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Relationship Between Oral Health and Physical Frailty in Patients With Cardiovascular Disease

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Abstract

Background: Oral health is important for maintaining general health and is associated with components of physical frailty among the elderly. Oral health problems are common in hospitalized patients; however, no reports on oral health problems pertain to patients with cardiovascular diseases (CVD). The present study aimed to evaluate the association between oral health and physical frailty in these patients.

Methods: In this retrospective cohort study, we included consecutive patients admitted for CVD to our hospital between May 2014 to December 2018. Physical frailty was assessed using the Short Physical Performance Battery (SPPB). Oral health characteristics, such as the number of remaining teeth, denture use, occlusal support, and periodontal status, were assessed.

Results: In our cohort (n = 457), 111 (24.3 %) patients had physical frailty. Univariate linear regression showed that the number of teeth present and the prevalence of occlusal support were significantly lower in patients with than without frailty. Pearson correlation indicated that the number of teeth significantly correlated with the nutritional status (r = 0.27) and physical function, as indicated by the SPPB score (r = 0.27), grip strength (r = 0.33) and exercise capacity (r = 0.26). Multiple linear regression analysis showed that the number of teeth was independently associated with physical function after adjusting for confounders.

Conclusions: Oral health was closely associated with physical function, frailty prevalence, and nutritional status in patients with CVD; thus, it could be an important screening marker for early frailty symptoms and a predictor of future malnutrition risk. (248/300 words)

Introduction

The frail population suffering from CVD is growing worldwide [1]. A recent systematic review showed that frailty is an independent predictor for mortality and morbidity among patients with heart failure [2]. Frailty is a complex systemic syndrome; a decline in physical function is a key component of frailty and of increased adverse health outcomes, including falls, hospitalization, and mortality [3]. Hence, preventive interventions for physical frailty are imperative, but remain a challenge because of the complexity of this condition. Several multifactorial processes including demographic, social, lifestyle, and biological factors compose frailty; these are interlinked with each other and may constitute a vicious cycle leading to further physical function decline [3]. Chief among these factors is malnutrition, which has attracted increasing attention as a key factor for the development of physical frailty [4].

Similarly, oral health decreases with aging, and oral diseases are a major public health problem [5]. Oral health was considered a broad concept, and defined as comfortable and functional dentition that allows individuals to continue in their desired social role, fundamental to overall health, well-being and quality of life [6]. Problems with oral health are very common and occur in as much as 70% of hospitalized patients [7]. Previous studies have reported that poor oral health, including tooth loss, periodontal disease, xerostomia, infections, and loss of dental occlusion, is a risk factor of malnutrition [8]. Based on these findings, it is suggested that oral health could be a notable trigger for the vicious cycle of frailty.

In community-dwelling adults, some studies have reported that oral health, evaluated based on dental occlusion, chewing ability, or number of teeth, was associated with the nutritional status, physical frailty, and cognitive function [9-11]. Interestingly, the

prevalence of oral health problems among those with CVD seems to be higher than among community-dwelling populations, as concluded by a large-scale epidemiological survey [12, 13]. Poor oral health, as exemplified by periodontitis or missing teeth, was associated with more than a two-fold increase in the risk of future CVD [12, 13]. Moreover, the prevalence of malnutrition among patients with CVD is high because of anorexia or intestinal edema, cytokine-induced catabolism, and cardiac cachexia [14].

Nevertheless, to our knowledge, no clinical studies have investigated the association between oral health and physical frailty in patients with CVD. Clarifying these relationships will serve as a breakthrough regarding the vicious cycle of frailty and help the development of preventive interventions. Thus, the purpose of the present study was to investigate the relationship between physical frailty and oral health in CVD patients.

Methods

Study Population

The study was a retrospective analysis conducted at a single center in Japan. Between May 2014 to December 2018, we screened 473 consecutive patients admitted to Kobe University Hospital for CVD, such as heart failure, valvular heart disease, and coronary artery diseases. Patients whose frailty was not assessed due to neurological or orthopedic disease and those who declined to undergo evaluation of their oral health were excluded. The present study complied with the principles of the Declaration of Helsinki regarding investigations in human subjects and was approved by the Kobe University Institutional Review Board (approved No. 190064). Due to the retrospective study design, we used opt-out method in the present study. All participants were notified regarding their participation in the study and explained that they were free to opt out of

participation at any time.

Clinical Characteristics of the Patients

We evaluated the baseline characteristics, including sociodemographic data, biochemical data, comorbidities, medications, and echocardiographic data at hospital discharge in a stable condition. Patient comorbidities included diabetes, chronic obstructive pulmonary disease (COPD), hypertension, previous stroke, dyslipidemia, chronic kidney disease (CKD), and atrial fibrillation. CKD was defined as eGFR <60 mL/min/1.73 m^2 or positive dipstick results for albuminuria according to a recent guideline [15]. Diabetes was defined by a clinical history, hemoglobin A1c levels ≥ 6.5%, and either a fasting plasma glucose (PG) level of ≥126 mg/dl or a PG level of ≥200 mg/dl 2 h after a 75-g oral glucose tolerance test [16]. Hypertension was defined as blood pressure > 140/90 mmHg or use of anti-hypertensive drugs. Dyslipidemia was defined as low-density lipoprotein cholesterol levels > 140 mg/dL, triglyceride levels > 150 mg/dL, or use of anti-dyslipidemic drugs, per the guidelines issued by the Japan Atherosclerosis Society [17]. The functional classification of the New York Heart Association was used to classify the extent of heart failure. Nutritional status at baseline was assessed using the Mini Nutritional Assessment Short Form (MNA-SF). The reliability and validity of the MNA-SF have been demonstrated for the detection of malnutrition [18].

