0.67	0.784
Grip power (kg)	36.7 ± 7.4	33.2 ± 5.6	**0.027**	1.45 ± 0.22	1.44 ± 0.24	0.810
Normal gait speed (m/s)	1.41 ± 0.23	1.34 ± 0.22	0.215	23.3 ± 4.3	22.5 ± 3.6	0.239
Cre (mg/dL)	0.91 ± 0.19	0.91 ± 0.17	0.930	0.66 ± 0.13	0.67 ± 0.17	0.818
CysC (mg/L)	0.99 ± 0.22	1.04 ± 0.20	0.276	0.89 ± 0.16	0.91 ± 0.21	0.418
Cre/CysC	0.93 ± 0.13	0.88 ± 0.14	0.162	0.75 ± 0.10	0.74 ± 0.11	0.426
eGFRcre (mL/min/1.73 m^2)	66.2 ± 14.0	64.6 ± 12.0	0.613	68.5 ± 12.9	69.1 ± 14.9	0.765
eGFRcys (mL/min/1.73 m^2)	74.1 ± 15.9	62.4 ± 14.3	0.111	76.5 ± 14.0	75.2 ± 16.8	0.615
eGFRcys/eGFRcre	1.13 ± 0.18	1.07 ± 0.19	0.158	1.13 ± 0.17	1.10 ± 0.17	0.273
Hemoglobin (g/dL)	14.3 ± 1.5	14.0 ± 1.1	0.282	13.2 ± 1.0	13.2 ± 1.1	0.715
Albumin (g/dL)	4.3 ± 0.3	4.2 ± 0.3	0.289	4.4 ± 0.2	4.3 ± 0.3	0.807
Number of teeth, n	21.2 ± 8.7	19.2 ± 9.0	0.304	21.4 ± 8.2	19.9 ± 8.3	0.247
Tongue pressure (kPa)	35.6 ± 9.2	32.6 ± 7.4	0.141	33.3 ± 8.3	34.0 ± 9.3	0.635

Table 4. *Cont.*

Results of First Survey	Men (n = 105)			Women (n = 224)		
	Improved or Unchanged (n = 78)	**Worsened (n = 27)**	***p***	**Improved or Unchanged (n = 177)**	**Worsened (n = 47)**	***p***
Low articulatory oral motor skills (times/s)	5.86 ± 1.11	5.75 ± 1.13	0.658	6.22 ± 0.82	6.02 ± 0.74	0.127
Item of oral frailty						
Fewer teeth, n(%)	22(28.2)	14(51.9)	**0.035**	51(28.8)	16(34.0)	0.480
Difficulty in chewing, n(%)	12(15.4)	6(22.2)	0.554	28(15.8)	14(29.8)	**0.036**
Difficulty in swallowing, n(%)	16(20.5)	8(29.6)	0.425	43(24.3)	20(43.6)	**0.018**
Dry mouth, n(%)	17(21.8)	8(29.6)	0.438	52(29.4)	18(38.3)	0.076
Low articulatory oral motor skills, n(%)	34(43.6)	13(48.1)	0.823	58(32.8)	16(34.0)	0.863
OF-5 score	**1.29 ± 1.01**	**1.81 ± 1.00**	**0.023**	**1.31 ± 1.17**	**1.79 ± 1.37**	**0.017**
0, n(%)	17(21.8)	4(14.8)	0.580	53(29.9)	9(19.1)	0.199
1, n(%)	32(41.0)	4(14.8)	**0.018**	54(30.5)	15(31.9)	0.860
2, n(%)	21(26.9)	12(44.4)	0.099	40(22.6)	7(14.9)	0.315
3, n(%)	5(6.4)	7(25.9)	**0.011**	24(13.6)	9(19.1)	0.357
4, n(%)	3(3.8)	0(0.0)	0.568	4(2.3)	7(14.9)	**0.002**
5, n(%)	0(0.0)	0(0.0)	1.000	2(1.1)	0(0.0)	1.000
Oral frailty states						
Oral non-frailty, 0–1 OF-5 score, n(%)	49(62.8)	8(29.6)	**0.004**	107(60.5)	24(51.0)	0.250
Oral frailty, ≥2 OF-5 score, n(%)	29(37.2)	19(70.4)		70(39.5)	23(49.0)	

Cre, creatinine; CysC, cystatin C; eGFRcys, cystatin-based estimated glomerular filtration rate; eGFRcre, creatinine-based estimated glomerular filtration rate; OF-5, oral frailty five-item checklist.

Univariate logistic regression analysis was conducted to calculate the odds ratios for each indicator at baseline in the worsening group in the second survey. For men, significant associations were found between reduced grip strength and tooth loss, whereas an OF-5 score of ≥2 and a diagnosis of oral frailty at the first visit were also significant worsening risk factors. Significant associations were observed between decreased chewing ability and swallowing function in the women. The OF-5 score was a significant worsening risk factor in both men and women; however, in women, there was no significant difference in those with an OF-5 score ≥2 (Table 5A).

Table 5. Regression analysis.

Variables	Men		Women	
	OR (95%CI)	***p* Value**	**OR (95%CI)**	***p* Value**
A. Univariate logistic regression analysis for baseline factors predicting worsening frailty according to sex				
Age (per 1SD)	1.43(0.92–2.22)	0.108	1.28(0.93–1.75)	0.129
Body mass index (per 1SD)	1.18(0.77–1.82)	0.450	1.30(0.94–1.78)	0.108
Skeletal muscle mass index (SMI) (per 1SD)	0.78(0.49–1.22)	0.268	1.05(0.76–1.44)	0.783
Grip power (per 1SD)	**0.57(0.34–0.95)**	**0.022**	0.82(0.58–1.14)	0.232
Normal gait speed (per 1SD)	0.76(0.49–1.18)	0.213	0.97(0.70–1.33)	0.837
Cre/CysC (per 1SD)	0.71(0.44–1.15)	0.149	0.87(0.63–1.22)	0.420
eGFRcys/eGFRcre (per 1SD)	0.71(0.44–1.15)	0.145	0.83(0.59–1.16)	0.265
Hemoglobin (per 1SD)	0.79(0.52–1.21)	0.285	0.94(0.68–1.30)	0.714
Albumin (per 1SD)	0.79(0.51–1.22)	0.287	0.96(0.70–1.33)	0.806
Number of teeth (per 1SD)	0.80(0.53–1.22)	0.307	0.84(0.62–1.13)	0.255

Table 5. *Cont.*

Variables	Men		Women	
	OR (95%CI)	***p* Value**	**OR (95%CI)**	***p* Value**
Tongue pressure (per 1SD)	0.72(0.46–1.12)	0.139	1.08(0.78–1.50)	0.632
Low articulatory oral motor skills (per 1SD)	0.91(0.59–1.40)	0.657	0.78(0.57–1.07)	0.128
Item of oral frailty				
Fewer teeth (absence = 0, presence = 1)	**2.74(1.11–6.75)**	**0.028**	1.28(0.64–2.53)	0.487
Difficulty in chewing (absence = 0, presence = 1)	1.57(0.53–4.70)	0.427	**2.26(1.07–4.75)**	**0.037**
Difficulty in swallowing (absence = 0, presence = 1)	1.63(0.60–4.40)	0.340	**2.31(1.18–4.52)**	**0.015**
Dry mouth (absence = 0, presence = 1)	1.51(0.56–4.05)	0.418	1.49(0.76–2.92)	0.297
Low articulatory oral motor skills (absence = 0, presence = 1)	1.20(0.50–2.89)	0.682	1.06(0.54–2.09)	0.869
OF-5 score (per 1 point)	**1.65(1.06–2.57)**	**0.023**	**1.36(1.05–1.76)**	**0.019**
Oral frailty states				
Oral frailty, ≥2 OF-5 score (absence = 0, presence = 1)	**4.01(1.56–10.33)**	**0.004**	1.46(0.77–2.80)	0.248
B. Multivariate logistic regression analysis for baseline factors associated with worsening of frailty according to sex				
Age (per 1SD)	0.98(0.56–1.70)	0.934	1.15(0.81–1.64)	0.436
Body mass index (per 1SD)	1.53(0.82–2.84)	0.172	1.39(0.88–2.20)	0.156
Grip power (per 1SD)	0.62(0.34–1.13)	0.106	0.96(0.64–1.42)	0.820
Normal gait speed (per 1SD)	0.86(0.53–1.42)	0.564	1.13(0.80–1.62)	0.479
Skeletal muscle mass index (SMI) (per 1SD)	0.82(0.39–1.71)	0.592	0.86(0.54–1.37)	0.536
Cre/CysC (per 1SD)	0.91(0.53–1.58)	0.740	1.03(0.72–1.49)	0.863
OF-5 score (per 1 point)	1.49(0.91–2.45)	0.107	**1.32(1.00–1.75)**	**0.049**
C. Multivariate logistic regression analysis for baseline factors associated with worsening of frailty in men				
Age (per 1SD)	0.96(0.55–1.69)	0.894		
Body mass index (per 1SD)	1.50(0.80–2.82)	0.209		
Grip power (per 1SD)	0.61(0.33–1.11)	0.097		
Normal gait speed (per 1SD)	0.87(0.52–1.44)	0.582		
Skeletal muscle mass index (SMI) (per 1SD)	0.83(0.39–1.75)	0.622		
Cre/CysC (per 1SD)	0.94(0.54–1.64)	0.830		
Oral frailty states				
Oral frailty, ≥2 OF-5 score (absence = 0, presence = 1)	**3.38(1.23–9.28)**	**0.018**		

OR, odds ratio; CI, confidence interval; SD, standard deviation; Cre, creatinine; CysC, cystatin C; eGFRcys, cystatin-based estimated glomerular filtration rate; eGFRcre, creatinine-based estimated glomerular filtration rate; OF-5, oral frailty five-item checklist.

A multivariate logistic regression analysis was performed using age, BMI, grip strength, gait speed, SMI, Cre/CysC ratio, and OF-5 score, which are associated with frailty and sarcopenia, as explanatory variables. In men, grip strength was identified as a significant risk factor in univariate analysis; consequently, OF-5 score did not remain a significant risk factor in multivariate analysis. However, in women, the OF-5 score remained a significant risk factor (Table 5B).

The same multivariate logistic regression analysis was repeated for men by adjusting the OF-5 score to ≥2, and a significant difference remained (Table 5C).

4. Discussion

This study offers a comprehensive examination of sex-specific differences in oral frailty and related factors in a cohort of older adults, highlighting the important aspects of oral and physical function. Oral dysfunction is regarded as a significant contributor to systemic decline. Oral frailty is defined as a mild decline in oral functions during the early and

reversible stages of frailty. Many community-dwelling older people have reduced oral function or oral hypofunction, which is significantly associated with frailty and aging. Appropriate evaluation of oral function and effective intervention to suppress oral function deterioration may be effective in extending the healthy life expectancy of older people [34].

Frailty, in contrast, is considered a state of increased vulnerability to disease onset and physical dysfunction due to a decline in several functions associated with aging. Sarcopenia, a state of reduced muscle mass, is a typical physical frailty phenotype. The prevalence of oral frailty is similar between men and women, affecting >40% of the population. The 40% prevalence of oral frailty was in agreement with several previous reports [4,35,36].

Women tended to report more fatigue and anemia, whereas men reported greater muscle strength, muscle mass, and tongue pressure. These findings underscore the need to consider sex-based physiological differences when evaluating frailty and sarcopenia, particularly oral-health-related parameters.

One of the key results of this study was the significant association between oral frailty and reduced physical functions, such as walking speed, muscle mass, and tongue pressure, confirming an intricate link between systemic frailty and oral health. In both sexes, a higher OF-5 score of $\geq$2, which indicates a diagnosis of oral frailty, was correlated with diminished physical and oral functions, including grip strength and the number of teeth. These findings suggest that oral frailty can serve as a valuable early marker of declining physical capacity and could help identify individuals at risk of sarcopenia or broader systemic frailty.

