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**Original article**

# Assessment of potential clinical cascade between oral hypofunction and physical frailty: Covariance structure analysis in a cross-sectional study

Short running title:

Cascade between oral function and physical frailty

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## Summary

**Background:** No report has yet examined the impact of oral hypofunction on physical frailty in relation to intra-relationships of physical frailty assessment items.

**Objectives:** The purpose of this study was to verify the potential of a clinical cascade between oral hypofunction and physical frailty, and especially to support the hypothesis that the influence of oral hypofunction on physical frailty is greater than the intra-relationships among elements of physical frailty, and that sex differences significantly affect these relationships.

**Methods:** The participants were 272 older adults (101 men and 171 women; mean age 75.1±7.5 years). Maximum occlusal force (MOF) and oral dryness (OD), as indicators of oral hypofunction, and grip strength (GS) and walking speed (WS), as indicators of physical frailty, were measured. Mutual relationship of four variables were verified using covariance structure analysis.

**Results:** In men, three paths from MOF to WS and GS and from WS to GS were confirmed, and those from MOF to WS and from WS to GS were found to be significant ($p<0.01$). In women, three paths from MOF to WS and GS and from WS to GS were also confirmed, as with the men, and those from MOF to WS and from MOF to GS were found to be significant ($p<0.01$). Model adaptability was shown to be good for both men and women.

**Conclusion:** The results suggest our hypothesis was verified, and it is expected that the early detection of oral hypofunction, that is, MOF, may be important for assessing physical frailty, especially in women.



## KEYWORDS

oral hypofunction, physical frailty, covariance structure analysis

## 1 BACKGROUND

Currently, the number of older people is increasing worldwide, and this tendency is especially prominent in Japan, which has the highest rate of population aging in the world.[1-3] With the increase in the older population, medical care costs will increase accordingly, and the need for preventative nursing care is becoming a critical Japanese social problem.[4] Frailty, a concept proposed by Fried et al. in 2001, is of particular interest in the field of gerontology; it is theoretically defined as a clinically recognizable state of increased vulnerability resulting from aging-associated decline in reserve and function across multiple physiologic systems, such as the compromising of the ability to cope with everyday or acute stressors.[5,6] Frailty is a multidimensional construct comprising not only physical but also psychological and social conditions. The criteria for the assessment of physical frailty specified by Fried et al., which include weight loss, exhaustion, physical activity, walking speed (WS), and grip strength (GS), have been widely used.[7] There is considerable research concerning the interrelationships among these five criteria, as well as the effects of each criterion on fatality risk and rate of nursing care service utilization.[8-10]

The relationship between oral and systemic diseases/conditions has been examined and is well documented;[11,12] consequently, in recent years the relationship between physical frailty and oral hypofunction (deterioration of oral function) has also been examined, in various epidemiological studies. For example, it has been reported that sarcopenia, one of the core components of physical frailty, is associated with decline in occlusal force and mastication efficiency, with a significant odds ratio; there are also sex differences in the relationship.[13] However, no report has yet examined the impact of oral hypofunction on physical frailty in relation to the intra-relationships among physical frailty assessment items.

In the present study, we hypothesized that the influence of oral hypofunction on physical frailty would be greater than the intra-relationships of physical frailty, and that sex differences would significantly affect these relationships. We focused on maximum occlusal force (MOF) and oral dryness (OD) as indicators of oral hypofunction and on GS and WS as indicators of physical frailty. We examined the mutual relationships among these four variables through covariance structure analysis in order to verify the above hypothesis.

## 2 MATERIALS AND METHODS

### 2.1 Participants

From among patients undergoing regular maintenance at a dental clinic, 272 participants (101 men and 171 women; mean age 75.1±7.5 years) were serially recruited from November 2016 to April 2018. Patients aged over 65 years who consented to participate in this study based on the relevant information provided to them were included. Each participant had complete dental arches from their incisors to their molar teeth, with/without prosthesis. The exclusion criterion was having more than one unmeasurable item among the four—GS, WS, MOF, and OD—due to the cognitive decline and physical impairment. The present study was approved by the Ethics

Committee of Tokushima University Hospital (approval number: 2404). It was conducted according to the criteria set out by the Declaration of Helsinki. Each participant signed an informed consent form before participating in the study.

