Validity of maximum isometric tongue pressure as a screening test for physical frailty: cross-sectional study in Japanese community-dwelling elderly people

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Short title

Tongue pressure as a frailty screening

ABSTRACT

Aim

Maximum isometric tongue pressure (MIP) seems to have a diagnostic value for oral phase dysphagia. This study aimed to examine the association between MIP and frailty and to assess the screening validity of MIP for physical frailty.

Methods

We conducted a cross-sectional study and enrolled participants aged ≥60 years from Japanese national medical check-ups in 2015 and 2016. The Fried frailty phenotype model was used. We analyzed odds ratios (OR) and 95% confidence intervals (CI) of physical frailty using one standard deviation (SD) increments of tongue pressure. Receiver operating characteristic (ROC) curves were obtained to predict physical frailty using MIP values.

Results

Out of 1603 participants, 968 were categorized as non-frail, 605 as pre-frail, and 30 as frail. In logistic regression analysis, one SD increment of MIP significantly differentiated frail and pre-frail: OR for frail with one SD increment in MIP was 0.37 (95% CI 0.26, 0.54, $P < 0.001$), and OR for pre-frail was 0.63 (95% CI 0.57, 0.70, $P < 0.001$). The area under the ROC curve for predicting frail with MIP score was as high as 0.776 (95% CI, 0.689, 0.862). A point of MIP 35kPa had a sensitivity of 90.0%, specificity of 40.4%, a positive likelihood ratio (LR) of 1.5, and a negative LR of 0.2 for predicting frail.

Conclusions

MIP performance is independently associated with frailty. MIP also can be used as a simple screening tool for frailty.

Keywords

Aging, Frailty, Geriatric Medicine, Maximum isometric tongue pressure, Screening

Introduction

Frailty is defined as increased vulnerability to stress and increased susceptibility to adverse outcomes due to declines in multiple body systems with age [1]. Frail elderly people are more likely to suffer falls, to have reduced activities of daily living, and to be at high risk of hospitalization and death [2]. International clinical guidelines recommend that all persons older than 70 years should be screened for frailty [3]; however, frailty evaluations take time [4]. Appropriate screening procedures for community-dwelling populations with frailty are lacking.

The human tongue has several essential tasks such as mastication, swallowing and speech. Tongue pressure produced by contact between the hard palate and tongue is a major propulsive force in the transport of a food bolus toward the pharynx [5]. The maximum voluntarily pressing tongue pressure was decreased with aging [6], and it was also decreased in individuals with impaired swallowing [7]. And down syndrome patients, and post-stroke patients had lower tongue pressure during swallowing than healthy controls [8,9].

The vicious cycle of frailty was proposed by Fried, who emphasized that chronic undernutrition leads to weight loss, which is one of the five components that define frailty [2]. Because dysphagia reduced or altered oral intake of food which, in turn, can contribute to lowered nutritional status [10], and maximum voluntarily pressing tongue pressure seems to have a diagnostic value for oral phase dysphagia [7], we hypnotized that maximum isometric tongue pressure (MIP) may be related to systemic physical frailty. Although two studies have investigated the association between MIP and handgrip strength among healthy adults [6,11], no study has examined the association between MIP and frailty. We aimed to clarify how MIP and frailty are related, and whether it can serve as a screen for frailty.

Methods

Study settings and subjects

We conducted this cross-sectional survey as a part of the Nagasaki Islands Study in Goto City, in the western part of Japan. In 2015, the population of Goto City was 39,808, with an increasing proportion of elderly people. The Nagasaki Islands Study is a community cohort study, which started in 2014 to investigate lifestyle and genetic risk factors for a broad array of diseases, such as cardiovascular disease, stroke, and frailty. We invited community dwellers for a medical health check-up. Details of the recruitment process have been described elsewhere [12]. In the present study, we excluded individuals younger than 60 years, those with a history of stroke, and those with missing data (tongue pressure or interview).

