#### **UROLOGY - ORIGINAL PAPER**



# Association between oral frailty and lower urinary tract symptoms among middle-aged and older adults in community-dwelling individuals: a cross-sectional study

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## Abstract

**Purpose** We assessed the association between oral frailty risk and LUTS among middle-aged and older adults in a community-dwelling population.

**Methods** This cross-sectional study was conducted among 586 subjects aged  $\geq$  40 years who participated in the Iwaki Health Promotion Project in Hirosaki, Japan. We used the International Prostate Symptom Score (IPSS) and the Overactive Bladder Symptom Score (OABSS) to assess LUTS. LUTS was defined as an IPSS score of 8 or higher or meeting diagnostic criteria for OAB. Oral frailty risk was defined as experiencing two or more of the following: decreased chewing ability, decreased biting force, and dry mouth sensation. Physical performance (10-m gait speed and grip strength) was used for analysis. The association between oral frailty risk and LUTS was examined using multivariate logistic regression analyses.

**Results** The study included 218 men and 370 women, of whom 140 had LUTS. The mean age of this cohort was 59 years. Significant differences were observed between the LUTS and non-LUTS groups, including age, hypertension, history of CVD, depressive status, sleep disturbance, and 10 m gait speed. The prevalence of oral frailty risk was significantly higher in the LUTS group than in the non-LUTS group (26% vs. 11%, P<0.001). Multivariate analysis revealed that age, male gender, and oral frailty risk (odds ratio: 2.67, 95% confidence interval: 1.57–4.51, P<0.001) were independent factors for LUTS. Moreover, oral frailty risk was an independent factor in both participants aged <65 years and participants aged  $\geq$ 65 years. **Conclusions** Oral frailty was independently associated with LUTS.

Keywords Lower urinary tract symptoms  $\cdot$  Oral frailty risk  $\cdot$  Aging

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### Introduction

Lower urinary tract symptoms (LUTS) are symptoms related to problems with the lower urinary tract, including the bladder, prostate, and urethra [1]. Common symptoms of LUTS include hesitancy, weak or intermittent stream, straining, urgency, frequency, nocturia, and incontinence. LUTS can have a significant impact on quality of life and is associated with various comorbidities, including aging, cardiovascular disease (CVD), metabolic syndrome, depression, dementia, and sleep disturbances [1-5]. Frailty is a condition characterized by impaired physical function and is associated with several adverse health outcomes, particularly in the older people [6]. Previous studies have suggested a possible association between LUTS and frailty [1, 7–9]. In particular, physical functions such as walking speed and grip strength are known to be indicators of LUTS [8, 10, 11]. However, only few studies have demonstrated an association between LUTS and oral frailty and hygiene [7, 12].

Oral frailty is a condition characterized by impaired oral function and is associated with several adverse health outcomes in the older people. Oral frailty has been associated with a higher risk of physical frailty and mortality [13, 14], suggesting that oral function may reflect systemic frailty more accurately than physical function. A recent cross-sectional study showed that older patients with LUTS-related disease had significantly lower oral function scores than those without LUTS-related disease [7]. However, to date, little is known about the independent association between LUTS and oral frailty. We hypothesized that oral frailty may be an important factor in the presence of LUTS. We cross-sectionally assessed the association of oral frailty with LUTS among middle-aged and older adults in a community population using the Community Health Promotion Program database.

# **Materials and methods**

#### **Design and ethics statement**

The research adhered to the ethical principles outlined in the Declaration of Helsinki, and the use of data from the Iwaki Health Promotion Project was approved by the Ethics Committee of the Hirosaki University School of Medicine (approval number 2018-062 and 2023-078). Since 2005, this annual health survey initiative has been conducted among residents of the Iwaki area of Hirosaki City. All individuals aged 20 years and older have voluntarily participated in this program. Anonymity of all participants is strictly preserved when researchers use information of this database. The primary objectives of the Iwaki Project were to prevent lifestyle-related diseases, promote healthconscious lifestyles, and improve the life expectancy of Hirosaki residents. To date, many researchers in various fields have done research by using the database of this project. We have also previously investigated the relationship between the LUTS and other conditions or factors, such as frailty, falls, sleep quality, gut microbiome, and oxidative stress [4, 15–18].