## 2.2 Assessment of physical frailty and oral function

Patient age and sex were recorded as basic attributes. GS and WS were measured as indicators of physical frailty. GS was measured using a digital grip dynamometer (Grip D・TKK5401, Takei Scientific Instruments Co., Ltd., Niigata, Japan) for each hand. To measure WS, patients were asked to walk at their normal pace down a 3-meter measuring zone, using an assistive device if needed. Their WS was calculated according to the time required to complete the 3-meter walking task. MOF and OD were measured as indicators of oral hypofunction. MOF was measured using an occlusal force meter (GM-10, Nagano Keiki Co., Ltd., Tokyo, Japan) with a load cell transducer at the first molar of each side.[14,15] OD was measured using an oral moisture checker (Mucus, Life Co., Ltd., Saitama, Japan). The oral moisture checker can easily measure the moisture level of a substance by calculating the capacitance from the dielectric constant of the substance. In this study, the oral moisture checker was applied to measure the moisture of the submucosal layer at the central tongue dorsum linguae, 10 mm backward from the apex linguae. The oral moisture checker has been validated[16-18]; Fukushima et al. reported that 241 participants with dry mouth showed 27.2±4.9, while 250 participants without dry mouth showed 29.5±3.1.[17] The cut-off value is 27.0, that is, a measured value less than 27.0 is evaluated as OD.[18] The measurements were repeated three times.

The mean of the multiple measurements on both sides was used as the representative value.

## 2.3 Statistical analysis

Statistical analyses were conducted using SPSS 24.0 (SPSS Inc., Chicago, USA) and AMOS (SPSS Statistics 17.0, SPSS Inc., Chicago, IL, USA). Sex-based comparisons of the four variables were conducted using a Mann–Whitney U test. Spearman's correlation and multiple regression analyses were conducted to clarify the mutual relationships among all the variables to develop a hypothetical path model. Statistical analyses were conducted with a significance level of 0.05. A path model analysis was then conducted from oral hypofunction to physical frailty using a covariance structure analysis.

We calculated the $\chi^2$ value, goodness-of-fit index (GFI), adjusted goodness-of-fit index (AGFI), comparative fit index (CFI), and root–mean–square error of approximation (RMSEA) to examine goodness of fit in the model. A p value of >0.05, and scores of >0.95, >0.90, >0.97, and <0.08 for GFI, AGFI, CFI, and RMSEA, respectively, were considered to indicate a good model data fit.[19]

## 3 RESULTS

Table 1 shows the means and standard deviations for the variable scores among the men and women. No significant difference in mean age was found between men and women. MOF and GS were significantly larger in men compared with women, whereas there were no sex differences in either WS or OD scores.

Figure 1 shows the two-dimensional scatter plot for the two variables, physical frailty (left) and oral hypofunction (right), with cut-off values at the normal level. Each cut-off value was selected based on previous study findings.[7,18] Regarding the characteristics of the elderly sample population, the values of GS and OD for most of the subjects were above the cut-off value, while the values of MOF and WS of for most of the subjects were less than the cut-off value.

Table 2 shows the results of correlation analysis among the variables. Significant positive correlations were found between the variables and GS, WS, and MOF scores for both sexes. No such correlations were found between the OD scores and the other variables.

Table 3 shows the results of the multiple regression analysis. When GS was the dependent variable, WS and MOF were significantly associated as independent variables for both sexes. When WS was the dependent variable, GS and MOF were significantly associated for both sexes. The partial regression coefficient of WS as a dependent variable of GS was larger than that of GS as a dependent variable of WS for both sexes. OD was not significantly associated in any of the multiple regression analyses.

Considering the above results, a covariance structure analysis was performed to investigate a path model in which oral hypofunction affects physical frailty as shown in Fig.2. In men, the three paths—from MOF to WS and GS and from WS to GS—were confirmed, and those from MOF to WS and from WS to GS were found to be significant ($p<0.01$). The adaptability of the model was good in men ($\chi^2=0.643$, $p=0.423$, GFI: 0.997, AGFI: 0.968, CFI: 1.000, RMSEA: 0.000). In women, the three passages—from MOF to WS and GS and from WS to GS—were also confirmed, as in the path model of men, but those from MOF to WS and from MOF to GS were found to be significant ($p<0.01$). The adaptability of the model was shown to be good with the women ($\chi^2=1.833$, $p=0.176$, GFI: 0.995, AGFI: 0.947, CFI: 0.972, RMSEA: 0.070), as with the men. None of the reverse path models from physical frailty to oral hypofunction had good adaptability.