Examinations

We examined tongue pressure according to the method proposed by Tsuga et al., using a JMS tongue pressure measurement device (JMS, Hiroshima Japan) with a disposable oral balloon probe [13,14]. Before measurement, we explained the procedure to each participant. The balloon was attached to the end of the plastic probe and inserted into the seated participant's mouth, between the front of the hard palate and the tongue. Participants then held the probe in place with their closed lips at the midpoint of their central incisors and pressed as firmly as possible against the balloon with their tongues for 5 seconds. We measured the resulting increase in air pressure in the balloon. Each measurement was repeated 3 times at 30-second intervals. MIP was defined as the best value of the three measurements.

Body weight and height were measured in the lightly clothed participants with an automatic body composition analyzer (BF-220; Tanita, Tokyo, Japan). Body mass

index (BMI) was calculated as weight divided by height in meters squared (kg/m^2) and categorized using cut-off points for Asian populations [4, 15]. Two measurements of handgrip strength were recorded for each hand with a handgrip dynamometer (Smedley, Matsumiya Ika Seiki Seisakujo, Tokyo, Japan), and the best value of the four measurements was used. The serum concentrations of HbA1c, low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL) cholesterol, triglycerides (TG), and creatinine were measured by standard laboratory procedures. The estimated glomerular filtration rate (GFR) was determined with an established method [16]. According to this adaptation,

GFR ($mL/min/1.73\ m^2$) = $194 \times (\text{serum creatinine (enzyme method)})^{-1.094} \times (\text{age})^{-0.287} \times (0.739 \text{ for women})$.

Researchers and trained nurses collected information on medical history of stroke and ischemic heart disease, use of antihypertensive agents, use of hypoglycemic drugs, use of lipid-lowering drugs, smoking status (current smoker, ex-smoker, never-smoker), drinking status (current drinker, ex-drinker, never-drinker), the Kessler 6 test [17], family unit, and marital status. Four of the frailty criteria (described in the next section) were assessed by questionnaire; the fifth was determined by handgrip strength measurement.

Physical frailty phenotype

We used the definition of frailty from the Fried frailty phenotype model [4], which was one of the two major existing frailty models. Fried et al. demonstrated the longitudinal risks of adverse outcomes in a group of frail or pre-frail individuals. According to the Fried model, a person is classified as frail when at least 3 of 5 criteria are met, as pre-frail when 1 or 2 criteria are met, and as non-frail when no

criterion is met [2]. Table 1 shows the 5 criteria: unintentional weight loss, weakness, exhaustion, slowness, and a low physical activity level.

Statistical analysis

We assessed the frailty phenotypes of participants as frail, pre-frail, or non-frail, and values of characteristics were calculated as means or proportions for each frailty category. The differences in means of continuous variables were analyzed using analysis of variance (ANOVA). The differences in proportions of categorical variables were analyzed with chi-square tests.

We performed a Pearson correlation analysis of MIP and number of frailty components (0 to 5). Multiple logistic regression analysis was performed to examine the association between MIP and frailty phenotypes. To build the multivariable model, we used stepwise regression algorithm [18]. All candidate variables of age, sex, height, weight, BMI, SBP, DBP, HbA1c, LDL cholesterol, HDL cholesterol, TG, GFR, history of ischemic heart disease, smoking status, alcohol intake, Kessler 6 test, number of household members, living alone, and marital status were divided into two classes: forced-in variables (age and sex), or non-forced variables (others). Model 1 only included forced-in variables. In Model 2, non-forced variables were selected or deleted by a stepwise algorithm [18]. To select or delete a variable, we compare the initial model with current model based on likelihood ratio test [LRT]. We retained a variable if the p value of LRT was statistically significant. As a cut-off point of p value, 0.1 was used because more traditional levels such as 0.05 can fail in identifying variables known to be important [19].