#### Data collection and evaluation of variables

Participants gave informed consent and answered a series of questions about their lifestyle and personal information. They also underwent several assessments, including blood tests. Blood samples were taken in the morning and immediately centrifuged to separate the serum, which was then stored in tubes containing EDTA at -80 °C until further study.

In 2015, a total of 1113 individuals participated in the study. A history of CVD included cardiac surgery, angina, myocardial infarction, stroke, or use of cardiotonic agents or coronary vasodilators. Diagnostic criteria for metabolic syndrome in Japan typically include the presence of at least three of the following risk factors: abdominal obesity (specific waist circumference thresholds), elevated triglycerides, reduced HDL cholesterol, elevated blood pressure, and elevated fasting glucose [19]. The Japanese version of the Pittsburgh Sleep Quality Index was used to assess sleep quality, with sleep disturbance defined as a PSQI score greater than 5 [18] mental health was assessed using the Center for Epidemiologic Studies Depression (CES-D) scale [20]. A CES-D score of 16 or higher generally indicates more severe symptoms of depression. Daily salt intake (in grams per day) was calculated for each participant using the Brief-type Selfadministered Diet History Questionnaire (BDHQ) [21]. This validated questionnaire is specifically tailored for Japanese adults and aims to estimate an individual's nutrient intake, such as salt and protein, based on the types and amounts of food consumed. Gait was assessed using the 10 m gait test. In the 10 m gait test, walking began 2 m from the start line of a 10 m walkway and slowed for 2 m after reaching the 10 m finish line [22]. Grip strength was measured with a digital pinch. Low grip strength was defined as of < 28 kg in men and < 19 kg in women, respectively [23]. Of the 1113 participants, we excluded data from individuals who were < 40 years of age and who were missing critical information needed for our analyses. In addition, participants taking anticholinergics and/or ß3 stimulants were also excluded from the study. The reason for this exclusion was that these medications may exacerbate dry mouth.

#### **Evaluation of oral frail risk**

We assessed the potential for oral frailty using the Kihon Checklist 6, a tool developed and validated by the Japanese Ministry of Health, Labor and Welfare. This checklist is widely used in Japan to identify elderly individuals who may need extended care. It's a simple self-report questionnaire with 25 yes/no questions about instrumental and social activities of daily living, physical function, nutritional status, oral function, cognitive function, and depressive mood. Oral frailty risk was defined as having two or more of the following oral function questions; decreased chewing ability (Do you have any difficulties eating tough foods compared to 6 months ago?), decreased swallowing ability (Have you choked on your tea or soup recently?), and dry mouth sensation (Do you often experience having a dry mouth?) [6].

#### **Evaluation of LUTS and classification of participants**

LUTS was evaluated using the International Prostate Symptom Score (IPSS) [24] and the Overactive Bladder Symptom Score (OABSS) [25]. The IPSS is a validated scoring system used to assess the severity of LUTS in patients with benign prostatic hypertrophy (BPH). The IPSS consists of seven questions related to urinary voiding and storage symptom [26]. Score ranges from 0 to 35, with higher scores indicating more severe symptoms. The IPSS consists of seven questions (Q1–Q7) related to urinary voiding (Q1, 3, 5, and 6) and storage symptoms (Q2, 4, and 7). The IPSS is commonly used in research studies and clinical practice to measure disease severity and assess response to therapy for in both male and female patients. A score of 0 to 7 indicates mild symptoms, 8 to 19 indicates moderate symptoms, and 20 to 35 indicates severe symptoms. The OABSS consists of four questions, daytime frequency, nocturia, urinary urgency, and urge incontinence. OAB was defined as the presence of two or more points in urinary urgency and an overall OABSS score of three or greater. The presence of LUTS was defined as having an IPSS total score of  $\geq 8$  (moderate to severe) and/or OAB in this study.