## 4 DISCUSSION

In this study, we aimed to examine the potential clinical cascade between oral hypofunction and physical frailty using covariance structure analysis. This analysis, proposed by Jöreskog in the 1960s, is a form of causal modeling that includes a diverse set of statistical models that fit networks of constructs to data.[20] The parameters used for measures of fit included the $\chi^2$ value, GFI, AGFI, CFI, and RMSEA. A p value of >0.05 is considered to indicate good path model fit, as are GFI, AGFI, CFI, and RMSEA scores of >0.95, >0.90, >0.97, and <0.08, respectively. The covariance structure analysis in which the structural relationships of the observation variables can be provided has been widely used in many studies not only in sociology and economics but also in epidemiology.[21,22] Therefore, covariance structure analysis was used to examine the mutual relationship between oral hypofunction and physical frailty in this study.

In order to reduce the burden on the older people in our sample, the assessments of oral hypofunction and physical frailty included only two variables each: MOF and OD, and GS and WS, respectively. Regarding physical frailty, GS and WS are included in the diagnostic criteria of sarcopenia, as well as physical frailty.[23] These are the most objective indexes in the five diagnostic criteria of physical frailty proposed by Fried.[6] Many studies have reported that GS and WS are significant indexes of general health condition, as well as risk factors in declining basic activities of daily living (ADL). Guralnik investigated the occurrence of ADL disability with a longitudinal study of community-dwelling elderly people, and reported that there is a quadruple risk for ADL disability in people with lower extremity function of WS at baseline compared with those with a higher WS at a 4-year follow-up.[24] Moreover, in Japan, Furuna performed similar research and reported that older people with reduced exercise capacity, including declines in GS and WS, had difficulty maintaining instrumental ADL, as well as a high risk of ADL disability occurrence after 4 years.[25]

The Japanese Society of Gerodontology proposed seven criteria for oral hypofunction: poor oral hygiene, OD, reduced occlusal force, decreased tongue-lip motor function, decreased tongue pressure, decreased masticatory function, and deterioration of swallowing function.[18] These seven criteria are not necessarily independent, but they are considered to be mutually related. Three criteria: poor oral hygiene, decreased masticatory function, and deterioration of swallowing function are comprehensive abilities and conditions of oral cavity, and the other four criteria: OD, reduced occlusal force, decreased tongue-lip motor function, and decreased tongue pressure are more fundamental assessments. MOF was selected as a factor of muscular strength in relation to oral function, because older people can easily understand the significance of that measurement compared with other muscle-related measurements, such as tongue-lip motor function and tongue pressure. In addition, numerous studies on the relationship between MOF and physical frailty have already been reported.[26,27] For instance, Iinuma reported that MOF was significantly related to GS and WS in community-living individuals aged 85 years and older.[26] Watanabe examined the relationship between MOF and frailty in participants aged 65 and older, and reported that the risk of frailty became significantly lower as MOF increased.[27] The meaning of OD, the other measurement of oral hypofunction, may be different from that of the other three fundamental criteria related to muscle activities. OD, which is often caused by essential disease or drug side effects, involves a lack of moisture derived chiefly from saliva. It considerably affects dental caries and periodontal disease development, as well as the stability of removable dentures, food bolus formation, smooth speech and swallowing behaviors, and oral health-related quality of life.[28] Although there is little information on the relationship between OD and physical frailty, OD was selected as the other assessment of oral hypofunction.