We obtained odds ratios (OR) and 95% confidence intervals (CI) for each single kilopascal (kPa) increment and for each standard deviation (SD) increment in MIP

between the groups. Non-frail subjects were treated as a reference group. To investigate sex differences, sex-specific analyses were also performed. A P value <0.05 was considered statistically significant, except for LRT.

We examined receiver operating characteristic (ROC) curves, sensitivity, specificity, positive likelihood ratio (LR), and negative LR to predict frail (or pre-frail) status by cut-off points of MIP, by sex. Statistical analyses were performed using STATA® (version 14.0; StataCorp, College Station, TX).

Ethical approval

This study was approved by the Ethics Committee in Nagasaki University Graduate School of Biomedical Sciences (project registration number: 14051404).

Results

Characteristics of participants

Of the 2018 people who participated in the Nagasaki Islands Study, we excluded 306 who were younger than 60 years, 83 with history of stroke, and 26 with missing data (16 MIP, and 10 interview), leaving 1603 participants (650 men and 953 women) aged 60 to 95 years for enrolment in the study.

Of these 1603 participants, we classified 30 as frail, 605 as pre-frail, and 968 as non-frail. Frail individuals were older than non-frail ones, and had a lower average MIP by 10 kPa compared with non-frail subjects (Table 2). Frail participants had lower height, body weight, DBP, HDL cholesterol, and GFR; higher SBP; higher proportions with medical history of ischemic heart disease, use of antihypertensive agents; lower proportions of current smokers and current drinkers; and higher scores of depressive mood. Frailty affected more women than men although it was not statistically

significant ($P = 0.293$). MIP was higher in men than women (32.0 ± SD 0.4 in men,29.5 ± 0.3 in women, $P < 0.001$).

MIP and frailty

In Pearson correlation analysis, MIP values were significantly associated with number of frailty components (r=-0.25, $P < 0.001$) (treated as a continuous variable of frailty components 0 to 5).

In logistic regression analysis, increments in MIP were significantly associated with lower risk of frail and pre-frail status (Table 3). OR for frailty in relation to 1 kPa increment in MIP was 0.90 (95% CI 0.87, 0.94, $P < 0.001$). OR for frailty in relation to 1 SD increment in MIP was 0.37 (95% CI 0.26, 0.54, $P < 0.001$), where one SD increment in MIP was 9.8 kPa in women, and 10.3 kPa in men. Even after multivariable adjustment for confounding factors, these associations remained significant. As for the association between MIP and pre-frailty, OR and 95% CI for pre-frailty were significant (1 kPa increment in MIP 0.96, 95% CI 0.95 to 0.97, $P < 0.001$; one SD increment in MIP 0.63, 0.57 to 0.70, $P < 0.001$).

We also conducted sex-specific logistic regression analyses. In women, an increment in MIP was significantly associated with lower risk of both frailty and pre-frailty. In men also, an increment in MIP was significantly associated with both frailty and pre-frailty, but the relationship was not statistically significant for frailty after multivariable adjustments. We additionally analyzed the association between MIP and frailty status after excluding the malnourished subjects (BMI <18.5 kg/m^2 in men, and BMI <19.0 kg/m^2 in women). The results did not differ (1 kPa increment in MIP 0.90, 95% CI 0.87 to 0.94, $P < 0.001$; 1 SD increment in MIP 0.37, 0.25 to 0.54, $P < 0.001$), and remained significant after multivariable adjustments (1 kPa increment in MIP

0.92, 95% CI 0.88 to 0.97, *P* = 0.001; one SD increment in MIP 0.46, 0.29 to 0.73, *P* = 0.001).

ROC curve of MIP to predict frailty

We tested whether we could predict frail or pre-frail status by using a simple cut-off score for MIP (Tables 4 and 5). The area under the ROC curve for predicting frailty was as high as 0.776 (95% CI, 0.689, 0.862) (Figure S1); that for predicting pre-frailty was 0.630 (95% CI, 0.602, 0.659) (Figure S2).