#### **Statistical analysis**

StatistaphPad Software, San Diego, CA, USA) and EzR: R commander (version 1.6-3). Data were presented as means (standard deviation [SD]) for normally distributed continuous variables, and as medians (interquartile range [IQR]) for non-normally distributed variables. Categorical variables were compared using the  $\chi^2$  test or Fisher's exact test. Differences between groups were assessed using Student's t test for normally distributed data and Mann–Whitney U test for non-normally distributed data. The association of each factor with LUTS was analyzed by multivariable

logistic regression. In Japan, people aged over 65 years or older are defined as pre-old age [27]. Therefore, we also performed subgroup analyses of multivariable logistic regression by age 65 (participants aged  $\geq$  65 years and < 65 years). The covariates selected for inclusion in the multivariate analyses were determined to account for factors that could potentially influence both frailty and LUTS. These variables consisted of age, nutritional status (serum albumin levels and BMI), gender, daily salt intake, depressive status, physical functions, history of CVD, sleep quality, and the presence of metabolic syndrome. To investigate the factors contributing to LUTS severity (IPSS and OABSS), multiple linear regression analysis was conducted. To assess the relative importance of the independent variables and to facilitate comparison among them, standardized  $\beta$  coefficients were calculated for each factor in the multiple linear regression model.

### Results

#### **Baseline characteristics**

Of 1,113 participants, we excluded 19 who were taking OAB medications, 312 who were missing important data (25 missing oral frailty assessment, 4 missing BMI, 244 missing physical tests, 32 missing IPSS, and 7 missing PSQI), and 196 who were aged < 40 years from further analysis. Finally, we evaluated 586 individuals (218 men and 368 women). The median age of this cohort was 59 years. The number of participants in the LUTS and non-LUTS groups was 140 and 446, respectively (Fig. 1). Of the 140 participants in the LUTS group, 7 were receiving medication for BPH.

# Comparison of characteristics between the LUTS and non-LUTS groups

Table 1 shows the baseline characteristics of the study participants, categorized into LUTS and non-LUTS groups. In the LUTS group, participants were significantly older (P<0.001), higher daily salt intake (P=0.041), and slower 10 m gait speeds (P=0.021) compared to those in the non-LUTS group. In addition, a significantly higher proportion of participants in the LUTS group had a history of CVD, metabolic syndrome, depressive status (CES-D  $\geq$  16) and sleep disturbances (PSQI > 5) compared to the non-LUTS group. The participants in the LUTS group had a significantly higher oral frailty score (0.91 vs. 0.57, P<0.001) and a higher prevalence of having an oral frailty risk (26% vs. 11%, P<0.001) compared to the non-LUTS group. Fig. 1 Participant selection and disposition. A cohort of 1113 community-dwelling participants were selected from the Iwaki Health Promotion Project. After excluding 527 participants, the remaining 586 were included in the analysis. The participants were stratified to one group of 140 with lower urinary tract symptoms (LUTS), and a second group of 446 with non-LUTS. IPSS, International Prostate Symptom Score; OABSS, Overactive Bladder Symptom Score; OAB, overactive bladder; BPH, benign prostatic hyperplasia

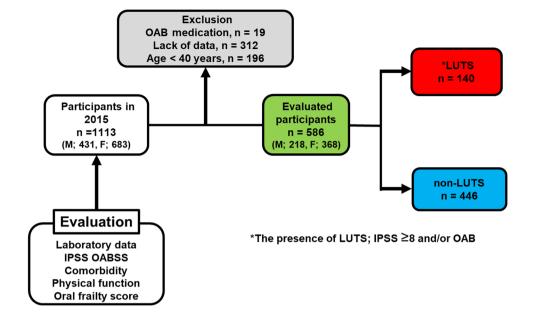


Table 1 Comparison of baseline characteristics between the LUTS and non-LUTS group