First, the relationship between GS and WS for physical frailty was examined in constructing the path model. As the partial regression coefficient of WS with GS as a dependent variable was larger than that of GS with WS as a dependent variable for both sexes, the possibility of a path from WS to GS was indicated. A significant positive correlation between GS and WS has been reported;[29] however, this relationship has not been verified using covariance structure analysis or logistic regression analysis. Although both GS and WS are included in the diagnostic criteria for both physical frailty, as proposed by Fried,[6] and sarcopenia, as defined by the Group on Sarcopenia in Older People, the diagnostic flows of the two are different. GS and WS are defined independently of each other in physical frailty, whereas WS is assessed before GS in the diagnosis of sarcopenia: WS is examined first, and then muscle volume is measured if WS is less than 0.8 m/sec; then, GS is measured, even if WS is 0.8 m/sec or more, and the greater measurement is judged as the cut-off value of GS.[23] This difference may be based on the idea that the critical outcome of sarcopenia is a physical dysfunction due to reduced skeletal muscle mass and skeletal muscle strength, which is typically referred to as "reduction in mobility." Furuna reported that WS was the most important predictor of ADL disability occurrence,[25] and Shinkai also reported a similar result.[30] Our model speculates that WS will be an upstream element of GS, and this is supported by these other studies.

Although no significant path was found from OD to GS and WS, the path model did not have good adaptability unless OD was selected as an observation variable. This result implies that OD does not directly influence both GS and WS, but may indirectly influence physical frailty through other factors of oral hypofunction, considering that patients with

OD and decline in oral moisture often complain about difficulties in mastication, speech, swallowing, and taste disorder.[28] Future studies will need to address this issue.

The potential path from MOF to WS and GS as physical frailty indicators, relative to the path between WS and GS, was strong among women. Past studies have reported that both systemic and oral function are significantly lower among women than men. Regarding physical frailty, Kojima et al. reported that prevalence of physical frailty in women was higher than that in men among participants aged over 75 years.[31] Ikebe et al. also reported that MOF in women was significantly lower than that in men among those aged 60–84 years who were living independently.[32] Regarding the perioral muscles, similar results in tongue pressure and masseter muscle thickness have been reported by Kamijo et al.[33] and Gaszynska et al.[34] These studies' findings support our present results.

Moreover, because the participants used in this study had complete dental arches from their incisors to their molar teeth with/without prosthesis and were receiving regular maintenance at a dental clinic, there was the possibility of sampling bias, in that many subjects with high health awareness may have been included. Regarding their general health condition, participants who consented to participate in this study based on relevant information and who completed all measurable items, were enrolled; thus, participants with extensive cognitive decline and physical impairment were excluded, and sampling bias may also have been present in this regard. The results of this study must be interpreted based on these limitations, and investigations of those with low oral literacy or those who cannot visit a dental clinic should be performed in future studies.

However, considering the distribution of each measurement item, as described in Figure 1, sampling have been performed without significantly deviating toward either oral hypofunction or physical frailty. Moreover, the sample of elderly people in this study is similar to those of previous studies, considering the averages for each variable.[35-37]

The present study also has limitations in terms of the different sample sizes of men and women, the paucity of measurements in the diagnostic criteria of physical frailty and oral hypofunction, and the nature of the cross-sectional study design. However, our hypothesis that the influence of oral hypofunction on physical frailty is greater than the interrelationships of the physical frailty variables, as well as the flowing order of clinical cascade from oral hypofunction to physical frailty being MOF-WS-GS, and that this relationship was strong among women, was verified in this study. The early detection of oral hypofunction, that is, decline in occlusal force, is expected to be significant in the assessment of physical frailty, especially in women.

## CONFLICT OF INTERESTS

The authors declare no conflict of interest.

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## TABLE AND FIGURE LEGENDS

**TABLE 1** Means and standard deviations of measurements in men and women

**TABLE 2** Spearman's correlation coefficients among four measurements in men and women: grip strength, walking speed, maximum occlusal force, and oral dryness

**TABLE 3** The result of multiple regression analysis. Each value presents standardized partial regression coefficients when the dependent factor is either grip strength or walking speed

**FIGURE 1** Scatter plots of two measurements, physical frailty and oral hypofunction (a: physical frailty, b: oral hypofunction). The dash lines show the cut-off values for each measurement

**FIGURE 2** The results of the covariance structure analysis for men (left) and women (right). The arrows with single and double lines represent the statistically significant paths with $p<0.05$ and $p<0.01$, respectively, and the dash lines show the non-significant paths. The numbers beside the arrows show the standardized path coefficients. The p values reveal the levels of statistical significance