Assessment of Physical Frailty

The Short Physical Performance Battery (SPPB) was used to assess physical frailty

[19]. The SPPB consists of three tests that include walking speed, chair stands, and standing balance. Each test is scored from zero (inability to complete the task) to four (highest level of performance). The sum of these scores (0–12) is used as a measurement of the level of physical performance. The reliability and validity of the SPPB have been demonstrated for the detection of frailty [20]. Patients were stratified into two groups: the frail group (SPPB score ≤ 9) and the non-frail group (SPPB score > 9), as per previous studies [19, 21].

Physical Function and Exercise Capacity

The psoas muscle index (PMI) was used as an index of total skeletal muscle mass. To calculate the PMI, the outer margin of the major psoas muscle cross-section at the level of the caudal end of the L3 vertebral body was manually traced on abdominal computed tomography (CT) images, and the sum of the left and right cross-sectional areas was divided by the height squared [22]. Handgrip strength was measured with a grip strength dynamometer (T.K.K.5401; Takei Scientific Instruments Co., Ltd., Niigata, Japan). To assess exercise capacity, we used the 6-minute walking distance test (6MWD), a submaximal exercise test of functional capacity. The 6MWD was performed according to the American Thoracic Society guidelines [23] in a 30-m long straight corridor under the guidance of a physiotherapist. For this test, participants were instructed to walk at a self-selected pace with the aim of covering as much distance as possible in 6 minutes.

Assessment of Oral Health

The participants received oral examinations by a trained dentist and a dental hygienist. All patients underwent panoramic radiography. The oral examination comprised counting of the number of teeth present and that of functional teeth. All dental diseases (caries, apical periodontitis, marginal periodontitis, and impacted wisdom teeth), unfitted dental restoration (inlay, crown, or bridge), and denture use were evaluated. The decayed, missing, and filled teeth (DMF-T) index was determined based on the evaluation of the number of decayed, missing, and filled teeth. All teeth were classified as decayed (D), filled (F) (teeth that were filled or crowned), or missing (M). The DMF-T enables conclusions regarding the history of caries in an individual [24]. Occlusal support was classified according to the Eichner Index (EI) [25], which is widely used to assess occlusal support status on the basis of existing natural teeth contact. According to the definition, we allocated patients into three groups: Group A, natural dentition with adequate function; Group B, partially or fully edentulous, but maintaining functional occlusion with dentures in either or both jaws; and Group C, functionally inadequate occlusion with no dentures. The Community Periodontal Index of Treatment Needs (CPITN) was used to assess periodontal health [26]. The CPITN assesses the following conditions: no treatment needs (CPITN 0), gingival bleeding on gentle probing (CPITN 1), presence of supra- or sub-gingival calculus or other plaque retentive factors (CPITN 2), 4- or 5-mm deep periodontal pockets (CPITN 3), and 6-mm or deeper periodontal pockets (CPITN 4).

Statistical Analysis

We conducted statistical analyses after confirming that the data were normally distributed using the Shapiro-Wilk test. Continuous variables were expressed as mean (standard deviation) or median (interquartile range). Category variables were expressed as numbers (%). Patients were assigned to two groups based on the presence or absence of frailty, and the clinical characteristics between these groups were compared using an independent *t*-test, Mann-Whitney U test, or chi-square test. To compare the oral health and other outcome variables, a univariate linear regression analysis was used. The correlations between various parameters were assessed using the Pearson correlation coefficient. Multiple linear regression analysis was used to determine the relationship between oral health and physical function. The dependent variable was physical function, whereas the independent variable was the number of teeth. Multiple linear regression analyses were adjusted for age, sex, body mass index, MNA-SF score, hemoglobin level, eGFR, brain natriuretic peptide (BNP) level, chronic kidney disease (CKD) and C-reactive protein (CRP) level. To compare the relationship between occlusal support or periodontal health and physical frailty, one-way analysis of variance was used. Post-hoc analyses were performed using Tukey's test when appropriate. A P-value < 0.05 indicated statistical significance. Statistical analyses were conducted using R ver. 2.8.1 (The R Foundation for Statistical Computing, Vienna, Austria).

Results

Clinical Characteristics

Of the 473 patients, 16 were excluded from the study based on the exclusion criteria. Among these 16 excluded patients, physical frailty could not be assessed completely due to neurological or orthopedic disease in nine, and seven declined to undergo

evaluation of oral health. Finally, 457 patients with a mean age of 67.1 ± 13.0 years were included.

In our cohort, physical frailty was noted in 111 patients (24.3%). Baseline characteristics according to the presence of frailty are shown in Table 1. Patients in the frail group were significantly older than those in the non-frail group ($P < 0.001$). Frail individuals had lower serum hemoglobin levels and eGFR, but higher BNP and CRP levels than non-frail patients ($P < 0.05$ for all). Furthermore, nutritional status, as indicated by the MNA-SF score, was significantly poorer in the frail than the non-frail group (12.1 ± 1.9 vs. 10.1 ± 2.6; $P < 0.001$). Regarding comorbidities, the prevalence of hypertension COPD, and CKD was much higher in the frail than that in the non-frail group ($P < 0.05$ for all). Each physical function parameter such as gait speed, handgrip strength and knee extensor muscle strength were significantly decreased in frail group than that in the non-frail group ($P < 0.05$ for all; Table 2). Exercise capacity measured by 6MWD in the frail group was 287.1m, which was approximately two-thirds of that in the non-frail group. The prevalence of sarcopenia in the frail group was 48.6%, whereas 27.7% in the non-frail group (Table 2).