	LUTS	Non-LUTS	P value
Number of participants	140	446	_
Male sex <sup>‡</sup> (presence), n (%)	80 (47%)	152 (34%)	0.007
Age* (years) (median, IQR)	65 (58–71)	58 (49–65)	< 0.001
History of $\text{CVD}^{\ddagger}$ (presence), n (%)	19 (14%)	24 (5.4%)	0.002
Metabolic syndrome <sup>‡</sup> (presence), n (%)	23 (16%)	38 (8.5%)	0.011
Smoking history <sup>‡</sup> (presence), n (%)	49 (35%)	151 (34%)	0.838
Sleep disturbance <sup><math>\ddagger</math></sup> (PSQI > 5) (presence), n (%)	35 (25%)	76 (17%)	0.047
Depressive status <sup>‡</sup> (CES-D $\geq$ 16) (presence), n (%)	34 (24%)	67 (15%)	0.015
BMI* (kg/m <sup>2</sup> ) (median, IQR)	22.9 (21.1-24.5)	22.6 (20.7-24.8)	0.515
Serum albumin* (mg/dL) (median, IQR)	4.4 (4.2–4.6)	4.5 (4.3-4.6)	0.154
Daily salt intake* (g/day)	10.4 (8.4–12.7)	11.1 (9.3–13.1)	0.041
Oral frailty score <sup>¶</sup> (mean, SD)	0.91 (0.83)	0.57 (0.73)	< 0.001
Oral frailty risk <sup>‡</sup> (presence), n (%)	37 (26%)	47 (11%)	< 0.001
10-m gait speed* (sec) (median, IQR)	4.1 (3.5–4.9)	3.9 (3.5–4.5)	0.021
Low grip strength <sup><math>\ddagger</math></sup> (M; <28 kg, F; <18 kg) (presence), n (%)	11 (7.9%)	23 (5.2%)	0.298

LUTS lower urinary tract symptoms, IQR interquartile range, CVD cardiovascular disease, PSQI Pittsburgh sleep quality index; The Center for Epidemiologic Studies Depression Scale, BMI body mass index, CES-D, SD standard deviation

 $^{\ddagger}\chi^{2}$  test

\*Mann-Whitney U test

<sup>¶</sup>Student t test

#### Multivariable logistic regression analyses for LUTS

Multivariate analysis revealed that age, male gender, sleep disturbance, oral frailty risk (odds ratio [OR]: 2.67, 95% confidence interval [CI]: 1.57–4.51, P<0.001) served as independent factors for LUTS (Table 2), whereas 10-m gait speed and lower grip strength were not independent factors for LUTS. A sensitivity analysis that included 9 participants who received OAB treatment and had no missing data showed that oral frailty risk remained an independent factor for LUTS (OR: 2.46, P<0.001).

Table 2 Multivariable logistic analysis of LUTS
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Variable	Risk factor	P value	OR	95% CI
Age (years)	Continuous	< 0.001	1.06	1.03-1.09
Gender	Male	< 0.001	2.44	1.49–3.99
Oral frailty risk	Presence	< 0.001	2.67	1.57-4.51
Low grip strength	Presence	0.500	0.75	0.32-1.77
10 m gait speed (sec)	Continuous	0.262	1.15	0.90-1.48

Model was adjusted by serum albumin levels, BMI, sleep disturbance, history of CVD, depressive status, daily salt intake, and metabolic syndrome

# Subgroup analyses of multivariable logistic regression by age 65

Figure 2A shows the subgroup analysis of the multiple logistic analysis for LUTS in patients with < 65 years. Among low grip strength, 10 m gait speed, and oral frailty risk, oral frailty risk was an independent factor for LUTS (OR: 2.53, P=0.015). In participants aged  $\geq$  65 years, 10 m gait speed and oral frailty risk (OR: 2.83, P=0.010) were independent factors for LUTS, whereas low grip strength was not (Fig. 2B).