**TABLE 1** Means and standard deviations of measurements in men and women

| Variable | Men (n=101) | Women (n=171) | P-value |
|---|---|---|---|
| Age (years) | 74.7±7.8 | 75.4±7.3 | p=0.32 |
| Grip strength (kgf) | 30.3±8.4 | 19.4±7.1 | p<0.01* |
| Walking speed (m/sec) | 0.83±0.25 | 0.83±0.25 | p=0.70 |
| Maximum occlusal force (N) | 231.0±172.7 | 170.9±133.1 | p<0.01* |
| Oral dryness | 27.9±4.1 | 28.6±6.2 | p=0.50 |

* Statistical difference (P-value <0.01)

**TABLE 2** Spearman's correlation coefficients among four measurements in men and women: grip strength, walking speed, maximum occlusal force, and oral dryness

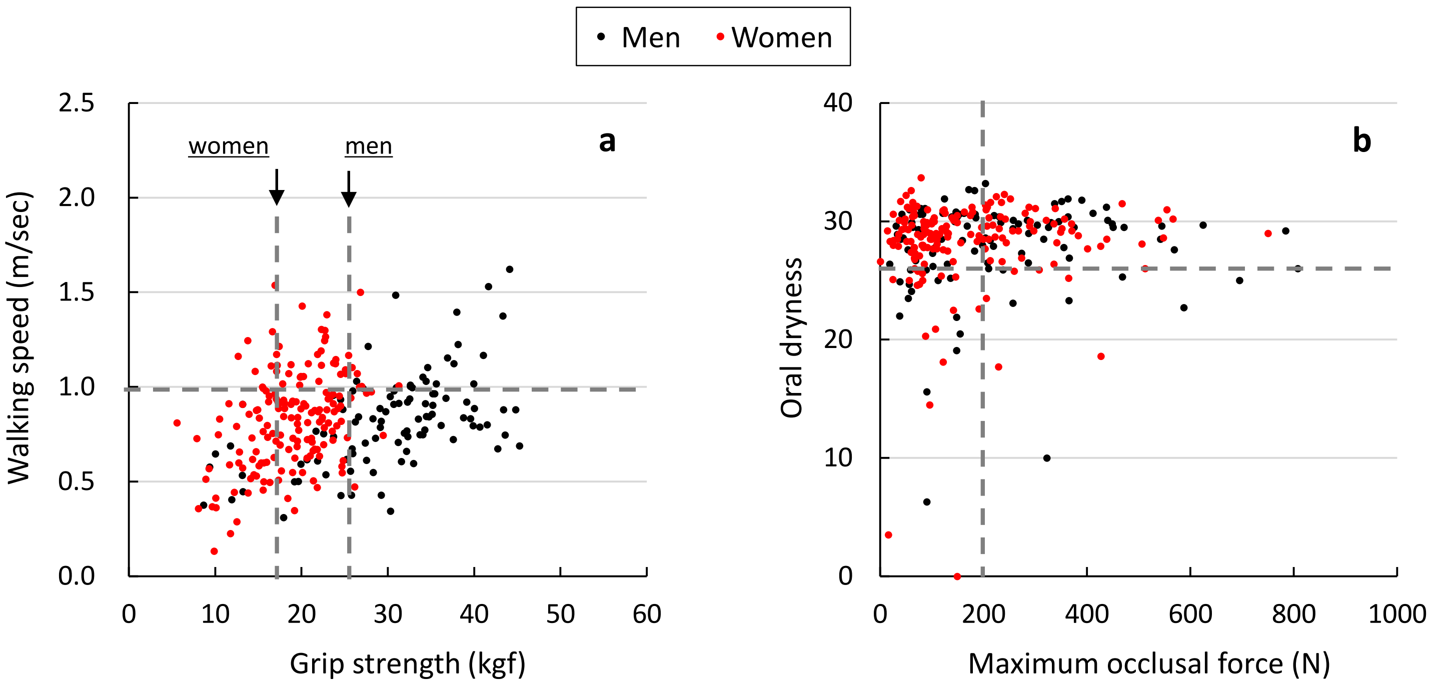
| Variable | Grip strength | Walking speed | Maximum occlusal force | Oral dryness |
|---|---|---|---|---|
| Grip strength | 1.000/1.000 | 0.528*/0.373* | 0.417*/0.431* | 0.060/-0.041 |
| Walking speed | | 1.000/1.000 | 0.403*/0.324* | 0.026/-0.053 |
| Maximum occlusal force | | | 1.000/1.000 | 0.126/0.241 |
| Oral dryness | | | | 1.000/1.000 |