The longitudinal component of this study provides further insights into the progression of oral frailty. Over a follow-up period of 2–3 years, significant declines in cystatin-C-related indices (Cre/CysC and eGFRcys) and oral functions, including tongue pressure and albumin levels, were observed, particularly in women. These changes were not accompanied by significant alterations in muscle strength, walking speed, or other systemic parameters, indicating that oral frailty may progress rapidly or independently of systemic physical decline. This underlines the importance of targeted interventions focusing on oral health to mitigate the progression of frailty.

Importantly, the logistic regression analysis identified distinct risk factors for the worsening of oral frailty. In men, reduced grip strength and tooth loss were significant predictors, consistent with previous studies linking oral health to systemic physical capacity. In contrast, impaired chewing and swallowing functions were more prominent risk factors in women, underscoring the role of oral function in overall health deterioration in older women. Notably, although the OF-5 score was a significant risk factor for worsening frailty in both sexes, its effect was more pronounced in women, suggesting a potential sex difference in the relationship between oral health and progression of systemic frailty.

Approximately one-fourth of the participants demonstrated improvements in J-CHS scores for both men and women during the second survey. Neither pharmacological nor exercise interventions specifically targeting frailty were implemented. Therefore, the observed improvement in J-CHS scores may be attributed to increased activity levels among older adults following the lifting of COVID-19-related restrictions in Japan, such as the state of emergency declarations.

This interpretation is supported by the findings in Table 3, which show a decrease in the number of participants categorized under 'Low Activity' during the second survey for both men and women. During the first survey, many older adults had limited outdoor activities due to self-imposed restrictions stemming from the pandemic. In contrast, by the second survey, a substantial number of these older adults had resumed their regular activities, potentially explaining the observed changes.

Despite these significant findings, it is important to acknowledge the limitations of this study. The sample size of frail individuals was relatively small, limiting the ability

to detect subtle differences between sexes or within subgroups. Additionally, although longitudinal data were collected, the follow-up period may not have been sufficiently long to fully capture the trajectory of oral frailty in this population. Future studies with larger, more diverse cohorts and extended follow-up periods are needed to clarify the dynamics between oral and systemic frailty, and to identify effective interventions that target both domains. Moreover, the inclusion of healthy volunteers may have influenced the representativeness of the study population. Previous reports indicated that the prevalence of frailty, according to the J-CHS criteria, is approximately 10% among older adults in the Japanese populations [37–39]. However, in this study, the prevalence of frailty was considerably lower at 3.2% for men and 5.0% for women.

During the 2–3-year observation period, no significant decline in grip strength, gait speed, or muscle mass was observed. However, even with a limited number of participants and short observation period, a diagnosis of oral frailty using the OF-5 was associated with an increase in J-CHS scores, suggesting that the OF-5 score is significantly linked to the worsening of long-term physical frailty. Oral frailty, as assessed using the OF-5, was also significantly associated with higher J-CHS scores after adjusting for age, BMI, grip strength, gait speed, SMI, and other frailty-related factors. These findings indicate that the OF-5 is a promising predictor of frailty onset. The novelty of this study lies in the significant relationship between OF-5 score and other frailty indices.

In the original article that introduced the OF-5 in 2023, difficulty in chewing, difficulty swallowing, and dry mouth were evaluated using subjective questionnaires, whereas objective data from dental examinations were used to assess the number of teeth and articulatory oral motor skills. Similarly, the present study evaluated articulatory oral-motor skills via ODK, and a dentist assessed the number of teeth, to objectively evaluate these aspects.

The results of the objective evaluation of ODK and subjective evaluation via questionnaires were in good agreement [39]. In April 2024, a joint consensus statement on "Oral Frailty" in Japan suggested that the objective assessment of ODK is no longer necessary and can be replaced with the following question: "Have you had difficulty with clear pronunciation recently?". This statement also allows for a self-reported assessment of whether respondents had >20 teeth. Future studies should investigate whether oral frailty, as assessed by the OF-5 subjective questionnaire, is associated with lower muscle mass, slower gait speed, and reduced physical function in cross-sectional studies, and whether it significantly correlates with the progression of physical frailty in longitudinal studies.

5. Conclusions

In conclusion, this study provides valuable evidence on the relationships between oral frailty, systemic frailty, and risk factors in older adults. These findings emphasize the importance of integrating oral health assessments into frailty screening protocols, particularly for older women in whom oral dysfunction may serve as an early marker of systemic health decline. These insights have implications for the development of interventions aimed at preventing or mitigating frailty and its associated adverse outcomes in aging populations.

Author Contributions: Conceptualization, H.K. (Hiroshi Kusunoki) and H.K. (Hiromitsu Kishimoto); Methodology, Y.H., K.N. and H.S.; Validation, H.K. (Hiromitsu Kishimoto); Investigation, H.K. (Hiroshi Kusunoki), Y.H., Y.N., K.S. (Kensaku Shojima), S.T., Y.W., K.T., K.N. and H.S.; Resources, H.Y., T.M., S.T., K.T. and R.M.; Data curation, H.Y., T.M., Y.W. and R.M.; Writing—original draft, H.K. (Hiroshi Kusunoki); Supervision, K.S. (Ken Shinmura). All authors have read and agreed to the published version of the manuscript.

Funding: This study was supported in part by JSPS KAKENHI (grant number: 22K19496) (2022–2024), the National Center for Geriatrics and Gerontology (Choujyu 20-1, 21-18) (2022–2023), and Health Labour Sciences Research Grant (24FA1005) (2024) (Shinmura).

Institutional Review Board Statement: The study was conducted in accordance with the Declaration of Helsinki and approved by the ethics committee of Hyogo College of Medicine (approval no. Rinhi 0342, approval date: 23 May 2017). All methods were carried out in accordance with relevant guidelines and regulations.

Informed Consent Statement: Written informed consent has been obtained from all subjects involved in the study to publish this paper.

Data Availability Statement: Data supporting the findings of this study are available from the corresponding author upon reasonable request. However, the data are not publicly available due to privacy and ethical restrictions.

Conflicts of Interest: The authors declare no conflict of interest. The funders had no role in the study design, data collection and analysis, manuscript preparation, or the decision to publish this study.

References

1. Dibello, V.; Zupo, R.; Sardone, R.; Lozupone, M.; Castellana, F.; Dibello, A.; Daniele, A.; De Pergola, G.; Bortone, I.; Lampignano, L.; et al. Oral frailty and its determinants in older age: A systematic review. *Lancet Healthy Longev.* **2021**, *2*, e507–e520. [CrossRef] [PubMed]
2. Dibello, V.; Lobbezoo, F.; Lozupone, M.; Sardone, R.; Ballini, A.; Berardino, G.; Mollica, A.; Coelho-Júnior, H.J.; De Pergola, G.; Stallone, R.; et al. Oral frailty indicators to target major adverse health-related outcomes in older age: A systematic review. *GeroScience* **2023**, *45*, 663–706. [CrossRef]
3. Tanaka, T.; Takahashi, K.; Hirano, H.; Kikutani, T.; Watanabe, Y.; Ohara, Y.; Furuya, H.; Tetsuo, T.; Akishita, M.; Iijima, K. Oral Frailty as a Risk Factor for Physical Frailty and Mortality in Community-Dwelling Elderly. *J. Gerontol. A Biol. Sci. Med. Sci.* **2018**, *73*, 1661–1667. [CrossRef] [PubMed]
4. Tanaka, T.; Hirano, H.; Ikebe, K.; Ueda, T.; Iwasaki, M.; Shirobe, M.; Minakuchi, S.; Akishita, M.; Arai, H.; Iijima, K. Oral frailty five-item checklist to predict adverse health outcomes in community-dwelling older adults: A Kashiwa cohort study. *Geriatr. Gerontol. Int.* **2023**, *23*, 651–659. [CrossRef] [PubMed]
5. Zhao, H.; Wu, B.; Zhou, Y.; Yang, Z.; Zhao, H.; Tian, Z.; Jiang, M.; Huang, D. Oral frailty: A concept analysis. *BMC Oral Health* **2024**, *24*, 594. [CrossRef]
6. Kugimiya, Y.; Iwasaki, M.; Ohara, Y.; Motokawa, K.; Edahiro, A.; Shirobe, M.; Watanabe, Y.; Obuchi, S.; Kawai, H.; Fujiwara, Y.; et al. Relationship between Oral Hypofunction and Sarcopenia in Community-Dwelling Older Adults: The Otassha Study. *Int. J. Environ. Res. Public Health* **2021**, *18*, 6666. [CrossRef] [PubMed]
7. Kawamura, K.; Maeda, K.; Miyahara, S.; Shimizu, A.; Ishida, Y.; Ueshima, J.; Nagano, A.; Kagaya, H.; Matsui, Y.; Arai, H.; et al. Association between oral frailty and sarcopenia among frailty clinic outpatients: A cross-sectional study. *Nutrition* **2024**, *124*, 112438. [CrossRef] [PubMed]
8. Tanaka, T.; Hirano, H.; Ikebe, K.; Ueda, T.; Iwasaki, M.; Minakuchi, S.; Arai, H.; Akishita, M.; Kozaki, K.; Iijima, K. Consensus statement on "Oral frailty" from the Japan Geriatrics Society, the Japanese Society of Gerodontology, and the Japanese Association on Sarcopenia and Frailty. *Geriatr. Gerontol. Int.* **2024**, *24*, 1111–1119. [CrossRef]
9. Kusunoki, H.; Hasegawa, Y.; Tsuji, S.; Wada, Y.; Tamaki, K.; Nagai, K.; Mori, T.; Matsuzawa, R.; Kishimoto, H.; Shimizu, H.; et al. Relationships between cystatin C and creatinine-based eGFR with low tongue pressure in Japanese rural community-dwelling older adults. *Clin. Exp. Dent. Res.* **2022**, *8*, 1259–1269. [CrossRef] [PubMed]
10. Nomura, Y.; Ishii, Y.; Suzuki, S.; Morita, K.; Suzuki, A.; Suzuki, S.; Tanabe, J.; Ishiwata, Y.; Yamakawa, K.; Chiba, Y.; et al. Nutritional Status and Oral Frailty: A Community Based Study. *Nutrients* **2020**, *12*, 2886. [CrossRef]
11. Tanaka, T.; Hirano, H.; Ohara, Y.; Nishimoto, M.; Iijima, K. Oral Frailty Index-8 in the risk assessment of new-onset oral frailty and functional disability among community-dwelling older adults. *Arch. Gerontol. Geriatr.* **2021**, *94*, 104340. [CrossRef] [PubMed]
12. Watanabe, D.; Yoshida, T.; Watanabe, Y.; Yokoyama, K.; Yamada, Y.; Kikutani, T.; Yoshida, M.; Miyachi, M.; Kimura, M. Oral frailty is associated with mortality independently of physical and psychological frailty among older adults. *Exp. Gerontol.* **2024**, *191*, 112446. [CrossRef]
13. Hart, A.; Paudel, M.L.; Taylor, B.C.; Ishani, A.; Orwoll, E.S.; Cawthon, P.M.; Ensrud, K.E.; Osteoporotic Fractures in Men Study Group. Cystatin C and frailty in older men. *J. Am. Geriatr. Soc.* **2013**, *61*, 1530–1536. [CrossRef] [PubMed]