# Multiple liner regression analyses for OABSS and IPSS

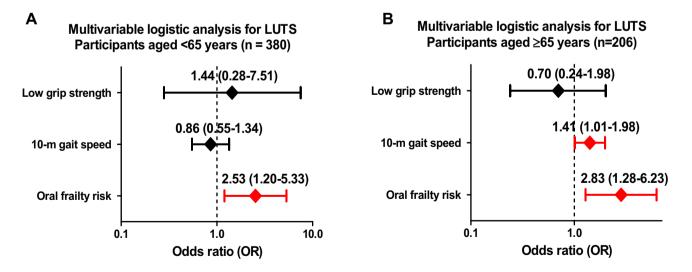
Table 3 shows the results of the oral frailty score in multiple regression analyses for LUTS severity. In the OABSS, multiple regression analyses showed that the oral frailty score was

not significantly correlated with the total OABSS, OABSS Q1, and Q2. On the other hand, it was significantly correlated with OABSS Q3 (standardized  $\beta = 0.100$ , P=0.009) and Q4 (standardized  $\beta = 0.046$ , P=0.035). In the IPSS, multiple regression analyses showed that the oral frailty score was significantly correlated with the total IPSS, IPSS voiding symptom domain, and IPSS storage symptom domain in each gender. On the other hand, the oral frailty score was significantly correlated with the IPSS storage symptom domain only in the male gender.

### Discussion

We showed the potential association between oral frailty and LUTS in community-dwelling individuals, using the community health promotion program database. We observed that participants with LUTS had a significantly higher prevalence of oral frailty risk compared to those without LUTS. Multivariable logistic regression analysis identified oral frailty risk as an independent factor associated with LUTS. Notably, we showed that oral frailty risk was independently associated with the presence of LUTS among factors closely associated with frailty, such as age, physical function, mental status, nutritional status, and comorbidities. To the best of our knowledge, this is the first study to demonstrate an independent association between oral frailty and LUTS.

It is well known that frailty and LUTS co-occur, especially in the older people. Frailty is characterized by reduced physical functioning, decreased physiological resilience, and increased susceptibility to adverse health outcomes



Models were adjusted by age, gender, sleep disturbance, serum albumin levels, BMI, history of CVD, depressive status, daily salt intake, and metabolic syndrome.

Fig. 2 Subgroup analyses of multivariable logistic regression for lower urinary tract symptoms (LUTS) by age 65. A Participants < aged 65 years. B Participants  $\geq$  aged 65 years

OABSS*	Standardized b coefficient	95% CI	<i>P</i> value	
Total OABSS	0.14	0.31 to 0.08	0.085	
OABSS Q1	0.01	- 0.04 to 0.05	0.750	
OABSS Q2	- 0.03	- 0.09 to 0.04	0.450	
OABSS Q3	0.10	0.03 to 0.18	0.009	
OABSS Q4	0.046	0 to 0.12	0.035	
IPSS**	Standardized b coefficient	95% CI	P value	
Total IPSS in male	1.18	0.31 to 2.05	0.008	
Total IPSS in female	0.57	0.10 to 1.03	0.017	
IPSS voiding symptom domain in male	0.92	0.24 to 1.59	0.022	
IPSS voiding symptom domain in female	0.48	0.16 to 0.80	0.004	
IPSS storage symptom domain in male	0.45	0.10 to 0.82	0.013	
IPSS storage symptom domain in female	0.090	- 0.14 to 0.32	0.423	

Table 3 Multiple linear regression analyses for OABSS and IPSS (Oral frailty score)

\*Models were adjusted by gender, serum albumin levels, BMI, PSQI, HbA1c, CES-D score, daily salt intake, 10 m gait speed, and grip strength \*\*Models were adjusted by serum albumin levels, BMI, PSQI, HbA1c, CES-D score, daily salt intake, 10 m gait speed, and grip strength

[28]. LUTS and frailty are two conditions which are associated with multiple comorbidities and adverse outcomes, including reduced physical activity and function, hospitalization, falls, and mortality [4, 29–34]. Several studies have suggested that frailty worsens LUTS [35, 36], whereas our previous study showed that LUTS has a greater impact on worsening frailty[9]. Psychosocial factors such as reduced physical activity and social engagement due to bothersome LUTS and frailty-related limitations, may also increase the impact of LUTS and frailty on quality of life [7, 37]. It is remains unclear whether frailty or LUTS is the antecedent factor, but both factors may influence each other and increase the risk of adverse outcomes.