Relationship Between Oral Health and Nutritional Status or Frailty

The mean number of teeth was lower in the frail than the non-frail group (15.6 ± 9.6 vs. 20.6 ± 9.2, $P < 0.001$; Table 3). Occlusal support evaluated using EI was more favorable in the non-frail than in the frail group ($P = 0.003$). More patients needed tooth extraction in the frail than the non-frail group ($P = 0.022$). Conversely, no significant inter-group differences were observed regarding CPITN ($P = 0.407$).

There was a positive correlation between the number of teeth and SPPB score (P <

0.0001; Figure 1). In addition, grip strength or exercise capacity measured by 6MWD also had a statistically significant positive correlations with the number of teeth ($P < 0.05$ for all; Figure 1). Poor occlusion support indicated by EI was associated with significantly lower SPPB scores; nevertheless, CPITN did not show a statistically significant association with SPPB score (Figure S1). Figure 2 shows the relationship between the number of teeth and MNA-SF with or without physical frailty. The number of teeth positively correlated with the MNA-SF score in non-frail patients ($p = 0.0001$), whereas there was no such statistically significant correlation among frail patients ($p = 0.100$; Figure 2). In the multiple linear regression analysis, both the number of teeth and MNA-SF were independently associated with each physical function measure, such as SPPB score, PMI, grip strength, 6MWD, and gait speed after adjustment for confounding factors ($p < 0.05$ for all; Table 4). Furthermore, the CRP level continued to have an independent association with the SPPB score and 6MWD ($p < 0.05$ for all).

Discussion

To the best of our knowledge, no previous study has investigated the relationship between oral health and physical frailty in patients with CVD. We elucidated that physical frailty was related to poor oral health, and that oral health, in turn, was independently associated with physical function, after adjusting for confounding variables. Furthermore, poor oral health was associated with a poorer nutritional status.

In this study, we focused the number of teeth as a determinant of comprehensive oral health. It was reported that healthy elderly individuals with more teeth met several oral function criteria throughout the aging process, including oral mucosal wetness, occlusal force, lip motor function, masticatory function, and swallowing function [27].

Furthermore, people with more teeth had a significantly lower mortality risk than that among people with fewer teeth [28]. Our results indicated that the number of teeth was independently associated with muscle mass, strength, and functional capacity after adjusting for confounding factors. In addition to physical frailty, decreased muscle mass (sarcopenia), grip strength, and functional capacity have been reported to be strong prognostic factors in patients with CVD [29, 30]. Further, a previous study that included community-dwelling elderly patients demonstrated that tooth loss is associated with weight loss [31], and Hung et al. demonstrated that dental impairment is associated with lower dietary intake, especially that of protein [32]. Unfavorable changes in diet because of tooth loss or decreased chewing ability can result in weight loss, and it is well known that adequate protein intake helps limit and treat age-related decline in muscle mass, strength, and functional abilities and to prevent the development of frailty [32]. Hence, the association between the number of teeth and physical frailty could be attributable to the association between the number of teeth and nutritional status.

In the present study, the number of teeth positively correlated with nutritional status, as assessed by the MNA-SF score. Mendonca et al. demonstrated that tooth loss associated with poor dietary intake of nutrients and healthy foods correlated with stable coronary disease [33]. In their study, individuals with less than 20 teeth showed a lower probability of attaining their recommended nutritional goals [33]. Furthermore, other studies have shown that patients with poor oral health indicated by the number of teeth have a tendency to select processed foods that are high in fat and sugar and show inadequate intake of vitamins and minerals, due to the difficulty in and fatigue experienced while chewing. Poor oral health could cause malnutrition, increased comorbidities, and physical frailty in patients with CVD, leading to future

cardiovascular events [31, 34-36]. In the present study, the number of teeth correlated with nutritional status in non-frail patients, but not in frail patients. A previous study reported that not only the total number of teeth, but also the occlusal status, swallowing function, and wearing dentures can significantly affected nutritional status especially in patients with fewer teeth [37]. For those in the frail group with fewer teeth, the association between the number of teeth and nutritional status did not demonstrate statistically significant differences because the factors other than number of teeth may be associated with nutritional status. Further studies that investigate comprehensive oral function including swallowing function are needed. However, in non-frail patients with more teeth remaining, the number of teeth had a significant positive correlation with nutritional status. It is possible that the number of teeth can be a good screening tool for nutritional status, and clinically useful indicator for the patients who are not frail.

Another important intervening factor between the number of teeth and physical frailty is inflammatory response. Previous studies have indicated that periodontal disease is associated with chronic systemic inflammation and oxidative stress and induces endothelial dysfunction that may lead to increased blood pressure [38-40]. On the contrary, standard treatment approaches for CVD, such as the administration of angiotensin converting enzyme inhibitor and angiotensin II receptor blockers, are known to cause periodontitis as a side effect [38]. Enhancement of the systemic inflammatory response due to periodontal disease is involved in the onset and progression of vascular disorders, which are in turn associated with an increased future risk of CVD. Furthermore, chronic inflammation plays an important role in muscle wasting and physical frailty [41]. Our results also confirmed that the serum CRP level was independently associated with physical frailty. However, periodontal status as

assessed by CPITN did not show a significant correlation with physical frailty. Thus, future studies are required to elucidate the mechanism underlying the effect of periodontal diseases on physical frailty in patients with CVD.