14. He, Q.; Jiang, J.; Xie, L.; Zhang, L.; Yang, M. A sarcopenia index based on serum creatinine and cystatin C cannot accurately detect either low muscle mass or sarcopenia in urban community-dwelling older people. *Sci. Rep.* **2018**, *8*, 11534. [CrossRef]
15. Kashani, K.; Sarvottam, K.; Pereira, N.L.; Barreto, E.F.; Kennedy, C.C. The sarcopenia index: A novel measure of muscle mass in lung transplant candidates. *Clin. Transplant.* **2018**, *32*, e13182. [CrossRef] [PubMed]
16. Komorita, Y.; Iwase, M.; Fujii, H.; Ide, H.; Ohkuma, T.; Jodai-Kitamura, T.; Sumi, A.; Yoshinari, M.; Nakamura, U.; Kitazono, T. The serum creatinine to cystatin C ratio predicts bone fracture in patients with type 2 diabetes: The Fukuoka Diabetes Registry. *Diabetes Res. Clin. Pract.* **2018**, *146*, 202–210. [CrossRef] [PubMed]
17. Kusunoki, H.; Tsuji, S.; Kusukawa, T.; Wada, Y.; Tamaki, K.; Nagai, K.; Itoh, M.; Sano, K.; Amano, M.; Maeda, H.; et al. Relationships between cystatin C- and creatinine-based eGFR in Japanese rural community-dwelling older adults with sarcopenia. *Clin. Exp. Nephrol.* **2020**, *25*, 231–239. [CrossRef] [PubMed]
18. Kusunoki, H.; Tabara, Y.; Tsuji, S.; Wada, Y.; Tamaki, K.; Nagai, K.; Itoh, M.; Sano, K.; Amano, M.; Maeda, H.; et al. Estimation of Muscle Mass Using Creatinine/Cystatin C Ratio in Japanese Community-Dwelling Older People. *J. Am. Med. Dir. Assoc.* **2021**, *23*, 902.e21–902.e31. [CrossRef]
19. Hirai, K.; Tanaka, A.; Homma, T.; Goto, Y.; Akimoto, K.; Uno, T.; Yoshitaka, U.; Miyata, Y.; Inoue, H.; Ohta, S.; et al. Serum creatinine/cystatin C ratio as a surrogate marker for sarcopenia in patients with chronic obstructive pulmonary disease. *Clin. Nutr.* **2021**, *40*, 1274–1280. [CrossRef]
20. Yoshida, S.; Nakayama, Y.; Nakayama, J.; Chijiiwa, N.; Ogawa, T. Assessment of sarcopenia and malnutrition using estimated GFR ratio (eGFRcys/eGFR) in hospitalized adult patients. *Clin. Nutr. ESPEN* **2022**, *48*, 456–463. [CrossRef]
21. Kusunoki, H.; Ekawa, K.; Kato, N.; Yamasaki, K.; Motone, M.; Shinmura, K.; Yoshihara, F.; Shimizu, H. Association between oral frailty and cystatin C-related indices-A questionnaire (OFI-8) study in general internal medicine practice. *PLoS ONE* **2023**, *18*, e0283803. [CrossRef]
22. Suzuki, N.; Goto, A.; Yokokawa, H.; Yasumura, S. Changes in ability- and performance-based IADL among community-dwelling elderly. *Nihon Ronen Igakkai Zasshi* **2009**, *46*, 47–54. [CrossRef] [PubMed]
23. Suzuki, N.; Makigami, K.; Goto, A.; Yokokawa, H.; Yasumura, S. Comparison of ability-based and performance-based IADL evaluation of community-dwelling elderly using the Kihon Checklist and TMIG Index of Competence. *Nihon Ronen Igakkai Zasshi* **2007**, *44*, 619–626. [CrossRef]
24. Chen, L.-K.; Liu, L.-K.; Woo, J.; Assantachai, P.; Auyeung, T.-W.; Bahyah, K.S.; Chou, M.-Y.; Chen, L.-Y.; Hsu, P.-S.; Krairit, O.; et al. Sarcopenia in Asia: Consensus report of the Asian Working Group for Sarcopenia. *J. Am. Med. Dir. Assoc.* **2014**, *15*, 95–101. [CrossRef]
25. Kusunoki, H.; Tsuji, S.; Wada, Y.; Fukai, M.; Nagai, K.; Itoh, M.; Sano, K.; Tamaki, K.; Ohta, Y.; Amano, M.; et al. Relationship between sarcopenia and the serum creatinine/cystatin C ratio in Japanese rural community-dwelling older adults. *JCSM Clin. Rep.* **2018**, *3*, e00057. [CrossRef]
26. Sato, K.; Iwabuchi, M.; Endo, T.; Miura, T.; Ito, T.; Shirado, O. Association between trunk extensor strength and gait-induced back pain in the elderly with adult spinal deformity: A cross-sectional study. *Eur. Spine J.* **2024**, *33*, 2770–2776. [CrossRef] [PubMed]
27. Fried, L.P.; Tangen, C.M.; Walston, J.; Newman, A.B.; Hirsch, C.; Gottdiener, J.; Seeman, T.; Tracy, R.; Kop, W.J.; Burke, G.; et al. Frailty in older adults: Evidence for a phenotype. *J. Gerontol. A Biol. Sci. Med. Sci.* **2001**, *56*, M146–M156. [CrossRef]
28. Satake, S.; Arai, H. The revised Japanese version of the Cardiovascular Health Study criteria (revised J-CHS criteria). *Geriatr. Gerontol. Int.* **2020**, *20*, 992–993. [CrossRef] [PubMed]
29. Chen, L.K.; Woo, J.; Assantachai, P.; Auyeung, T.W.; Chou, M.Y.; Iijima, K.; Jang, H.C.; Kang, L.; Kim, M.; Kim, S.; et al. Asian Working Group for Sarcopenia: 2019 Consensus Update on Sarcopenia Diagnosis and Treatment. *J. Am. Med. Dir. Assoc.* **2020**, *21*, 300–307.e2. [CrossRef] [PubMed]
30. Utanohara, Y.; Hayashi, R.; Yoshikawa, M.; Yoshida, M.; Tsuga, K.; Akagawa, Y. Standard values of maximum tongue pressure taken using newly developed disposable tongue pressure measurement device. *Dysphagia* **2008**, *23*, 286–290. [CrossRef] [PubMed]
31. Tun, T.Z.; Thwin, K.M.; Takehara, S.; Ogawa, H. Oral Diadochokinesis and Potential Associated Factors in Japanese Older Adult Outpatients. *Oral. Health Prev. Dent.* **2024**, *22*, 601–608. [CrossRef] [PubMed]
32. Matsuo, S.; Imai, E.; Horio, M.; Yasuda, Y.; Tomita, K.; Nitta, K.; Yamagata, K.; Tomino, Y.; Yokoyama, H.; Hishida, A.; et al. Revised equations for estimated GFR from serum creatinine in Japan. *Am. J. Kidney Dis.* **2009**, *53*, 982–992. [CrossRef] [PubMed]
33. Horio, M.; Imai, E.; Yasuda, Y.; Watanabe, T.; Matsuo, S. Modification of the CKD epidemiology collaboration (CKD-EPI) equation for Japanese: Accuracy and use for population estimates. *Am. J. Kidney Dis.* **2010**, *56*, 32–38. [CrossRef]
34. Shimazaki, Y.; Nonoyama, T.; Tsushita, K.; Arai, H.; Matsushita, K.; Uchibori, N. Oral hypofunction and its association with frailty in community-dwelling older people. *Geriatr. Gerontol. Int.* **2020**, *20*, 917–926. [CrossRef] [PubMed]
35. Miyahara, S.; Maeda, K.; Kawamura, K.; Matsui, Y.; Onaka, M.; Satake, S.; Arai, H. Concordance in oral frailty five-item checklist and oral hypofunction: Examining their respective characteristics. *Arch. Gerontol. Geriatr.* **2024**, *118*, 105305. [CrossRef]

36. Iwasaki, M.; Shirobe, M.; Motokawa, K.; Tanaka, T.; Ikebe, K.; Ueda, T.; Minakuchi, S.; Akishita, M.; Arai, H.; Iijima, K.; et al. Prevalence of oral frailty and its association with dietary variety, social engagement, and physical frailty: Results from the Oral Frailty 5-Item Checklist. *Geriatr. Gerontol. Int.* **2024**, *24*, 371–377. [CrossRef] [PubMed]
37. Satake, S.; Shimada, H.; Yamada, M.; Kim, H.; Yoshida, H.; Gondo, Y.; Matsubayashi, K.; Matsushita, E.; Kuzuya, M.; Kozaki, K.; et al. Prevalence of frailty among community-dwellers and outpatients in Japan as defined by the Japanese version of the Cardiovascular Health Study criteria. *Geriatr. Gerontol. Int.* **2017**, *17*, 2629–2634. [CrossRef]
38. Watanabe, D.; Yoshida, T.; Watanabe, Y.; Yamada, Y.; Miyachi, M.; Kimura, M. Validation of the Kihon Checklist and the frailty screening index for frailty defined by the phenotype model in older Japanese adults. *BMC Geriatr.* **2022**, *22*, 478. [CrossRef] [PubMed]
39. Iwasaki, M.; Shirobe, M.; Motokawa, K.; Hayakawa, M.; Miura, K.; Kalantar, L.; Edahiro, A.; Kawai, H.; Fujiwara, Y.; Ihara, K.; et al. Validation of self-reported articulatory oral motor skill against objectively measured repetitive articulatory rate in community-dwelling older Japanese adults: The Otassha Study. *Geriatr. Gerontol. Int.* **2023**, *23*, 729–735. [CrossRef] [PubMed]

Geriatrics & Gerontology International

DOI: 10.1111/ggi.70003

REVIEW ARTICLE

Multidimensional insights about healthy aging from the cohort study for community-dwelling older adults: The SONIC study

Kei Kamide,[1] Kazunori Ikebe,[2] Yukie Masui,[3] Takeshi Nakagawa,[4] Mai Kabayama,[1] Hiroshi Akasaka,[5] Tomoaki Mameno,[2] Yuki Murotani,[2] Madoka Ogawa,[4] Saori Yasumoto,[4] Koichi Yamamoto,[5] Takumi Hirata,[3] Yasumichi Arai,[6] and Yasuyuki Gondo,[4] the SONIC study group

[1]Division of Health Science, Graduate School of Medicine, Osaka University, Osaka, Japan
[2]Department of Prosthodontics, Gerodontology and Oral Rehabilitation, Graduate School of Dentistry, Osaka University, Osaka, Japan
[3]Research Team for Human Care, Tokyo Metropolitan Institute of Gerontology, Tokyo, Japan
[4]Department of Clinical Thanatology and Geriatric Behavioral Science, Graduate School of Human Sciences, Osaka University, Osaka, Japan
[5]Department of Geriatric and General Medicine, Graduate School of Medicine, Osaka University, Osaka, Japan
[6]Center for Supercentenarian Medical Research, Keio University School of Medicine, Tokyo, Japan

Correspondence
Kei Kamide MD PhD, Division of Health Sciences, Osaka University Graduate School of Medicine, 1-7 Yamadaoka, Suita City, Osaka 565-0871, Japan.
Email: kamide@sahs.med.osaka-u.ac.jp

Yasuyuki Gondo PhD, Department of Clinical Thanatology and Geriatric Behavioral Science, Osaka University Graduate School of Human Sciences, 1-2 Yamadaoka, Suita City, Osaka 565-0871, Japan.
Email: y.gondo.hus@osaka-u.ac.jp

Received: 9 November 2024
Revised: 10 January 2025
Accepted: 23 January 2025

The Septuagenarian, Octogenarian, Nonagenarian Investigation with Centenarian (SONIC) study was established considering population trends and targeting the oldest-old population. This study is unique in its narrow age range, consisting of individuals aged in their 70s, 80s and 90s, and is carried out as a longitudinal cohort study with follow ups every 3 years in urban and rural areas of eastern and western Japan. The aims of the SONIC study are primarily to clarify aging-related changes in multiple domains of human functioning, explore the dynamics of interactions among these domains and identify factors influencing healthy longevity, including psychological well-being. Investigations spanning medical, dental, nutritional, psychological and sociological fields were carried out by specialists, yielding important results. Findings from the SONIC study in Japan, a super-aged society, will provide valuable information for addressing the global aging trend. This review introduces the results from the SONIC study, and explains factors contributing to healthy longevity and happy aging. **Geriatr Gerontol Int 2025; 25: 346–355**.