For predicting frail status, an MIP value of 35kPa had a sensitivity of 90.0%, specificity of 40.4%, a positive LR of 1.5, and a negative LR of 0.2 (Table 4). For predicting pre-frail status, the MIP value 35kPa had a lower sensitivity of 77.9%, specificity of 40.3%, a positive LR of 1.3, and a negative LR of 0.5 (Table 5). Sex-specific results showed an MIP of 35kPa had a sensitivity of 87.5% in men and 90.9% in women for predicting frail status, and 72.6% in men and 81.2% in women for predicting pre-frail status.

Discussion

We found that MIP was associated with the frailty phenotype. To the best of our knowledge, this is the first report that shows a link between the objective parameter of tongue muscle strength and physical frailty. We also propose that such tongue pressure measurement can serve as a simple, non-invasive screening test for physical frailty. A decrease of approximately 10 kPa (1 SD decrement) in MIP was a strong predictor of risk for frailty.

Two possible cause of frailty in participants with lower MIP values is altered oral intake and malnutrition. Dysphagia is a major problem in elderly people with/without

disease [7-9]. Several studies supported a decline of tongue pressure, one of the physiological indicator of swallowing difficulty, has a leading cause of malnutrition [5, 10, 20-22]. Several interventional studies showed lingual exercise enabled community-dwelling older adults and stroke patients with dysphagia to increase swallowing pressure significantly and to reduce airway invasion [5,20]. Another cohort study of Spanish community-dwelling older adults has shown that oropharyngeal dysphagia can result in reduced or otherwise altered oral intake of food which, in turn, can contribute to lower nutritional status at a 1-year follow up visit [21]. Malnutrition has been reported to be highly prevalent among Japanese community-dwelling older adults who receive home dental care, and dysphagia risk has been independently associated with malnutrition [22]. These studies suggest that dysphagic community-dwelling older adults are likely to present with an elevated risk of malnutrition [10].

Furthermore, dysphagic patients did not consume sufficient protein to meet their requirement level. And lower protein intake has also been associated with a significant risk of loss of lean body mass over 3 years in US community-dwelling older adults [23]. Protein intake, especially from animal sources, has been linked to better preservation of muscle mass in healthy Canadian women [24]. Those with altered MIP in our study might have higher risk of poor nutritional status or lower protein intake, both of which have a potential relationship with frailty [2].

However, the analysis after excluding low BMI subjects showed the same pattern of results, which means that the association between MIP and frailty was unrelated to BMI status, which is an indicator of current nutritional status. The study to evaluate cumulative effect of malnutrition during their middle or younger age will be needed.

Another possible cause of frailty in lower MIP participants is sarcopenic dysphagia, defined as decline in swallowing capabilities of elderly adults with age-related loss of muscle mass named as sarcopenia [25,26]. Decreased MIP has been related to sarcopenia or to causes of sarcopenia in Japanese hospitalized adults [25], and severe dysphagia has been linked to the skeletal muscle index in hospitalized cancer patients [27]. Lower MIP associated with loss of muscle mass might be associated with frailty because sarcopenia poses an increased risk of disability, limited mobility [28], and frailty [29].

In this study, the apparent sex difference in OR for frailty in relation to MIP was not found. As for the frailty prevalence, several studies reported frailty affects more women than men [2, 30-33]. It can be explained by several reasons as: higher baseline levels of muscle mass to protect men from muscle mass loss; neuroendocrine and hormonal factors (testosterone and growth hormones), which may provide advantages in muscle mass maintenance; lower levels of activity and lower caloric intake in women as compared to men [30]. On the other hand, the difference between the tongue pressure in men and women is less robust across studies. Some earlier studies found a significant higher MIP in men than in women [6, 7, 34], whereas others did not [35, 36]. In our study, frailty prevalence did not significantly differ. And MIP was higher in men than women, but the difference was not large. Therefore, the sex difference in the association between frailty and MIP may not be clinically relevant in our study.