Community-dwelling elderly patients with more remaining teeth are reportedly less frail and have better quality of life than edentulous individuals [8]. The present study appears to not only support these results in patients with CVD, but also further suggests that the number of teeth might be a significant factor in the mechanism of frailty development. The number of teeth was increasing awareness especially in the Japanese population such as 8020 Movement. Thus, the number of teeth as a simple, easy to understand, and clinically applicable index of oral health. The Japanese Society of Gerodontology proposed oral hypofunction as the stage at which recovery can be expected through dental treatment before oral dysfunction occurs [42]. Early detection of oral problems to facilitate and evaluate oral care procedures is required to appropriately manage sarcopenia and malnutrition in older patients. We believe that it is possible to prevent malnutrition by detecting and responding early to the reversible decline in oral function.

Study Limitations

There are several limitations to this study. First, this was a single, high-volume center retrospective cohort study, and thus, generalizability of the results may be limited. Moreover, we could not evaluate sex-related differences or disease severity, because of insufficient data. Second, we could not consider the status of perioral muscles or swallowing function, such as the masticatory muscle, or the occlusal force. Thus, the relationship between physical function and perioral muscle status or dysphagia remains unknown. Finally, as the study had a cross-sectional design, causal relationships

between oral health and physical frailty could not be established. Therefore, the long-term effects of oral health remain to be evaluated. Further studies are needed to clarify the impact of oral health on long-term prognosis and future CVD events.

Conclusion

This study investigated the relationship between oral health and physical frailty in patients with CVD. Frail patients were found to have a lower number of teeth than non-frail patients. After adjustment for confounding factors, the number of teeth was independently associated with physical function. These results suggest that oral health assessment can be used as a screening tool for early symptoms of frailty and to predict future risk of malnutrition. The findings of such assessment can facilitate early intervention to maintain and improve nutritional status and physical function.

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Conflict of Interest

The authors declare that there are no conflicts of interest.

References

[1] Denfeld QE, Winters-Stone K, Mudd JO, Gelow JM, Kurdi S, Lee CS. The prevalence of frailty in heart failure: A systematic review and meta-analysis. Int J Cardiol. 2017;236:283-9.

[2] Yang X, Lupon J, Vidan MT, Ferguson C, Gastelurrutia P, Newton PJ, et al. Impact of Frailty on Mortality and Hospitalization in Chronic Heart Failure: A Systematic Review and Meta-Analysis. J Am Heart Assoc. 2018;7:e008251.

[3] Walston J, Hadley EC, Ferrucci L, Guralnik JM, Newman AB, Studenski SA, et al. Research agenda for frailty in older adults: toward a better understanding of physiology and etiology: summary from the American Geriatrics Society/National Institute on Aging Research Conference on Frailty in Older Adults. J Am Geriatr Soc. 2006;54:991-1001.

[4] Bonnefoy M, Berrut G, Lesourd B, Ferry M, Gilbert T, Guerin O, et al. Frailty and nutrition: searching for evidence. J Nutr Health Aging. 2015;19:250-7.

[5] Rapp L, Sourdet S, Vellas B, Lacoste-Ferre MH. Oral Health and the Frail Elderly. J Frailty Aging. 2017;6:154-60.

[6] Baiju RM, Peter E, Varghese NO, Sivaram R. Oral Health and Quality of Life: Current Concepts. J Clin Diagn Res. 2017;11:ZE21-ZE6.

[7] Andersson P, Hallberg IR, Lorefalt B, Unosson M, Renvert S. Oral health problems in elderly rehabilitation patients. Int J Dent Hyg. 2004;2:70-7.

[8] Watanabe Y, Hirano H, Arai H, Morishita S, Ohara Y, Edahiro A, et al. Relationship Between Frailty and Oral Function in Community-Dwelling Elderly Adults. J Am Geriatr Soc. 2017;65:66-76.

[9] Zhang Y, Ge M, Zhao W, Hou L, Xia X, Liu X, et al. Association Between

Number of Teeth, Denture Use and Frailty: Findings from the West China Health and Aging Trend Study. J Nutr Health Aging. 2020;24:423-8.

[10] Kikutani T, Yoshida M, Enoki H, Yamashita Y, Akifusa S, Shimazaki Y, et al. Relationship between nutrition status and dental occlusion in community-dwelling frail elderly people. Geriatr Gerontol Int. 2013;13:50-4.

[11] Tanaka T, Takahashi K, Hirano H, Kikutani T, Watanabe Y, Ohara Y, et al. Oral Frailty as a Risk Factor for Physical Frailty and Mortality in Community-Dwelling Elderly. J Gerontol A Biol Sci Med Sci. 2018;73:1661-7.

[12] Tonetti MS, Van Dyke TE. Periodontitis and atherosclerotic cardiovascular disease: consensus report of the Joint EFP/AAP Workshop on Periodontitis and Systemic Diseases. J Clin Periodontol. 2013;40 Suppl 14:S24-9.

[13] Liljestrand JM, Havulinna AS, Paju S, Mannisto S, Salomaa V, Pussinen PJ. Missing Teeth Predict Incident Cardiovascular Events, Diabetes, and Death. J Dent Res. 2015;94:1055-62.

[14] von Haehling S, Ebner N, Dos Santos MR, Springer J, Anker SD. Muscle wasting and cachexia in heart failure: mechanisms and therapies. Nat Rev Cardiol. 2017;14:323-41.

[15] Ando Y, Ito S, Uemura O, Kato T, Kimura G, Nakao T, et al. CKD Clinical Practice Guidebook. The essence of treatment for CKD patients. Clin Exp Nephrol. 2009;13:191-248.