Keywords: healthy longevity, longitudinal cohort, multidimensional aspects, oldest-old population, SONIC study.

Introduction

Recent epidemiological studies on aging have identified factors related to health outcomes and longevity. In Japan, life expectancy has increased to 81.1 years for men and 87.1 years for women in 2024. The number of centenarians has surpassed 95 000, and is expected to quintuple by 2060. The most rapidly growing age group over the next decade will be the oldest-old (≥85 or ≥90 years). The Septuagenarian, Octogenarian, Nonagenarian Investigation with Centenarian (SONIC) study was established with this trend in mind, targeting the oldest-old population (Fig. 1).[1]

The SONIC study has two primary objectives: first, to clarify aging-related changes across various domains of human functioning and the interactions between these domains, and second, to identify factors that influence healthy longevity, including psychological well-being. The SONIC study's framework includes several unique characteristics. The first feature is its interdisciplinary nature, involving researchers from diverse fields, including medicine, biology, dentistry, nutrition, psychology and sociology.

The second characteristic is the participant diversity. The study spans four urban and non-urban areas in Kanto (Itabashi Ward and Nishitama area: Hinohara Village, Hinode Town, Okutama Town,

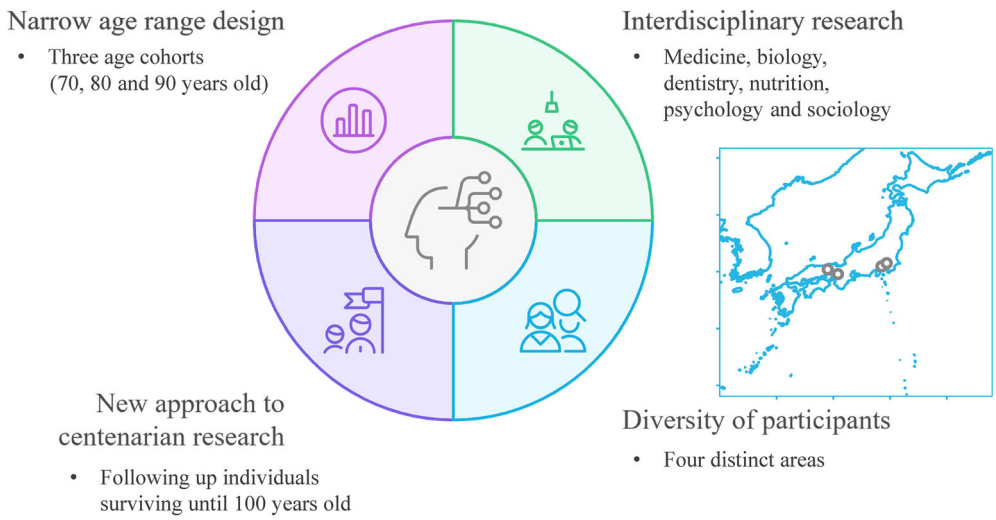


Figure 1 The features of the Septuagenarian, Octogenarian, Nonagenarian Investigation with Centenarian (SONIC) study.

and part of Ome City) and Kansai (Itami City and Asago City), each with distinct demographic and regional attributes. Participants represent varied sociodemographic backgrounds, including education, work experience, family structure and residential environment.

A third unique feature is the study's narrow age range design, which sets up three age cohorts (70, 80 and 90 years), each with a 3-year age span rather than a broader range. Follow-up surveys are carried out every 3 years for each cohort. By maintaining a narrow age range, the results can reflect individual differences without needing age as an adjustment variable.

A fourth feature positions the SONIC study as a novel approach to centenarian research, as indicated by its acronym. The study includes a large cohort with the potential to reach 100 years. For example, of the oldest cohort (90th) venue survey participants recruited in 2012 for the first time ($n = 325$, 140 men, 185 women), >47 survived until 100 years-of-age, and two could participate in the invitation-type study over the age of 100 years.

Participants completed various examinations in a random order at survey venues: verifying pre-filled questionnaires, answering additional psychosocial questions in interviews, undergoing cognitive tests, physical function tests, medical tests (including blood samples, blood pressure, breathing capacities, carotid ultrasonography) and dental assessments. (including natural teeth count, occlusal force, taste sensitivity and masticatory performance).

Data collection varied by cohort due to participant volume. The first wave began in 2010 for the 70s cohort, 2011 for the 80s cohort and 2012 for the 90s cohort. The second wave started in 2013 in the same sequence. For the 90s cohort, due to lower participation, additional recruitment occurred in 2015 and 2018.

All participants were recruited through residential registries, providing their name, sex, birth date and address within specific birth date ranges. These ranges differed slightly across the four study regions due to local government database schedules, time allocations for data transcription and regional recruitment start dates.

The SONIC study uses an invitation-based survey method, inviting participants to nearby survey venues, primarily local community centers owned by local governments. Invitations explained the study's purposes and methods. Participants confirmed their participation by returning an agreement letter specifying their preferred date and time. Additionally, invitees received a questionnaire booklet covering socioeconomic status, psychosocial variables, medical and dental conditions, and food intake to complete in advance. Participants who could not fill out the booklet themselves or with help from family completed it at the survey venue.

Tables 1 and 2 show participant totals and follow-up study participation by age cohort and sex.

Medical aspects

The main aim of the SONIC study is to investigate factors associated with healthy longevity, focusing on the decline of physical and cognitive function, diseases that influence the definition of healthy longevity, and related biomarkers, which are crucial for health promotion in Japan's super-aging society.[2]

Genetic factors in longevity

In the SONIC study, we explored genetic factors, focusing on genes associated with longevity and cardiovascular diseases (CVD). The Forkhead box transcription factor 3A (*FOXO3A*) gene is a strong candidate gene for longevity.[3,4] It has been reported that the single-nucleotide polymorphism, rs2802292, in *FOXO3A* is associated with both longevity[3] and protection against CVD[5] in Japanese Americans. We investigated the association of rs2802292 in *FOXO3A* with heart diseases in participants aged 70 and 80 years in the SONIC study, finding a newly clarified sex difference in this association.[6] Additionally, rs2802292 in *FOXO3A* was associated with hypertension in older women in the SONIC study.[7] The tumor suppressor genes, *CDKN2A/CDKN2B*, and the long non-coding RNA, ANRIL, at chromosome region 9p21 are known susceptibility loci for CVD.[8] We examined the association of several single-nucleotide polymorphisms in this region with CVD and longevity among the SONIC study participants and centenarians/supercentenarians, finding a positive association with CVD, but not with longevity.[9] We also explored mechanisms involving the expression of ANRIL and *CDKN2A/CDKN2B* in SONIC participants with carotid atherosclerosis.[10]

Factors related to cognitive decline and dementia

Dementia is a major threat to healthy longevity in Japan. In the SONIC study, we examined factors related to cognitive decline and dementia, particularly lifestyle-related diseases, such as hypertension, dyslipidemia and diabetes mellitus, which are prevalent in older adults and are potential risk factors for cognitive decline.[11]

Table 1 Invitation type participants of the Septuagenarian, Octogenarian, Nonagenarian Investigation with Centenarian (SONIC) study by data collection waves and years

		Sampled			Total			1st Wave			2nd Wave			3rd Wave			4th Wave			5th Wave		
Survey years							70	2010			2013	2014		2016	2017		2019	2020		2022	2023	
							80	2011			2014	2015		2017	2018		2020	2021		2023	2024	
							90	2012	2015	2018	2015	2018	2021	2018	21/22	23/24	2021	23/24	2027	23/24	2027	2030
		M	F	Total	M	F	Total	M	F	total	M	F	Total	M	F	Total	M	F	Total	M	F	Total
70	*n*	2247	2451	4698	576	653	1229	478	521	999	426	484	910	380	442	822	272	278	550	198	221	419
	%				25.6	26.6	26.2	83.0	79.8	81.3	74.0	74.1	74.0	66.0	67.7	66.9	47.2	42.6	44.8	34.4	33.8	34.1
80	*n*	2406	3451	5857	582	631	1213	460	513	973	487	497	984	272	268	540	85	83	168	60	59	119
	%				24.2	18.3	20.7	79.0	81.3	80.2	83.7	78.8	81.1	46.7	42.5	44.5	14.6	13.2	13.8	10.3	9.4	9.8
90	*n*	8441	15 566	24 007	422	461	883	393	414	807	151	189	340	57	51	108						
	%				5.0	3.0	3.7	93.1	89.8	91.4	35.8	41.0	38.5	13.5	11.1	12.2						

(1) Sampled indicates total number of people invited to the Septuagenarian, Octogenarian, Nonagenarian Investigation with Centenarian (SONIC) study.

(2)Total indicates the total number of participants in the SONIC study.

(3) We performed the 70s and 80s cohorts' first wave survey in 2010 and 2011. About the 90s cohort's, we recruited 90 years participants and performed first wave survey in 2012. In addition, we also recruited new 90 years participants and performed first wave survey both in 2015 and 2018.

(4) During the second wave of survey recruitment, we recruited the new 70s and 80s participants to compensate for the dropouts by sending an invitation letter.

(5) To increase participation, we recruited participants for two consecutive years from the second wave.

(6) We could not perform the invitation-type survey in 2020, because of the COVID-19 pandemic.

(7) In the 90s cohort, we will collect fifth wave data for participants recruted in 2015 future in 2027 and 2030, and we will collect fourth wave data for participants recruted in 2018 fourth wave data in 2030.

F, female; M, male.

Table 2 Number of mail survey participants during the COVID-19 pandemic

		2020				2021			
		Summer		Winter		Summer		Winter	
		M	F	M	F	M	F	M	F
70		366	456	298	353	339	410	300	358
80		269	306			178	227		
90	2012	24	42			10	23		
	2015	63	71			39	46		
	2018	106	94			70	71		

Mail surveys were performed four times for participants aged in their 70s, and twice for participants aged in their 80s and 90s.
F, female; M, male.

Blood pressure (BP) level is associated with cognitive decline, showing age-related differences.[12,13] Daily BP variability, measured at home, is also a factor associated with cognitive decline in individuals age >85 years.[14] Additionally, white coat and masked hypertension showed distinct characteristics across age groups.[15] Comorbid hypertension and diabetes mellitus[16] or dyslipidemia[17] were strong predictors of future cognitive decline. Silent strokes, commonly seen in older adults with hypertension, were also identified as a risk factor for cognitive decline.[18] Conversely, cognitive decline might lead to anemia in older adults.[19] Biomarkers for cognitive decline identified in the SONIC study include inflammation indicators, such as serum A/G ratio,[20] high-sensitivity C-reactive protein,[21] respiratory function[22] and a novel N-glycopeptide.[23] Daily alcohol intake might increase cognitive decline risk, whereas wine consumption might offer protective benefits.[24]

Factors related to physical frailty/sarcopenia and long-term care

The SONIC study also explored factors contributing to physical frailty and sarcopenia. Advanced age and musculoskeletal diseases are strongly associated with physical frailty.[25] However, we identified factors associated with future physical frailty that were stratified by the presence of musculoskeletal diseases.[26] Heart disease was a significant risk factor for future frailty in community-dwelling older adults.[27] Age differences were also evident in the associations between sleep status and frailty,[28] and the relationship of frailty with heart disease and social factors.[29] Low BP control among participants with hypertension at age 80 years was found to increase frailty risk.[13] Furthermore, no association was observed between daily salt intake and systolic BP in participants with physical frailty. In contrast, robust participants showed a positive association between systolic BP and salt intake.[30] Thus, salt intake restriction might be careful in older adults with frailty. Novel biomarkers related to frailty and sarcopenia included plasma adiponectin,[31] serum vitamin D[32] and the serum creatinine/cystatin C ratio.[33] Bodyweight loss was a strong predictor of frailty/sarcopenia, and we examined age-specific factors associated with weight loss in the 70s, 80s and 90s cohorts.[34] For long-term care certifications, diseases, such as stroke, musculoskeletal diseases and cancer, were linked to social subgroups.[35] Slow walking speed was a predictor of future long-term care certifications.[36] During the COVID-19 pandemic, we observed declines in daily activities and identified related factors in the SONIC study.[37]

Characteristics of diseases and geriatric syndrome in older adults

In the SONIC study, we investigated disease characteristics in older adults. Anemia is common among older adults and is a major factor in geriatric syndromes, potentially linked to low self-rated health in community-dwelling older adults.[38] Depressive symptoms, another common geriatric syndrome, might correlate with IADL decline, with differences across age groups.[39] Strict diabetes management might negatively impact mental health in older adults.[40] For atherosclerosis risk, we found that elevated uric acid levels were associated with carotid atherosclerosis in women at age 70 years, suggesting uric acid as a risk factor limited to certain age groups.[41] Additionally, adequate protein intake might not only slow chronic kidney disease progression in older adults, but also protect against frailty.[42]

Polypharmacy in older populations

Polypharmacy is a significant health concern in older adults, leading to frailty and increased healthcare costs in Japan. The SONIC study found that higher neuroticism in men and lower extraversion in women were associated with polypharmacy.[43] Taking ≥10 medications was linked to reduced grip strength and walking speed, whereas taking one to four medications was associated with increased walking speed.[44] Polypharmacy was also linked to a higher risk of falls.[45] Effective health management for older adults should emphasize minimizing unnecessary medication to improve health outcomes.