Application to clinical setting

Our findings suggest non-invasive and simple measurement of MIP can help identify those at high risk of frailty. The MIP test is not a time-consuming measurement, and the device is light weight and portable. Therefore, it can be used as a screening test in the community.

Furthermore, the new concept of "oral frailty" [37] suggests that recognition of frailty in oral function is important, and that pre-clinical sarcopenia and frailty might be prevented by recognition of oral function in its early stages of decline, because early nutritional or physical intervention could be implemented for those at risk. This study implies the need for future investigations of the mechanism of association between physical frailty and oral functional decline.

The ROC curve for predicting frail status using MIP values showed adequate validity of MIP as a screening tool. We could not detect a single cut-off point of MIP to distinguish frail from robust subjects because our study had a small sample size in the frail group, and it was difficult to fulfill both high sensitivity and high specificity simultaneously. However, the MIP value of 35 kPa had a sufficient negative LR to detect frail from robust elderly in both sexes, and such a tongue pressure measurement device would be a simple, non-invasive evaluation tool for screening out robust individuals among Japanese community-dwelling elderly.

On the other hand, screening for pre-frail status using the MIP value of 35 kPa had less sensitive, and higher negative LR than that for frail status. In this case, tongue pressure measurement has a trade-off sensitivity for specificity. The test has an over-diagnosis bias in higher cut-off point and it overlooks pre-frailty in lower cut-off point [38]. Therefore, we need careful consideration in assessing the utility of this screening test for pre-frailty.

Limitations of the study

First, because this is a cross-sectional study, we do not know the direction of causality between MIP and frailty. A longitudinal study is needed to investigate MIP decrement and adverse outcome. Second, recruitment of the sample was based on a pool of individuals attending a medical health check-up; therefore, we cannot generalize the results to other settings. However, a systematic review of age-stratified prevalence studies has shown a relatively low prevalence of frailty in Japan: 1.9% in those aged 65–69 years and 3.8% in those aged 70–74 years [39]. Because these prevalences are similar to the 1.9% frailty in our sample (mean age, 72.8 years), the selection bias in our study may be low. Third, our study did not have the data about dentition. The tongue pressure at a various position in the mouth were reported to be different [40]. And tongue-tip motion was different between dentulous and edentulous older people [41]. Furthermore, even in edentulous older adults, maximal magnitude of tongue pressure was statistically different between those with or without prostheses [42]. These factors about dentition might bias the analyses.

Our study shows that MIP values are independently associated with the Fried frailty phenotype. MIP also can be used as a simple screening tool for frailty. Prospective research is needed to validate the future risk of frailty as a function of present MIP performance.

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Disclosure Statement

The authors declare no conflict of interest.

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Supporting Information

Figure S1. Receiver operating characteristic curve for predicting physical frailty using maximum isometric tongue pressure

Figure S2. Receiver operating characteristic curve for predicting physical pre-frailty using maximum isometric tongue pressure

Table 1. Frailty criteria

(1) Unintentional weight loss	Defined as unwanted weight loss of 3 kg or more 3 kg or more in the past 6 months, based on an interview.
(2) Weakness	Defined as the maximum handgrip strength from a total of 4 trails (2 per hand), and stratified into quintiles according to sex and BMI, based on an Asian population reference. The lowest quintile was defined as weakness. Participants who were unable to perform the test were also classified weak.
(3) Exhaustion	Determined using the K6 screening scale instead of the original version of the Center for Epidemiologic Studies Depression Scale (CES-D) because its comparability to CES-D has already validated (13). The following 2 statements were read: (a) "During the past 30 days, how often did you feel so depressed that nothing could cheer you up?"; and (b) "During the past 30 days, how often did you feel that everything was an effort?" Answers were scored as 1=all of the time, 2=most of the time, 3=some of the time, 4=a little of the time, or 5=none of the time. Participants who answered "1" or "2" to either of these questions were categorized as meeting the exhaustion criterion.
(4) Slowness	Determined using a questionnaire with the following questions: Question a - "Can you walk as fast as others your age?" Question b - "Can you walk continuously for 1 km or more?" Answers were scored as 1=yes or 2=no. Participants who answered "2" to both of these questions were categorized as meeting the slowness criterion.
(5) A low physical activity level	Determined using the question of (a) "How often do you go out for daily activities, such as walking, shopping and working?" Answers were scored as 1="more than 2 days a week" or 2="less than once a week". Participants who answered "1" to this question were categorized as meeting the low physical activity level criterion.