[16] Association AD. Diagnosis and classification of diabetes mellitus. Diabetes Care. 2010;33 Suppl 1:S62-9.

[17] Teramoto T, Sasaki J, Ishibashi S, Birou S, Daida H, Dohi S, et al. Diagnosis of atherosclerosis. Executive Summary of the Japan Atherosclerosis Society (JAS)

Guidelines for the Diagnosis and Prevention of Atherosclerotic Cardiovascular Diseases in Japan—2012 Version. J Atheroscler Thromb. 2014;21:296-8.

[18] Guigoz Y. The Mini Nutritional Assessment (MNA) review of the literature--What does it tell us? J Nutr Health Aging. 2006;10:466-85; discussion 85-7.

[19] da Camara SM, Alvarado BE, Guralnik JM, Guerra RO, Maciel AC. Using the Short Physical Performance Battery to screen for frailty in young-old adults with distinct socioeconomic conditions. Geriatr Gerontol Int. 2013;13:421-8.

[20] Pritchard JM, Kennedy CC, Karampatos S, Ioannidis G, Misiaszek B, Marr S, et al. Measuring frailty in clinical practice: a comparison of physical frailty assessment methods in a geriatric out-patient clinic. BMC Geriatr. 2017;17:264.

[21] Bandinelli S, Lauretani F, Boscherini V, Gandi F, Pozzi M, Corsi AM, et al. A randomized, controlled trial of disability prevention in frail older patients screened in primary care: the FRASI study. Design and baseline evaluation. Aging Clin Exp Res. 2006;18:359-66.

[22] Hamaguchi Y, Kaido T, Okumura S, Kobayashi A, Hammad A, Tamai Y, et al. Proposal for new diagnostic criteria for low skeletal muscle mass based on computed tomography imaging in Asian adults. Nutrition. 2016;32:1200-5.

[23] ATS statement: guidelines for the six-minute walk test. Am J Respir Crit Care Med. 2002;166:111-7.

[24] Organization WWH. oral health surveys, basic methods. 4th edition. : WHO; Oral Health Unit, Geneva; 1997.

[25] Eichner K. [Renewed examination of the group classification of partially edentulous arches by Eichner and application advices for studies on morbidity statistics]. Stomatol DDR. 1990;40:321-5.

[26] Ainamo J, Barmes D, Beagrie G, Cutress T, Martin J, Sardo-Infirri J. Development of the World Health Organization (WHO) community periodontal index of treatment needs (CPITN). Int Dent J. 1982;32:281-91.

[27] Iyota K, Mizutani S, Oku S, Asao M, Futatsuki T, Inoue R, et al. A Cross-Sectional Study of Age-Related Changes in Oral Function in Healthy Japanese Individuals. Int J Environ Res Public Health. 2020;17: 1376.

[28] Hayasaka K, Tomata Y, Aida J, Watanabe T, Kakizaki M, Tsuji I. Tooth loss and mortality in elderly Japanese adults: effect of oral care. J Am Geriatr Soc. 2013;61:815-20.

[29] Chainani V, Shaharyar S, Dave K, Choksi V, Ravindranathan S, Hanno R, et al. Objective measures of the frailty syndrome (hand grip strength and gait speed) and cardiovascular mortality: A systematic review. Int J Cardiol. 2016;215:487-93.

[30] Prescher S, Schoebel C, Koehler K, Deckwart O, Wellge B, Honold M, et al. Prognostic value of serial six-minute walk tests using tele-accelerometry in patients with chronic heart failure: A pre-specified sub-study of the TIM-HF-Trial. Eur J Prev Cardiol. 2016;23:21-6.

[31] Lee JS, Weyant RJ, Corby P, Kritchevsky SB, Harris TB, Rooks R, et al. Edentulism and nutritional status in a biracial sample of well-functioning, community-dwelling elderly: the health, aging, and body composition study. Am J Clin Nutr. 2004;79:295-302.

[32] Hung HC, Colditz G, Joshipura KJ. The association between tooth loss and the self-reported intake of selected CVD-related nutrients and foods among US women. Community Dent Oral Epidemiol. 2005;33:167-73.

[33] Mendonca DD, Furtado MV, Sarmento RA, Nicoletto BB, Souza GC, Wagner TP, et al. Periodontitis and tooth loss have negative impact on dietary intake: A cross-sectional study with stable coronary artery disease patients. J Periodontol. 2019;90:1096-105.

[34] Hutton B, Feine J, Morais J. Is there an association between edentulism and nutritional state? J Can Dent Assoc. 2002;68:182-7.

[35] Sheiham A, Steele JG, Marcenes W, Lowe C, Finch S, Bates CJ, et al. The relationship among dental status, nutrient intake, and nutritional status in older people. J Dent Res. 2001;80:408-13.

[36] Wada H, Dohi T, Miyauchi K, Jun S, Endo H, Doi S, et al. Relationship between the prognostic nutritional index and long-term clinical outcomes in patients with stable coronary artery disease. J Cardiol. 2018;72:155-61.

[37] Sahyoun NR, Lin CL, Krall E. Nutritional status of the older adult is associated with dentition status. J Am Diet Assoc. 2003;103:61-6.

[38] Macedo Paizan ML, Vilela-Martin JF. Is there an association between periodontitis and hypertension? Curr Cardiol Rev. 2014;10:355-61.

[39] Lockhart PB, Bolger AF, Papapanou PN, Osinbowale O, Trevisan M, Levison ME, et al. Periodontal disease and atherosclerotic vascular disease: does the evidence support an independent association?: a scientific statement from the American Heart Association. Circulation. 2012;125:2520-44.