Validation of the health assessment questionnaire in older adults

To prevent lifestyle-related diseases and frailty, the Japanese government has implemented a screening program for older adults, especially those aged ≥75 years. This program includes a 15-item health assessment questionnaire focusing on frailty (12 items), general health (2 items) and smoking habits (1 item). Confirmatory factor analysis showed that a model with a higher-order factor of "frailty" with five subfactors (physical function, nutritional status, oral function, cognitive function and social aspects) was a good fit.[46] The 12 frailty-related items showed high predictive power for frailty prevalence based on the Japanese Cardiovascular Health Study criteria, with cut-off points of 3 and 4, yielding 55.9% sensitivity and 85.8% specificity, respectively.[47] These results suggest the questionnaire is effective for screening frailty in community-dwelling older adults.

Dental and nutritional aspects

Tooth loss and oral function

Tooth loss is one of the most prevalent oral health issues associated with aging. Our studies have shown that a reduction in posterior occlusal support is linked to an increased risk of tooth loss.[48,49] Hatta *et al.* reported that dental implants placed in free-end edentulous spaces might help extend the longevity of adjacent teeth.[50] The mechanism linking reduced occlusal support to tooth loss likely involves increased occlusal load or trauma to the remaining teeth. Tooth loss has a profound impact on masticatory function. Higashi *et al.* found that reduced occlusal support was associated with decreased masticatory performance.[51] Seto *et al.* showed that the number of teeth, occlusal force and depression can influence subjective evaluations of chewing difficulty.[52] Additionally, Hatta *et al.* showed that although tongue pressure decreased significantly over time, occlusal force did not, suggesting that tongue muscles might be more susceptible to aging than masticatory muscles.[53]

Impact of periodontal disease

Miki *et al.* identified that the periodontal inflamed surface area, which measures the severity and extent of periodontitis, was associated with high-sensitivity C-reactive protein, a marker of systemic inflammation.[54] Kitamura *et al.* suggested that maintaining good periodontal health might be important for preventing atherosclerosis development and progression.[55] Furthermore, periodontal probing depth correlated significantly with occlusal force and self-rated food acceptability, even among individuals with complete posterior occlusal contacts and no tooth mobility.[56]

Oral health-related quality of life

Takeshita *et al.* reported that personality traits are associated with oral health-related quality of life, independently of objective oral health measures.[57] Mihara *et al.* suggested that oral health-related quality of life correlates significantly with the degree of gerotranscendence, independent of objective oral health status.[58]

Association with nutritional intake

Inomata *et al.* examined the relationship between occlusal force, number of teeth and nutritional intake using a self-administered diet quality questionnaire.[59,60] The results showed that lower occlusal force was significantly associated with lower intake of vegetables and antioxidant vitamins. In the 70s age group, the number of teeth was associated with intake of calcium and zinc, whereas no significant associations were observed in the 80s group, suggesting that nutrient intake might be more closely related to occlusal force than to the number of teeth. Inomata *et al.* also reported that removable partial denture wearers consumed more vegetables, n-3 fatty acids, calcium, vitamin A and dietary fiber than non-wearers.[61] Mameno *et al.* found that occlusal force and occlusal contact area were significantly associated with dietary hardness.[62] These findings underscore the importance of prosthetic rehabilitation for maintaining adequate nutritional intake. Additionally, Fukutake *et al.* found that oral stereognostic ability was significantly associated with green and yellow vegetable intake in older complete denture wearers.[63] Tada *et al.* suggested that reduced posterior occlusion was associated with an increased prevalence of atherosclerosis due to declines in key dietary intakes, such as fish, shellfish, vitamin B6 and n-3 fatty acids.[64]

Association with physical function

Fukutake *et al.* assessed the impact of occlusal force and the number of teeth on body mass index reduction in older adults over a 3- to 6-year follow-up period.[65] The analysis showed that although the number of teeth was not significantly associated with body mass index reduction, lower occlusal force correlated with a decline in body mass index, suggesting that reduced occlusal force might contribute to weight loss. Okada *et al.* found that slow walking speed (<0.8 m/s) was significantly linked to occlusal force, with lower protein intake mediating this association.[66] Hatta *et al.* concluded that a lack of posterior occlusal support at baseline predicted reduced walking speed over 3 years.[67] These findings suggest that dental treatments to preserve occlusal support might help prevent a decline in walking speed. Our studies also identified that occlusal force, masticatory performance and tongue pressure were significantly associated with grip strength.[68,69] Murotani *et al.* found that tongue–lip motor and swallowing functions were good indicators of walking speed.[69] These measures could serve as proxies for physical decline in older adults, and may be valuable for screening physical frailty.

Association with cognitive function

In our study, the relationship between cognitive function and oral status was examined from multiple perspectives.[70–76] Ikebe *et al.* comprehensively explored this relationship, concluding that occlusal force correlated with cognitive function.[73] Path analysis showed both direct and indirect associations through dietary intake, even after controlling for potential confounding factors. Okubo *et al.* reported that a diet rich in vegetables, soy products, fruits, fish, and foods with dietary hardness might benefit cognitive function in older adults.[71,74] These findings suggest that decreased oral function might coincide with early cognitive decline. Longitudinal studies also support the role of maintaining occlusal force in preventing cognitive decline. Hatta *et al.* found that the number of teeth and occlusal force were associated with cognitive function at follow up, even after adjusting for other risk factors.[75] Mameno *et al.* observed that the intake of green and yellow vegetables, and meat, influenced by the number of teeth, was associated with cognitive function in a 9-year study.[76] These findings imply that preserving teeth and occlusal force might protect against cognitive decline.

Conversely, the impact of cognitive function on taste and dietary habits has also been studied. Uota *et al.*[77] and Ogawa *et al.*[78] evaluated taste sensitivity for sweetness, bitterness, saltiness and sourness. They found that individuals with lower cognitive function had reduced sensitivity to saltiness.[77,78] Additionally, sex was identified as a major factor affecting taste sensitivity, with sensitivity to sweetness being less affected by aging.[77–79] Fukutake *et al.* reported that cognitive decline was associated with reduced oral perception, which is crucial for effective mastication, appetite and food enjoyment.[80]

Association with psychological status

Akema *et al.* assessed the relationship between occlusal force and psychological frailty, defined as a World Health Organization-5 Well-Being Index score of <13 and a Montreal Cognitive Assessment in Japanese score of <23.[81] After controlling for potential confounding factors, occlusal force was associated with a reduced

prevalence of psychological frailty. Mameno *et al*. found a significant association between oral function and mental health status, mediated by fruit and vegetable intake, and social interactions.[82]

Summary

Tooth loss and reduced occlusal force are linked to dietary changes, weight loss and declines in walking speed, suggesting that maintaining oral function is crucial for physical health in community-dwelling older adults. The findings also underscore the relationship between oral function and cognitive and psychological health. Maintaining oral health is essential for promoting the overall well-being of older adults.

Psychosocial aspects

The psychosocial study in the SONIC study has two main aims. The first is to develop appropriate scales and confirm the applicability of pre-existing tools for evaluating long-term aging-related changes. The second aim is to clarify the influence of psychosocial factors on physical and cognitive function, and psychological well-being, covering a wide age range in the older population. Both qualitative and quantitative approaches were applied.

Regarding psychological well-being, we reported on elements that constitute the well-being of centenarians and the process of achieving this state, based on interviews with centenarians.[83,84] These unique findings helped develop a core framework to uncover the structure and longitudinal change of well-being, especially in the oldest-old population. One example is the development of the Japanese version of the Valuation of Life scale.[85] The Valuation of Life scale includes a positive evaluation of the future, and positive emotions that compensate for the loss of physical and social resources. We found that the Valuation of Life scale is related to mental health and individual differences in the desired remaining years of life. We also developed and confirmed the applicability of the Gerotranscendence Scale. The Gerotranscendence Scale describes a shift in behavior from active engagement in life to innate disengagement, with a change in thinking from a realistic view to a more abstract and cosmic view. We found that the construct of gerotranscendence differs for Japanese older people compared with Western populations, leading us to develop a Japanese-specific scale.[86,87] In relation to psychological well-being, a higher Gerotranscendence Scale score is associated with better subsequent mental health[6] and with greater well-being in individuals who experience a decline in physical functioning.[88] Longitudinal data over 9 years from four collection points showed that the Gerotranscendence Scale score increases in the 70s, and remains stable in the 80s and 90s, showing positive psychological development through the oldest years.[88]

Using the SONIC study's wide age coverage, we reported age-related physical and psychosocial characteristics among participants aged in their 70s, 80s and 90s. In physical functioning, using the Short Physical Performance Battery tool, we found only slight differences between the 70s and 80s, whereas differences were larger between the 80s and 90s.[89] Regarding social activities, we reported fewer leisure activities in the older age groups.[90] These studies highlight the importance of personal and internal resources for the daily activities of older adults. We also confirmed that the Montreal Cognitive Assessment is a highly reliable tool for evaluating cognitive function across a wide age range in a normal population, showing both construct validity and reliability.[91] An analysis of factors influencing well-being in participants aged in their 90s showed that living with family, economic conditions and a sense of being useful to others are important for men and women, respectively.[92]

We showed the importance of lifestyle and environmental factors on health outcomes. Variables, such as educational background, work style in middle age and leisure activities in older age, were examined. Regarding current lifestyle, we reported a simple relationship between leisure activity involvement and cognitive function.[93] Further complex analysis showed a direct influence of leisure activities on physical and cognitive function, and mental health, which are components of successful aging.[94] Additionally, a reciprocal relationship between cognitive and physical function was confirmed. In interviews about lifelong job experience, the complexity of the longest-held job was related to higher memory, reasoning test scores[95] and global cognition.[96] Combined analysis of job complexity and current leisure activities showed that both variables are important for global cognition.[96] Regarding social participation and subjective well-being, associations varied depending on the type of social participation.[97] A detailed analysis showed that participation in regional organizations had the highest association with well-being compared with participation in nonprofit organizations, volunteer groups, sports clubs or hobby groups.[97] However, these findings are limited by the use of retrospective and single-cohort data; we are planning to confirm these results using longitudinal data.

In addition to the aforementioned studies, we introduced new methods in the SONIC study data collection. We confirmed that body analogy assists in carrying out cognitive tasks (mental rotation), even in participants aged in their late 90s,[98] suggesting that pre-existing cognitive frameworks can help compensate for cognitive decline throughout life. To better assess emotional states in older people, we applied short-interval sampling methods in a small sample of SONIC study participants.[99] Using a daily diary method, we found that emotional stability was higher in older adults compared with younger counterparts. This method was also used to analyze the relationship between pre-night sleep and daytime fatigue.[100] To expand this approach, a smartphone app for microscopic data sampling is in development. We also found associations between salivary testosterone levels and cognitive function in 70-year-olds.[101] Testing new methodologies in the SONIC study is essential for developing a gerontology-based biopsychosocial model of successful aging.