Participants were classified as frail when at least 3 of the 5 criteria were met, as pre-frail as when 1 or 2 criteria were met, and as non-frail when no criterion was met.

Table 2. Characteristics of participants according to the Fried frailty model

Factor	Total 1603	Non-frail 968 (60.4)	Pre-frail 605 (37.7)	Frail 30 (1.9)	Trend *p*
Age, year	72.8 ± 7.4	70.5 ± 6.6	76.0 ± 7.3	80.3 ± 6.9	<0.001
Male sex	650 (40.6)	394 (40.7)	248 (41.0)	8 (26.7)	0.293
Height, cm	154.6 ± 8.6	155.9 ± 8.2	152.9 ± 8.9	146.6 ± 8.6	<0.001
Body weight, kg	56.3 ± 10.3	56.9 ± 10.0	55.6 ± 10.7	50.7 ± 11.8	0.001
BMI, kg/m ^{2}	23.5 ± 3.4	23.3 ± 3.2	23.7 ± 3.6	23.5 ± 4.5	0.122
Maximum isometric tongue pressure, kPa	30.5 ± 10.1	32.4 ± 9.5	28.0 ± 10.3	22.5± 9.2	<0.001
Maximum handgrip strength,	26.0 ± 8.8	28.6 ± 8.2	22.2 ± 8.3	16.2 ± 5.3	<0.001
SBP, mmHg	140.1 ± 18.2	139.2 ± 17.7	141.4 ± 18.3	143.5 ± 28.1	0.038
DBP, mmHg	79.7 ± 10.7	80.3 ± 10.3	78.7 ± 11.2	76.4 ± 12.5	0.003
HbA1c, %	5.8 ± 0.6	5.8 ± 0.6	5.8 ± 0.6	5.7 ± 0.6	0.689
LDL cholesterol, mg/dl	118.5 ± 29.3	121.1 ± 29.9	114.4 ± 27.6	118.7 ± 32.4	<0.001
HDL cholessterol, mg/dl	58.6 ± 14.1	59.6 ± 14.0	57.3 ± 14.2	53.6 ± 11.9	0.002
Triglycerides, mg/dl	104.9 ± 59.3	105.6 ± 60.9	102.8 ± 53.3	122.5 ± 104.3	0.172
GFR, mL/min/1.73m ^{2}	69.7 ± 15.3	71.0 ± 14.6	67.6 ± 16.0	67.4 ± 17.5	<0.001
Medical history of ischemic heart disease	117 (7.3)	55 (5.7)	56 (9.3)	6 (20.0)	0.001
Use of antihypertensive	824 (51.4)	440 (45.5)	362 (59.8)	22 (73.3)	<0.001
Use of hypoglycemic drugs	139 (8.7)	69 (7.1)	68 (11.2)	2 (6.7)	0.017
Use of lipid-lowering drugs	387 (24.1)	218 (22.5)	160 (26.5)	9 (30.0)	0.157
Smoking status					0.010
Current smoker	126 (7.9)	93 (9.6)	32 (5.3)	1 (3.3)	
Ex-smoker	391 (24.4)	238 (24.6)	149 (24.6)	4 (13.3)	
Never-smoker	1086 (67.8)	637 (65.8)	424 (70.1)	25 (83.3)	
Drinking status					<0.001
Current drinker	552 (34.4)	382 (39.5)	166 (27.4)	4 (13.3)	
Ex-drinker	99 (6.2)	45 (4.7)	52 (8.6)	2 (6.7)	
Never-drinker	952 (59.4)	541 (55.9)	387 (64.0)	24 (80.0)	
Kessler 6 test, score	1.2 ± 2.5	0.8 ± 1.6	1.7 ± 3.1	3.3 ± 5.3	<0.001
No. Household members	2.0 ± 0.9	2.0 ± 0.8	2.0 ± 0.9	2.0 ± 0.8	0.197
Living alone	392 (24.5)	208 (21.5)	176 (29.1)	8 (26.7)	0.003
Marital status					<0.001
Married	1107 (69.1)	700 (72.3)	388 (64.1)	19 (63.3)	
Bereaved	367 (22.9)	182 (18.8)	174 (28.8)	11 (36.7)	
Divorced	57 (3.6)	39 (4.0)	18 (3.0)	0	
Unmarried	70 (4.4)	47 (4.9)	23 (3.8)	0	
Unknown	2 (0.1)	0	2 (0.3)	0	