[40] Nakajima T, Honda T, Domon H, Okui T, Kajita K, Ito H, et al. Periodontitis-associated up-regulation of systemic inflammatory mediator level may increase the risk of coronary heart disease. J Periodontal Res. 2010;45:116-22.

[41] Phan HM, Alpert JS, Fain M. Frailty, inflammation, and cardiovascular disease:

evidence of a connection. Am J Geriatr Cardiol. 2008;17:101-7.

[42] Minakuchi S, Tsuga K, Ikebe K, Ueda T, Tamura F, Nagao K, et al. Oral hypofunction in the older population: Position paper of the Japanese Society of Gerodontology in 2016. Gerodontology. 2018;35:317-24.

Figure Legends

Fig. 1 Relationship between number of teeth and physical functions

(A), Scatter plot of the correlation between number of teeth and hand grip strength. (B), Scatter plot of the correlation between number of teeth and 6MWD. (C), Scatter plot of the correlation between number of teeth and psoas muscle index. (D), Scatter plot of the correlation between number of teeth and SPPB score.

6MWD, 6-minute walking distance; SPPB, Short Physical Performance Battery.

Fig. 2 Relationship between number of teeth and nutritional status

(A), Scatter plot of the correlation between number of teeth and MNA-SF score for all participants. (B), Scatter plot of the correlation between number of teeth and MNA-SF score grouped according to the presence of physical frailty.

Red squares: Frail group; Black squares: Non-frail group. MNA-SF, Mini Nutritional Assessment Short Form

Fig. S1 SPPB score stratified by occlusal support and periodontal status

(A), SPPB score stratified by Eichner index. (B), SPPB score stratified by CPITN.

SPPB, Short Physical Performance Battery; CPITN, Community Periodontal Index of

Treatment Needs; ANOVA, analysis of variance. *$p<0.05$. Post hoc Tukey's test.

Table 1. Baseline clinical characteristics of patients with or without physical frailty

Variables	Total	Non-frail group	Frail group	P-value
Number of patients, n	457	346 (75.7)	111 (24.3)	
Age, years	67.1 (13.0)	64.5 (12.6)	76.0 (8.9)	<0.001
Sex, female, n (%)	170 (37.2)	120 (34.7)	50 (45.0)	0.09
BMI, kg/m^2	23.0 (4.4)	22.9 (4.4)	23.0 (4.1)	0.85
Lab data				
Albumin, g/dL	4.0 (1.8)	4.0 (0.6)	4.0 (3.4)	0.69
BNP, pg/mL	88.0 (22.8-262.3)	84.0 (21.9-228.5)	135.0 (138.5-446.6)	0.01
Hemoglobin, g/dL	12.6 (2.3)	12.9 (2.1)	11.6 (2.4)	<0.001
eGFR, mL/min/1.73 m^2	55.3 (25.5)	57.7 (26.0)	45.5 (22.6)	<0.001
CRP, mg/dL	0.5 (1.1)	0.4 (0.8)	0.9 (1.7)	<0.001
Total cholesterol, mg/dL	171.9 (47.9)	174.7 (47.8)	170.6 (44.0)	0.42
HDL, mg/dL	52.9 (18.5)	54.2 (17.3)	50.5 (21.6)	0.06
LDL, mg/dL	86.8 (51.1)	87.6 (52.8)	83.9 (50.5)	0.52
HbA1c, %	5.7 (1.5)	5.7 (1.5)	5.5 (1.6)	0.47
Comorbidity, n (%)				
Diabetes	101 (22.1)	75 (21.7)	26 (23.4)	0.82
COPD	142 (31.1)	97 (28.0)	45 (40.5)	0.02
Hypertension	286 (62.6)	206 (59.5)	80 (72.1)	0.03
Previous stroke	12 (2.6)	8 (2.3)	4 (3.6)	0.58
Dyslipidemia	171 (37.4)	126 (36.4)	45 (40.5)	0.46
Previous cardiac surgery	39 (8.5)	31 (9.0)	8 (7.2)	0.14
Chronic kidney disease	247 (54.0)	166 (48.0)	81 (73.0)	<0.001
Atrial fibrillation	67 (14.7)	52 (15.0)	15 (13.5)	0.82

Family history of CAD	74 (16.2)	62 (17.9)	12 (10.8)	0.28
Smoking	24 (5.3)	20 (5.8)	4 (3.6)	0.60
Hemodialysis	34 (7.4)	24 (6.9)	10 (9.0)	0.64
Etiology				
Heart failure	393 (86.0)	295 (85.3)	98 (88.3)	0.53
Ischemic heart disease	64 (14.0)	47 (13.6)	17 (11.7)	0.75
LVEF, %	55.2 (15.0)	57.5 (14.6)	53.1 (13.9)	0.66
NYHA class n (%)				
I	118 (25.8)	95 (27.5)	23 (20.7)	0.10
II	279 (61.0)	208 (60.1)	71 (64.0)	
III	51 (11.2)	39 (11.3)	12 (10.8)	
IV	9 (2.0)	4 (1.2)	5 (4.5)	
MNA-SF	11.7 (2.3)	12.2 (1.9)	10.1 (2.6)	<0.001
Waist circumference, cm	82.3 (10.8)	82.2 (10.4)	82.6 (10.6)	0.72
CTR, %	49.1 (15.3)	48.4 (15.5)	51.4 (14.2)	0.07
Medications, n (%)				
β-blocker	172 (37.6)	131 (37.9)	41 (36.9)	0.99
ACE-I	51 (11.2)	37 (10.7)	14 (12.6)	0.45
ARB	168 (36.8)	123 (35.5)	45 (40.5)	0.65
Statin	132 (28.9)	96 (27.7)	36 (32.4)	0.60
Diuretics	181 (39.6)	136 (39.3)	45 (40.5)	0.94
Digitalis	19 (4.2)	14 (4.0)	5 (4.5)	0.93