* Statistical difference (P-value <0.01)

**TABLE 3** The result of multiple regression analysis. Each value presents standardized partial regression coefficients when the dependent factor is either grip strength or walking speed

| Dependent valuable | Independent valuables | | | |
|---|---|---|---|---|
| | Grip strength | Walking speed | Maximum occlusal force | Oral dryness |
| Grip strength | — | 0.463**/0.189* | 0.187*/0.207** | 0.008/-0.029 |
| Walking speed | 0.427**/0.185* | — | 0.287**/0.241** | -0.133/-0.096 |

Statistical difference ( *P-value <0.05, ** P-value <0.01)

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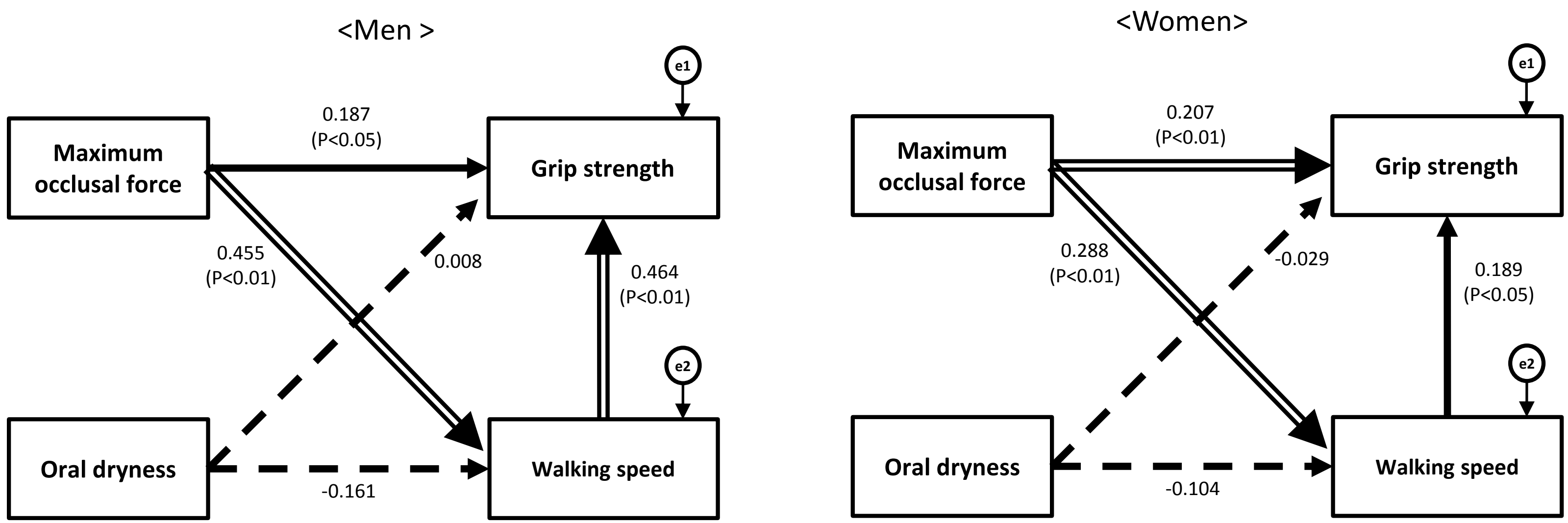


**FIGURE 2** The results of the covariance structure analysis for men (left) and women (right). The arrows with single and double lines represent the statistically significant paths with p<0.05 and p<0.01, respectively, and the dash lines show the non-significant paths. The numbers beside the arrows show the standardized path coefficients. The p values reveal the levels of statistical significance