Study under the COVID-19 pandemic

As aforementioned, the COVID-19 pandemic affected longitudinal data collection in the SONIC study. During the restricted period, we carried out a mail survey for all participants, regardless of the pre-planned invitation schedule. The mail survey enabled us to analyze longitudinal changes in participants' behavior and adaptation processes. In the early phase, participants restricted their activities, influenced by COVID-19 anxiety.[37] Women with lower COVID-19 anxiety had more direct interactions, whereas those with higher anxiety tended toward indirect interactions.[102] Additionally, younger individuals and those living in cities restricted their activities more than others.[37] Pre-COVID walking speed was also associated with a decrease in activity.[37] In contrast, we observed that 80-year-old participants increased the frequency of exercise and

social interactions in the later phase of the pandemic, with exercise frequency especially increasing among those living alone.[103] Details of preventive behaviors were reported based on face-to-face interviews with participants.[104] These studies provide new insights into older adults, highlighting a shift from viewing them as "weak and frail" to recognizing their adaptability and resilience.

Conclusion

The SONIC study was established considering population trends and specifically targeting the oldest-old population. This study is characterized by its unique narrow-age range of participants in their 70s, 80s and 90s, and by a longitudinal cohort design with 3-year intervals, conducted in both urban and rural areas of eastern and western Japan. The main aims of the SONIC study are to clarify aging-related changes across multiple domains of human functioning, to explore the dynamics of interaction among these domains and to identify factors influencing healthy longevity, including psychological well-being. Investigations in the SONIC study are carried out through a multidimensional approach encompassing medical, dental, nutritional, psychological and sociological perspectives contributed by professionals from each field. The greatest advantage of the SONIC study is its integration of various multidimensional studies to examine factors contributing to healthy longevity. Nowadays, not everyone wants to live a long life, so it is hoped that the factors that lead to happy aging and well-being will be clarified.

As detailed above, many important findings have been obtained so far, and these results are already being referenced in medical and dental care for older adults, as well as in guidelines for elderly care in Japan.

Overall, based on the study's characteristics, it can be said that old age spans a long period from age 65 years to >100 years, and physical and mental changes occur throughout this period, indicating correlations between various factors depending on age. Furthermore, it is important to consider differences between men and women, as well as regional differences. Figure 2 provides a summary of the achievements from the SONIC study. We are confident that the results obtained from the SONIC study in Japan's super-aged society will provide significant and valuable information for addressing the global aging trend.

Acknowledgements

We are grateful to all SONIC study participants who participated in these studies. We sincerely appreciate all staff involved in the SONIC study. The members of the SONIC Study Group (in addition to the authors) are as follows: Hiromi Rakugi, Ken Sugimoto, Ryosuke Oguro, Ada Congrains, Tatsuo Kawai, Hiroshi Kusunoki, Chikako Nakama, Miyuki Onishi-Takeya, Yasushi Takeya, Hiroko Hanasaki-Yamamoto, Yoichi Takami, Serina Yokoyama, Satomi Maeda, Motonori Nagasawa, Taku

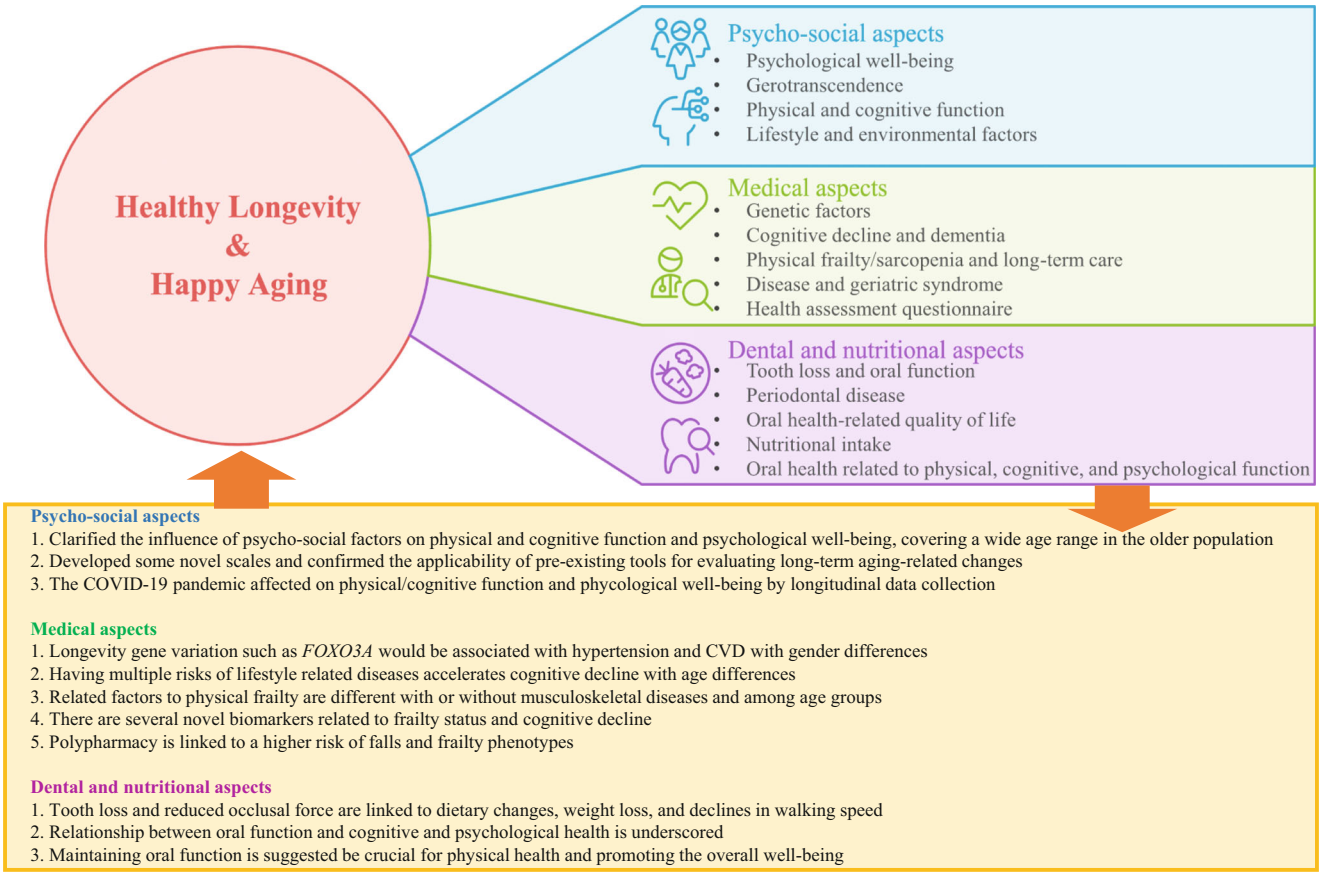


Figure 2 The overview of findings from the Septuagenarian, Octogenarian, Nonagenarian Investigation with Centenarian (SONIC) study. CVD, cardiovascular disease.

Fujimoto, Yoichi Nozato, Yuri Onishi, Ken Terashima, Shino Yoshida, Ryoichi Ohara, Masaaki Isaka at the Department of Geriatric and General Medicine, Osaka University Graduate School of Medicine; Kayo Godai, Michiko Kido, Yuya Akagi, Hirochika Ryuno, Eri Kiyoshige, Tomoko Noma, Kentaro Tanaka, Werayuth Srithumsuk, Nonglak Klinpudtan, Jinmei Tuo, Toshiaki Sekiguchi, Yuko Nakamura, Toshiki Mizuno, Tomoko Yano, Weng Fang, Yuka Ohata, Yuka Tachibana, Mariko Hosokawa, Arisa Wada, Hiroko Yoshida, Saya Terada, Takako Inoue, Yasuka Sawayama, Naoko Wada, Atsuko Higuchi, Chizuru Kuruma, Atsuto Hirose, Hitomi Tsunai, Yurie Maeyama, Keigo Kobayashi, Ayano Tamura, Motoko Nogami, Mayuka Iguchi, Mio Kubo, Minori Eguchi, Haruna Kikuchi, Riko Kinjo, Ayaka Hiratsuka, Yui Toshimitsu, Kaoru Hatta, Chisato Hori, Maya Mitani and Reina Yokokawa, at the Division of Health Sciences, Osaka University Graduate School of Medicine; Yoshinobu Maeda, Sinya Murakami, Kodai Hatta, Chisato Inomata, Yusuke Mihara, Motoyoshi Fukutake, Tadashi Okada, Hajime Takeshita, Sayaka Tada, Masahiro Uota, Masaki Yoshinaka, Taiji Ogawa, Masahiro Kitamura, Koji Miki, Hitomi Sato, Kotaro Higashi, Eri Seto and Suzuna Akema at Osaka University Graduate School of Dentistry; Satoshi Sasaki and Hitomi Okubo at Department of Social and Preventive Epidemiology, School of Public Health, The University of Tokyo; Ayaka, Kasuga, Yoshiko Ishioka, Kiyoaki Matumoto, Giovanni Sala, Hwang Choe, Hiroyuki Muto, Kumi Hirokawa, Yumi Kimura, Kokoro Shirai, Keitaro Numata, Megumi Tabuchi, Yukiko Tatsuhira, Marina Kozon, Fumika Goto, Yuki Mino, Akari Kikuchi, Xinyu Zhang, Yuchun Tsai, Yutian Cheng, Can Wang, Chihiro Nakajima, Yumi Tsuji, Momoho Kakuta, Nao Sakaguti, Marin Fujii, Momoko Furuno, Sayo Iio, Chihana Izuriha, Yuko Masuda, Yuki Matsubara, Takuto Nakanishi, Eriko Tasaka, Meina Tsujikura and Kazuko Yasumura at Department of Human Science, Osaka University Graduate School; Tatsuro Ishizaki, Ryutaro Takahashi, Tamao Endo, Shuichi Awata, Kae Ito, Yuri Miura, Hiroki Inagaki, Yuko Yoshida, Hiroki Tsumoto, Keitaro Umezawa, Kyojiro Kawakami, Mayuko Ono, Noriko Hori, Takeshi Kurinobu, Wataru Onoguchi, Fumi Yoshimatsu and Takuro Okuyama at TMIG; and Nobuyoshi Hirose, Michiyo Takayama and Yukiko Abe at Center for Supercentenarian Medical Research, Keio University School of Medicine.

Disclosure statement

The SONIC study was mainly supported by a grant-in-aid from JSPS KAKENHI (21330152, 22510211, 23390440, 24530905, 25780388, 25293394, 25780401, 26310104, 26380882, 26460905, 26780377, 15K08910, 15H05025, A15H063920, 15K04176, 16J02993, 16K12336, 16H05523, 16K16254, 16K21696, 16K01852, 17H02633, 17K17553, 17K17844, 17H06850, 18K18456, 18J00674, 18H02990, 18K09658, 19K07888, 19K11138, 19K10203, 19K19122, 19K22790, 19K14390, 19K11736, JP20ta0127004, 20H03576, 20K07803, 20K10975, 20K18598, 20K18628, 20K03354, 20K11327, 20K11664, 20K03475, 21H05331, 21H00943, 21H05330, 21K17039, 21KK0168, 22H00089, 22K10055, 22K10074, 22K17339, 22H03352, 23H03888, 23K09274, 23K16085, 23K19743, 23K24672, 24K02632, 24K06517), MHLW Research on Policy Planning and Evaluation Program (23AA2006, K24FA1005), AMED (24dk0110049h0002), CiDER Center For Infectious Disease Education And Research (JM00000160) and other multiple foundation research grants.