ACE-I, angiotensin converting enzyme inhibitor; ARB, angiotensin II receptor blocker; BMI, body mass index; BNP, brain natriuretic peptide; BP, blood pressure; CAD, coronary artery disease; COPD, Chronic obstructive pulmonary disease; CRP, C-reactive protein; CTR, cardiothoracic ratio; eGFR, estimated glomerular filtration rate; GNRI, Geriatric Nutritional Risk Index; HDL, high density lipoprotein; HbA1c, hemoglobin A1c; LDL, low density lipoprotein;

LVEF, left ventricular ejection fraction; MNA-SF, Mini Nutritional Assessment Short Form; NYHA, New York Heart Association.

Data are expressed as mean (standard deviation), median (interquartile range), or number (percentage).

Table 2. Baseline physical functions of patients with or without physical frailty

Variables	Total	Non-frail group	Frail group	P-value
Number of patients, n	457	346 (75.7)	111 (24.3)	
Gait speed, m/s	1.0 (0.2)	0.9 (0.1)	1.2 (0.4)	<0.001
Handgrip strength, kg	27.2 (9.0)	29.5 (8.4)	19.6 (6.6)	<0.001
Knee extensor muscle strength, N/kg	3.9 (1.2)	4.2 (1.1)	3.0 (1.0)	<0.001
SPPB, points	11.0 (1.6)	11.8 (0.4)	8.6 (1.5)	<0.001
Sarcopenia, n (%)	150 (32.8)	96 (27.7)	54 (48.6)	<0.001
6MWD, m	390.2 (113.7)	423.7 (100.0)	287.1 (90.8)	<0.001
PMI, cm^2/m^2	5.5 (1.9)	5.7 (1.9)	4.8 (1.5)	<0.001

PMI, psoas muscle index; SPPB, Short Physical Performance Battery.

Data are expressed as mean (standard deviation), or number (percentage).

Table 3. Comparison of oral health among patients with and without physical frailty.

Variables	Total	Non-frail group	Frail group	P-value
Number of patients, n (%)	457	346 (75.7)	111 (24.3)	
Number of teeth, n	19.3 (9.6)	20.6 (9.2)	15.6 (9.6)	<0.001
Dentures, n (%)	156 (34.1)	108 (31.2)	48 (43.2)	0.01
CPITN, points	2.78 (1.6)	2.7 (1.5)	2.8 (1.7)	0.41
Patients with CPITN ≥4, n (%)	147 (32.2)	107 (30.9)	40 (36.0)	0.35
DMF-T				
D-T	0.4 (1.4)	0.5 (1.6)	0.4 (1.0)	0.44
M-T	12.7 (9.6)	11.4 (9.2)	16.5 (9.6)	<0.001
F-T	8.0 (5.6)	8.4 (5.6)	7.4 (5.6)	0.10
Occlusal support (Eichner Index), n (%)				<0.001
Class A	192 (42.0)	167 (48.3)	25 (22.5)	
Class B	158 (34.6)	113 (32.7)	45 (40.5)	
Class C	107 (23.4)	66 (19.1)	41 (36.9)	
Need for tooth extraction, n (%)	129 (28.2)	88 (25.4)	41 (36.9)	0.022

CPITN, Community Periodontal Index of Treatment Needs; D, decayed teeth; F, filled teeth; M, missing teeth.

Data are expressed as mean (standard deviation) or number (percentage).

Table 4. Association of oral function and each physical function by multiple liner regression analyses.

	SPPB score		PMI		Grip strength		6MWD		Gait speed	
	$R^2 = 0.35$		$R^2 = 0.45$		$R^2 = 0.50$		$R^2 = 0.43$		$R^2 = 0.21$	
	Adjusted R^2 0.34		Adjusted R^2 0.44		Adjusted R^2 0.49		Adjusted R^2 0.42		Adjusted R^2 0.19	
	$P < 0.0001$, F = 27.0		$P < 0.0001$, F = 41.5		$P < 0.0001$, F = 49.6		$P < 0.0001$, F = 34.3		$P < 0.0001$, F =13.1	
Variables	β	p-value	β	p-value	β	p-value	β	p-value	β	p-value
Age	-0.04	<0.001	-0.03	0.001	-0.23	<0.001	-3.79	<0.001	-0.23	<0.001
Sex, female	-0.04	0.85	-1.79	<0.001	-6.44	<0.001	-6.99	0.05	-6.44	0.01
BMI	-0.006	0.002	0.16	<0.001	0.08	0.30	-2.58	0.01	0.07	0.30
MNA-SF score	0.28	<0.001	0.07	0.02	1.05	<0.001	12.75	<0.001	1.05	<0.001
Remaining teeth	0.08	0.02	0.07	0.02	0.09	0.01	0.93	0.02	0.09	0.04
BNP	0.01	0.33	-0.001	0.24	-0.01	0.41	-0.02	0.02	-0.01	0.41
Hemoglobin	0.05	0.06	0.01	0.84	0.35	0.02	6.38	0.01	-0.35	0.02
CKD	-0.01	0.87	-0.02	0.52	-0.40	0.56	-0.36	0.97	0.41	0.56
CRP	-0.09	0.04	-0.02	0.72	-0.06	0.83	-7.51	0.04	-0.06	0.83

BMI, body mass index; BNP, brain natriuretic peptide; CKD, chronic kidney disease; MNA-SF, Mini Nutritional Assessment Short Form; CRP; C-reactive protein; 6MWD, 6-minute walking distance; PMI, psoas muscle index; SPPB, Short Physical Performance Battery.