The association between LUTS and frailty may also be explained by age-related decline in physical performance and muscle mass (i.e., sarcopenia). [38]. Sarcopenia is thought to reflect lower pelvic floor muscles which are deeply associated with urinary continence [39]. Similar to the present study, previous studies have found that sarcopenia indicators such as slow walking speed and gait function are correlated with the presence and severity of LUTS [11, 29, 36]. However, grip strength, which was strongly associated with LUTS in women reported by Yang et al. [10], was not an independent factor for LUTS in this study (Table 1, Fig. 2 A, B). These contradictory results may be explained by the difference in the prevalence of lower grip strength. The prevalence of lower grip strength in this study was only 5.8%, which is a lower prevalence than in Chen's study (13.7%). In addition, a longitudinal study showed that walking speed declined more rapidly than hand grip strength in women [40]. These findings may suggest that grip strength may not be an optimal frailty indicator for LUTS in relatively healthy and robust individuals.

The association between oral frailty and LUTS deserves further discussion. Oral frailty refers to a condition in which oral functions deteriorate. As oral functions decline, daily activities such as chewing, drinking, and speaking become more difficult, and mouth ulcers are more likely to occur [41, 42]. Oral frailty can lead to reduced food intake, resulting in physical frailty and general weakness [13, 14, 41]. Furthermore, a longitudinal study in Japan showed that subjective symptoms such as decreased swallowing and chewing ability could independently predict future sarcopenia or physical frailty [13]. A previous cross-sectional study showed that chronic periodontal disease (strongly associated with systemic chronic inflammation and oral frailty) was independently correlated with LUTS severity [12]. Thus, it is not surprising that oral frailty risk was an independent factor for LUTS which is strongly associated with frailty and sarcopenia. Our subgroup analyses showed that oral frailty risk was an independent factor for LUTS in both participants aged < 65 years and aged  $\ge 65$  years (Fig. 2A, B). Oral frailty risk may be an accurate indicator of LUTS in the older people, but also in the non-older people. In contrast, 10 m gait speed was not an independent factor for LUTS in participants aged < 65 years (Fig. 2A). This result may reflect the finding that oral functional decline begins before physical functional decline in the aging process [13, 14]. In sum, the oral frailty risk may be a more accurate indicator of LUTS than the decline in physical function, especially in the non-older people. In addition, multiple regression analyses for LUTS severity suggested that oral frailty was more associated with urinary voiding symptoms than urinary storage symptoms (Table 3). This finding suggests that oral frailty risk may also be a more useful indicator of voiding symptoms than storage symptoms.

This study has several limitations. The underlying mechanism responsible for oral frailty in participants with LUTS remains unknown. The cross-sectional design does not allow for the determination of cause-and-effect relationships. Of the participants who were excluded from further analyses due to missing information, 244 without a physical examination were significantly older than those included in this study (data not shown). These participants may be frailer than those included in this study, which results in selection bias. Lack of information on the number of participants who were actually examined and diagnosed with LUTS. Caution should be exercised in generalizing the results to other populations, as regional bias may have influenced the results. The study participants may have been predominantly individuals with milder comorbidities who were already healthconscious, given their voluntary participation in the health survey. It should be noted that the actual number of participants diagnosed with LUTS and oral frailty actually remains unknown. Therefore, our future study should address this issue in a clinical study. Despite these limitations, the strength of our study is to show that simple 3 questions about oral frailty can be significantly associated with the presence of LUTS, suggesting that subjective symptoms related to oral function may be an indicator of LUTS and frailty.

In conclusion, oral frailty may be a significant indicator of LUTS. Further studies are warranted to clarify the exact relationship between LUTS and oral frailty. Clinicians may note that individuals with LUTS are also at risk for oral frailty.

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#### Declarations

**Conflict of interest** All authors declare that they have no conflicts of interest.

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