Data Availability Statement

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

References

1 Gondo Y, Masui Y, Kamide K, Ikebe K, Arai Y, Ishizaki T. SONIC study, a longitudinal cohort study of the older people as part of a centenarian study. *Encyclopedia Geropsychol* 2017: 2227–2236. doi: 10.1007/978-981-287-082-7_182
2 Kamide K, Tseng W, Kabayama M. Health promotion for older population in Japan: importance of preventive care and successful assisted living (review). *Gerontol Geriatr Res* 2021; **7**: 2.
3 Willcox BJ, Donlon TA, He Q *et al*. FOXO3A genotype is strongly associated with human longevity. *PNAS* 2008; **105**: 13987–13992.
4 Morris BJ, Willcox DC, Donlon TA *et al*. FOXO3: a major gene for human longevity--a mini-review. *Gerontology* 2015; **61**: 515–525.
5 Willcox BJ, Morris BJ, Tranah GJ *et al*. Longevity-associated FOXO3 genotype and its impact on coronary artery disease mortality in Japanese, whites, and blacks: a prospective study of three American populations. *J Gerontol A Biol Sci Med Sci* 2017; **72**: 724–728.
6 Klinpudtan N, Allsopp RC, Kabayama M *et al*. The association between longevity-associated FOXO3 allele and heart disease in septuagenarians and octogenarians: the SONIC study. *J Gerontol A Biol Sci Med* 2022; **77**: 1542–1542021.
7 Morris BJ, Chen R, Donlon TA *et al*. Association analysis of *FOXO3* longevity variants with blood pressure and essential hypertension. *Am J Hypertens* 2016; **29**: 1292–1300.
8 The Wellcome Trust Case Control Consortium. Genomewide association study of 14,000 cases of seven common diseases and 3,000 shared controls. *Nature* 2007; **447**: 661–678.
9 Congrains A, Kamide K, Hirose N *et al*. Disease-associated polymorphisms in 9p21 are not associated with extreme longevity. *Geriatr Gerontol Int* 2015; **15**: 797–803.
10 Congrains A, Kamide K, Oguro R *et al*. Genetic variants at the 9p21 locus contribute to atherosclerosis through modulation of ANRIL and CDKN2A/B. *Atherosclerosis* 2012; **220**: 445–455.
11 Livingston G, Huntley J, Liu KY *et al*. Dementia prevention, intervention, and care: 2024 report of the lancet standing commission. *Lancet* 2024; **404**: 572–628.
12 Ryuno H, Kamide K, Gondo Y *et al*. Differences of association between high blood pressure and cognitive functioning among general Japanese population aged 70 and 80 years: the SONIC study. *Hypertens Res* 2016; **39**: 557–563.
13 Kabayama M, Kamide K, Gondo Y *et al*. The association of blood pressure with physical frailty and cognitive function in community-dwelling septuagenarians, octogenarians, and nonagenarians: the SONIC study. *Hypertens Res* 2020; **43**: 1421–1429.
14 Godai K, Kabayama M, Gondo Y *et al*. Day-to-day blood pressure variability is associated with lower cognitive performance among Japanese community dwelling oldest-old population: the SONIC study. *Hypertens Res* 2020; **43**: 404–411.
15 Tuo J, Godai K, Kabayama M *et al*. Self-monitoring home blood pressure in community dwelling older people: age differences in white-coat and masked phenomena and related factors -the SONIC study. *Int J Hypertens* 2022: 1–9. doi:10.1155/2022/5359428
16 Ryuno H, Kamide K, Gondo Y *et al*. Longitudinal Association of Hypertension and Diabetes Mellitus with cognitive functioning in a general 70-year-old population: the SONIC study. *Hypertens Res* 2017; **40**: 665–670.
17 Nakamura Y, Kabayama M, Godai K *et al*. Longitudinal association of hypertension and dyslipidemia with cognitive function in community-dwelling older adults: the SONIC study. *Hypertens Res* 2023; **46**: 1829–1839.
18 Srithumsuk W, Kabayama M, Gondo Y *et al*. The importance of stroke as a risk factor of cognitive decline in community dwelling older and oldest peoples: the SONIC study. *BMC Geriatr* 2020; **20**: 24.
19 Noma T, Kayo G, Kabayama M *et al*. Lower cognitive function as a risk factor for anemia among older Japanese women from the longitudinal observation in the SONIC study. *Geriatr Gerontol Int* 2023; **23**: 334–340.
20 Maeda S, Takeya Y, Oguro R *et al*. Serum albumin/globulin ratio is associated with cognitive function in community-dwelling elderly people: the SONIC study. *Geriatr Gerontol Int* 2019; **19**: 967–971.

21 Hosokawa M, Kabayama M, Godai K *et al*. Cross-sectional association between high-sensitivity C-reactive protein and cognitive function in community-dwelling older adults: the SONIC study. *BMC Geriatr* 2024; **24**: 756.
22 Tachibana Y, Godai K, Kabayama M *et al*. Relationship between respiratory function assessed by spirometry and mild cognitive impairment among community-dwelling older adults. *Geriatr Gerontol Int* 2024; **24**: 1001–1007. https://doi.org/10.1111/ggi.14962. Online ahead of print.
23 Miura Y, Tsumoto H, Masui Y *et al*. A characteristic N-glycopeptide signature associated with diabetic cognitive impairment identified in a longitudinal cohort study. *Biochim Biophys Acta Gen Subj* 2023; **1867**: 130316.
24 Akagi Y, Kabayama M, Gondo Y *et al*. Alcohol drinking patterns have a positive association with cognitive function among older people: a cross-sectional study. *BMC Geriatr* 2022; **22**: 158.
25 Fried LP, Tangen CM, Walston J *et al*. Frailty in older adults: evidence for a phenotype. *J Gerontol A Biol Sci Med Sci* 2001; **56**: M146–M156.
26 Ohata Y, Godai K, Kabayama M *et al*. Risk factors predicting subtypes of physical frailty incidence stratified by musculoskeletal diseases in community-dwelling older adults: the SONIC study. *Geriatr Gerontol Int* 2024; **24**: 797–805.
27 Klinpudtan N, Kabayama M, Godai K *et al*. Association between physical function and onset of coronary heart disease in a cohort of community-dwelling older populations: the SONIC study. *Arch Gerontol Geriatr* 2021; **95**: 104386.
28 Mizuno T, Godai K, Kabayama M, Akasaka H *et al*. Age group differences in the association between sleep status and frailty among community-dwelling older adults: the SONIC study. *Gerontol Geriatr Med* 2023; **14**: 9. https://doi.org/10.1177/23337214231205432.
29 Klinpudtan N, Kabayama M, Gondo Y *et al*. The association between heart diseases, social factors, and physical frailty in community-dwelling older populations: the septuagenarians, octogenarians, nonagenarians investigation with centenarians study. *Geriatr Gerontol Int* 2020; **20**: 974–979.
30 Yoshida H, Kabayama M, Kido M *et al*. Association between salt intake and blood pressure among community-dwelling older adults based on their physical frailty status. *Hypertens Res* 2025. doi: 10.1038/s41440-024-02066-y (in press).
31 Nagasawa M, Takami Y, Akasaka H *et al*. High plasma adiponectin levels are associated with frailty in a general old-old population: the SONIC study. *Geriatr Gerontol Int* 2018; **18**: 839–846.
32 Onishi Y, Akasaka H, Hatta K *et al*. Association between serum vitamin D levels and skeletal muscle indices in an older Japanese population: the SONIC study. *Geriatr Gerontol Int* 2024; **24**: 898–903. https://doi.org/10.1111/ggi.14951.
33 Fang W, Godai K, Kabayama M *et al*. Usefulness of the serum creatinine/cystatin C ratio as a blood biomarker for sarcopenia components among age groups in community-dwelling older people: the SONIC study. *Geriatr Gerontol Int* 2024; **24**: 529–536.
34 Yano T, Godai K, Kabayama M *et al*. Factors associated with weight loss by age among community-dwelling older people. *BMC Geriatr* 2023; **6**: 277.
35 Kiyoshige E, Kabayama M, Gondo Y *et al*. Association between long-term care and chronic and lifestyle-related disease modified by social profiles in community-dwelling people aged 80 and 90: SONIC study. *Arch Gerontol Geriatr* 2019; **81**: 176–181.
36 Srithumsuk W, Kabayama M, Godai K *et al*. Relation between physical function and long-term care in community-dwelling older and oldest people: the SONIC study. *Environ Health Prev Med* 2020; **5**: 46.
37 Godai K, Kabayama M, Kamide K *et al*. Decrease in activity and its related factors under COVID-19 crisis in community-dwelling older people (Japanese). *Nihon Ronen Igakkai Zasshi* 2021; **58**: 591–601.
38 Noma T, Kabayama M, Gondo Y *et al*. Association of anemia with self-rated health in older community-dwelling people: the SONIC study. *Geriatr Gerontol Int* 2020; **20**: 720–726.
39 Kiyoshige E, Kabayama M, Gondo Y *et al*. Age group differences in association between IADL decline and depressive symptoms in community-dwelling elderly. *BMC Geriatr* 2019; **19**: 309.
40 Maeyama Y, Kabayama M, Godai K *et al*. Relationship between glycemic control and mental health in community-dwelling older people with diabetes mellitus: the SONIC study (Japanese). *Nihon Ronen Igakkai Zasshi* 2023; **60**: 141–152.
41 Tanaka K, Kabayama M, Sugimoto K *et al*. Association between uric acid and atherosclerosis in community-dwelling older people: the SONIC study. *Geriatr Gerontol Int* 2021; **21**: 94–101.
42 Sekiguchi T, Kabayama M, Ryuno H *et al*. Association between protein intake and changes in renal function among Japanese community-dwelling old people: the SONIC study. *Geriatr Gerontol Int* 2022; **22**: 286–291.
43 Yoshida Y, Ishizaki T, Masui Y *et al*. Association of personality traits with polypharmacy among community-dwelling older adults in Japan: a cross-sectional analysis of data from the SONIC study. *BMC Geriatr* 2022; **22**: 372. https://doi.org/10.1186/s12877-022-03069-5.
44 Yoshida Y, Ishizaki T, Masui Y *et al*. Effects of multimorbidity and polypharmacy on physical function in community-dwelling older adults: a 3-year prospective cohort study from the SONIC. *Arch Gerontol Geriatr* 2024; **126**: 105521.
45 Yoshida Y, Ishizaki T, Masui Y *et al*. Effect of number of medications on the risk of falls among community-dwelling older adults: a 3-year follow up of the SONIC study. *Geriatr Gerontol Int* 2024; **24**: 306–310.
46 Ishizaki T, Masui Y, Nakagawa T *et al*. Construct validity of a new health assessment questionnaire for the national screening program of older adults in Japan: the SONIC study. *Int J Environ Res Public Health* 2022; **19**: 10330.
47 Hori N, Ishizaki T, Masui Y *et al*. Criterion validity of the health assessment questionnaire for the national screening program for older adults in Japan: the SONIC study. *Geriatr Gerontol Int* 2023; **23**: 437–443.
48 Mihara Y, Matsuda K, Takahashi T *et al*. Occlusal support predicts tooth loss in older Japanese people. *Community Dent Oral Epidemiol* 2020; **48**: 163–170.
49 Sato H, Hatta K, Murotani Y *et al*. Predictive factors for tooth loss in older adults vary according to occlusal support: a 6-year longitudinal survey from the SONIC study. *J Dent* 2022; **121**: 104088.
50 Hatta K, Takahashi T, Sato H, Murakami S, Maeda Y, Ikebe K. Will implants with a fixed dental prosthesis in the molar region enhance the longevity of teeth adjacent to distal free-end edentulous spaces? *Clin Oral Implants Res* 2021; **32**: 242–248.
51 Higashi K, Hatta K, Mameno T *et al*. The relationship between changes in occlusal support and masticatory performance using 6-year longitudinal data from the SONIC study. *J Dent* 2023; **139**: 104763.
52 Seto E, Kosaka T, Hatta K *et al*. Factors related to subjective evaluation of difficulty in chewing among community-dwelling older adults. *Geriatr Gerontol Int* 2024; **24**: 327–333.
53 Hatta K, Murotani Y, Takahashi T *et al*. Decline of oral functions in old-old adults and their relationship with age and sex: the SONIC study. *J Am Geriatr Soc* 2022; **70**: 541–548.
54 Miki K, Kitamura M, Hatta K *et al*. Periodontal inflamed surface area is associated with hs-CRP in septuagenarian Japanese adults in cross-sectional findings from the SONIC study. *Sci Rep* 2021; **11**: 14436.
55 Kitamura M, Ikebe K, Kamide K *et al*. Association of periodontal disease with atherosclerosis in 70-year-old Japanese older adults. *Odontology* 2021; **109**: 506–513.
56 Okada T, Ikebe K, Inomata C *et al*. Association of periodontal status with occlusal force and food acceptability in 70-year-old adults: from SONIC study. *J Oral Rehabil* 2014; **41**: 912–919.
57 Takeshita H, Ikebe K, Kagawa R *et al*. Association of personality traits with oral health-related quality of life independently of objective oral health status: a study of community-dwelling elderly Japanese. *J Dent* 2015; **43**: 342–349.
58 Mihara Y, Matsuda K, Hatta K *et al*. Relationship between gerotranscendence and oral health-related quality of life. *J Oral Rehabil* 2018; **45**: 805–809.
59 Inomata C, Ikebe K, Kagawa R *et al*. Significance of occlusal force for dietary fibre and vitamin intakes in independently living 70-year-old Japanese: from SONIC study. *J Dent* 2014; **42**: 556–564.
60 Inomata C, Ikebe K, Okubo H *et al*. Dietary intake is associated with occlusal force rather than number of teeth in 80-year-old Japanese. *JDR Clin Trans Res* 2017; **2**: 187–197.
61 Inomata C, Ikebe K, Okada T, Takeshita H, Maeda Y. Impact on dietary intake of removable partial dentures replacing a small number of teeth. *Int J Prosthodont* 2015; **28**: 583–585.
62 Mameno T, Tsujioka Y, Fukutake M *et al*. Relationship between the number of teeth, occlusal force, occlusal contact area, and dietary hardness in older Japanese adults: the SONIC study. *J Prosthodont Res* 2023; **68**: 400–406.
63 Fukutake M, Ikebe K, Okubo H *et al*. Relationship between oral stereognostic ability and dietary intake in older Japanese adults with complete dentures. *J Prosthodont Res* 2019; **63**: 105–109.
64 Tada S, Ikebe K, Kamide K *et al*. Relationship between atherosclerosis and occlusal support of natural teeth with mediating effect of atheroprotective nutrients: from the SONIC study. *PLoS One* 2017; **12**: e0182563.