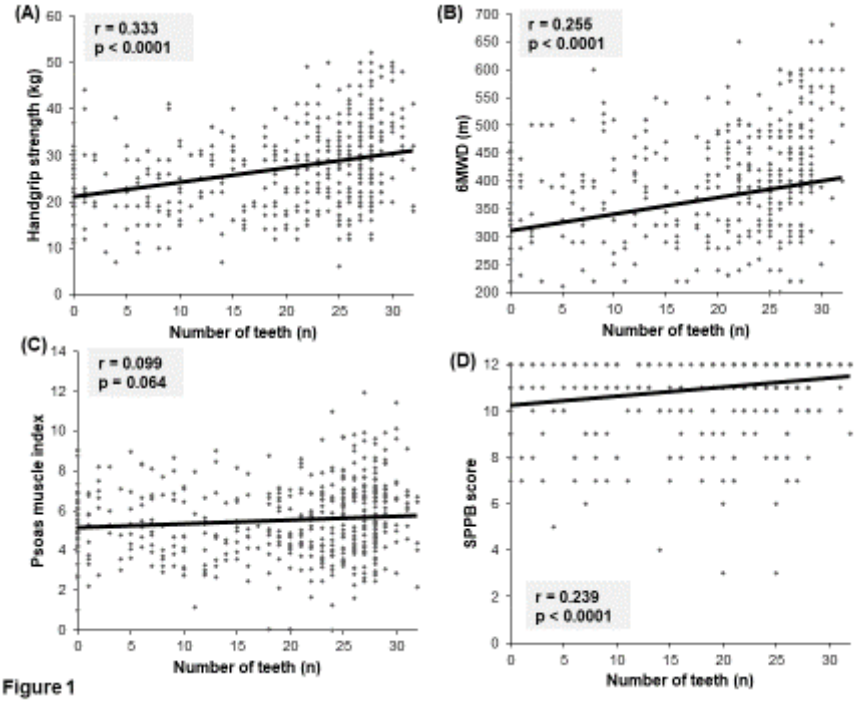
(A)
r = 0.333
p < 0.0001
Handgrip strength (kg)
Number of teeth (n)
(B)
r = 0.255
p < 0.0001
6MWD (m)
Number of teeth (n)
(C)
r = 0.099
p = 0.064
Psoas muscle index
Number of teeth (n)
(D)
r = 0.239
p < 0.0001
SPPB score
Number of teeth (n)

Figure 1

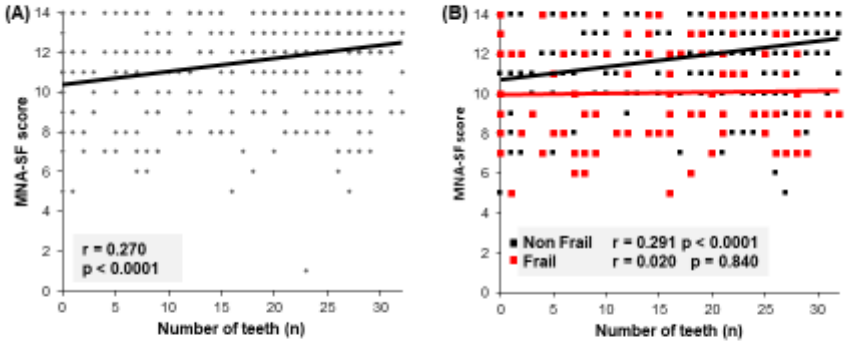
(A)
MNA-SF score
Number of teeth (n)
r = 0.270
p < 0.0001
(B)
MNA-SF score
Number of teeth (n)
Non Frail r = 0.291 p < 0.0001
Frail r = 0.020 p = 0.840

Figure 2

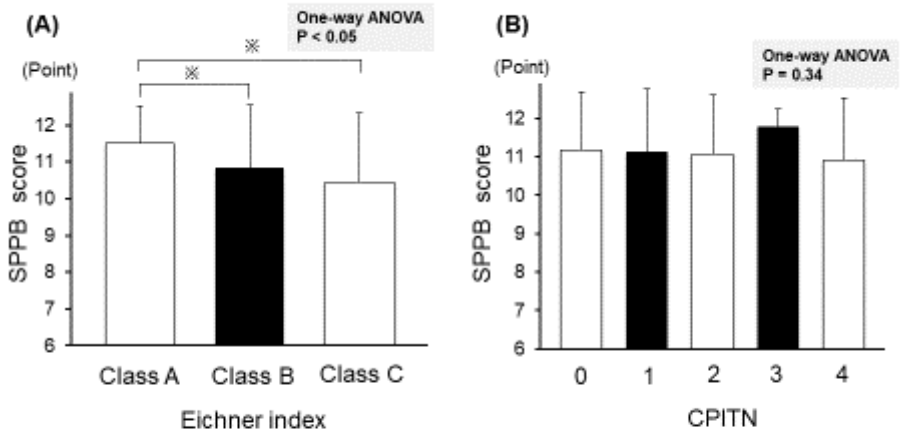

Figure. S1

(※ $p < 0.05$)