65 Fukutake M, Takahashi T, Gondo Y *et al*. Impact of occlusal force on decline in body mass index among older Japanese adults: finding from the SONIC study. *J Am Geriatr Soc* 2021; **69**: 1956–1963.
66 Okada T, Ikebe K, Kagawa R *et al*. Lower protein intake mediates association between lower occlusal force and slower walking speed: from the septuagenarians, octogenarians, nonagenarians investigation with centenarians study. *J Am Geriatr Soc* 2015; **63**: 2382–2387.
67 Hatta K, Ikebe K, Mihara Y *et al*. Lack of posterior occlusal support predicts the reduction in walking speed in 80-year-old Japanese adults: a 3-year prospective cohort study with propensity score analysis by the SONIC study group. *Gerodontology* 2019; **36**: 156–162.
68 Mihara Y, Matsuda K, Ikebe K *et al*. Association of handgrip strength with various oral functions in 82- to 84-year-old community-dwelling Japanese. *Gerodontology* 2018; **35**: 214–220.
69 Murotani Y, Hatta K, Takahashi T *et al*. Oral functions are associated with muscle strength and physical performance in old-old Japanese. *Int J Environ Res Public Health* 2021; **18**: 13199.
70 Takeshita H, Ikebe K, Gondo Y *et al*. Association of occlusal force with cognition in independent older Japanese people. *JDR Clin Trans Res* 2016; **1**: 69–76.
71 Okubo H, Inagaki H, Gondo Y *et al*. Association between dietary patterns and cognitive function among 70-year-old Japanese elderly: a cross-sectional analysis of the SONIC study. *Nutr J* 2017; **16**: 56.
72 Hatta K, Ikebe K, Gondo Y *et al*. Influence of lack of posterior occlusal support on cognitive decline among 80-year-old Japanese people in a 3-year prospective study. *Geriatr Gerontol Int* 2018; **18**: 1439–1446.
73 Ikebe K, Gondo Y, Kamide K *et al*. Occlusal force is correlated with cognitive function directly as well as indirectly via food intake in community-dwelling older Japanese: from the SONIC study. *PLoS One* 2018; **13**: e0190741.
74 Okubo H, Murakami K, Inagaki H *et al*. Hardness of the habitual diet and its relationship with cognitive function among 70-year-old Japanese elderly: findings from the SONIC study. *J Oral Rehabil* 2019; **46**: 151–160.
75 Hatta K, Gondo Y, Kamide K *et al*. Occlusal force predicted cognitive decline among 70- and 80-year-old Japanese: a 3-year prospective cohort study. *J Prosthodont Res* 2020; **64**: 175–181.
76 Mameno T, Moynihan P, Nakagawa T *et al*. Exploring the association between number of teeth, food intake, and cognitive function: a 9-year longitudinal study. *J Dent* 2024; **145**: 104991.
77 Uota M, Ogawa T, Ikebe K *et al*. Factors related to taste sensitivity in elderly: cross-sectional findings from SONIC study. *J Oral Rehabil* 2016; **43**: 943–952.
78 Ogawa T, Uota M, Ikebe K *et al*. Longitudinal study of factors affecting taste sense decline in old-old individuals. *J Oral Rehabil* 2017; **44**: 22–29.
79 Yoshinaka M, Ikebe K, Uota M *et al*. Age and sex differences in the taste sensitivity of young adult, young-old and old-old Japanese. *Geriatr Gerontol Int* 2016; **16**: 1281–1288.
80 Fukutake M, Ogawa T, Ikebe K *et al*. Impact of cognitive function on oral perception in independently living older people. *Clin Oral Investig* 2019; **23**: 267–271.
81 Akema S, Mameno T, Nakagawa T *et al*. Relationship between occlusal force and psychological frailty in Japanese community-dwelling older adults: the septuagenarians, octogenarians, nonagenarians investigation with centenarians study. *J Am Geriatr Soc* 2023; **71**: 1819–1828.
82 Mameno T, Moynihan P, Nakagawa T *et al*. Mediating role of fruit and vegetable intake and social interaction between oral function and mental health in older adults aged ≥75 years: the SONIC study. *J Prosthodont Res* 2024 in press. doi:10.2186/jpr.JPR_D_24_00103
83 Yasumoto S, Gondo Y, Nakagawa T, Masui Y. Components of well-being in centenarians. *Jpn J Social Gerontol* 2017; **39**: 365–373.
84 Nakagawa T, Gondo Y, Masui Y *et al*. Development of a Japanese version of the valuation of life(VOL)scale. *Jpn J Psychol* 2013; **84**: 37–46.
85 Masui Y, Nakgawa T, Gondo Y *et al*. Validity and reliability of Japanese Gerotranscendence scale revised (JGS-R). *Jpn J Gerontol* 2013; **35**: 49–59.
86 Masui Y, Nakgawa T, Gondo Y *et al*. The characteristics of gerotranscendence in frail oldest-old individuals who maintain a high level of psychological well-being : a preliminary study using the new gerotranscendence questionnaire for Japanese elderly. *Jpn J Gerontol* 2010; **32**: 33–47.
87 Masui Y, Gondo Y, Nakgawa T *et al*. Longitudinal effect of gerontranscendence on the mental health of community-dwelling older adults. *Jpn J Gerontol* 2019; **41**: 247–258.
88 Masui Y, Nakgawa T, Yasumoto S *et al*. Development in Gerotranscendence in community-dwelling older adults in Japan: a longitudinal study over a nine-year period. *J Adult Dev* 2024. https://doi.org/10.1007/s10804-024-09488-5.
89 Matsumoto K, Gondo Y, Masui Y *et al*. Physical performance reference values for Japanese oldest old: a SONIC study. *BMC Geriatr* 2022; **22**: 748.
90 Kikuchi A, Ishioka R, Ogawa M *et al*. Leisure activities of older adults--relations with gender, regions, residence forms. *Appl Gerontol* 2024; **17**: 32–41.
91 Sala G, Inagaki H, Ishioka YL *et al*. The psychometric properties of the Montreal cognitive assessment (MoCA): a comprehensive investigation. *Swiss J Psychol* 2020; **79**: 155–161.
92 Ito K, Okamura T, Awata S *et al*. Factors associated with psychological well-being among nonagenarians: well-being in the era of 100 years of life. *Geriatr Gerontol Int* 2022; **22**: 364–366.
93 Kozono M, Gondo Y, Ogawa M *et al*. The relationship between leisure activities and cognitive function in community-dwelling older adults. *Jpn J Gerontol* 2016; **38**: 32–44.
94 Sala G, Jopp D, Gobet F *et al*. The impact of leisure activities on older adults' cognitive function, physical function, and mental health. *PLoS One* 2019; **14**: e0225006.
95 Ishioka Y, Gondo Y, Masui Y *et al*. Occupational complexity and late-life memory and reasoning abilities. *Jpn J Psychol* 2015; **86**: 219–229.
96 Ishioka YL, Masui Y, Nakagawa T *et al*. Early- to late-life environmental factors and late-life global cognition in septuagenarian and octogenarians: the SONIC study. *Acta Psychol (Amst)* 2023; **233**: 103844.
97 Choe H, Gondo Y, Masui Y *et al*. Social participation, social capital, and subjective well-being among older adults. *Jpn J Gerontol* 2020; **43**: 5–14.
98 Muto H, Gondo Y, Inagaki H *et al*. Human-body analogy improves mental rotation performance in people aged 86 to 97 years. *Collabra Psychol* 2023; **9**: 177–184.
99 Nakagawa T, Yasumoto S, Kabayama M *et al*. Intraindividual variability in daily a ect in young and older adults: a pilot daily diary study. *Jpn J Pers* 2021; **29**: 162–171.
100 Nakagawa T, Yasumoto S, Kabayama M *et al*. Association between prior-night sleep and next-day fatigue in older adults: a daily diary study. *BMC Geriatr* 2023; **23**: 04539.
101 Hirokawa K, Kasuga A, Matsumoto K *et al*. Associations between salivary testosterone levels and cognitive function among 70-year-old Japanese elderly: a cross-sectional analysis of the SONIC study. *Geriatr Gerontol Int* 2022; **22**: 1040–1046.
102 Choe H, Gondo Y, Kasuga A *et al*. The relationship between social interaction and anxiety regarding COVID-19 in Japanese older adults. *Gerontol Geriatr Med* 2023; **9**: 1–7.
103 Kasuga A, Yasumoto S, Nakagawa T *et al*. Older Adults' resilience against impact of lifestyle changes during the COVID-19 pandemic. *Gerontol Geriatr Med* 2022; **8**: 1–6.
104 Kimura Y, Akasaka H, Takahashi T *et al*. Factors related to preventive behaviors against a decline in physical fitness among community-dwelling older adults during the COVID-19 pandemic: a qualitative study. *Int J Environ Res Public Health* 2022; **19**: 6008.

How to cite this article: Kamide K, Ikebe K, Masui Y, et al. Multidimensional insights about healthy aging from the cohort study for community-dwelling older adults: The SONIC study. Geriatr. Gerontol. Int. 2025;25:346–355. https://doi.org/10.1111/ggi.70003