Data are mean ± standard deviation or n (%). Ex-smoker indicates those who quit smoking at least 2 months before the interview. Ex-drinker indicates those who quit drinking alcohol at least 2 months before the interview. SBP, systolic blood pressure; DBP, diastolic blood pressure; LDL, low-density lipoprotein; HDL, high-density lipoprotein; GFR, glomerular filtration rate.

Table 3. Odds ratios and 95% confidence intervals for physical frailty in the study population, in relation to maximum isometric tongue pressure

	Frail				Pre-frail			
	OR (95% CI) for 1 kPa increment in MIP	*p*	OR (95% CI) for 1 SD increment in MIP	*p*	OR (95% CI) for 1 kPa increment in MIP	*p*	OR (95% CI) for 1 SD increment in MIP	*p*
Men and Women (n=998)					Men and Women (n=1573)			
Crude	0.90 (0.87, 0.94)	<0.001	0.37 (0.26, 0.54)	<0.001	0.96 (0.95, 0.97)	<0.001	0.63 (0.57, 0.70)	<0.001
Model 1	0.93 (0.89, 0.97)	<0.001	0.47 (0.31, 0.71)	<0.001	0.98 (0.96, 0.99)	<0.001	0.78 (0.69, 0.88)	<0.001
Model 2	0.92 (0.88, 0.97)	0.001	0.46 (0.29, 0.72)	0.001	0.97 (0.96, 0.98)	<0.001	0.76 (0.67, 0.86)	<0.001
Men (n=402)					Men (n=642)			
Crude	0.91 (0.86, 0.98)	0.008	0.40 (0.20, 0.79)	0.008	0.96 (0.94, 0.97)	<0.001	0.63 (0.53, 0.75)	<0.001
Model 1	0.94 (0.87, 1.02)	0.123	0.52 (0.23, 1.19)	0.123	0.98 (0.96, 1.00)	0.029	0.81 (0.67, 0.98)	0.029
Model 2	0.93 (0.85, 1.02)	0.135	0.48 (0.18, 1.26)	0.135	0.97 (0.95, 0.99)	0.007	0.76 (0.62, 0.93)	0.007
Women (n=596)					Women (n=931)			
Crude	0.90 (0.86, 0.94)	<0.001	0.36 (0.23, 0.56)	<0.001	0.95 (0.94, 0.97)	<0.001	0.63 (0.55, 0.73)	<0.001
Model 1	0.92 (0.88, 0.97)	0.001	0.44 (0.27, 0.72)	0.001	0.97 (0.96, 0.99)	<0.001	0.76 (0.65, 0.88)	<0.001
Model 2	0.93 (0.88, 0.98)	0.006	0.47 (0.28, 0.81)	0.006	0.97 (0.96, 0.99)	0.001	0.76 (0.65, 0.90)	0.001

OR odds ratio, CI confidence interval, SD standard deviation, and MIP maximum isometric tongue pressure. The non-frail group was treated as a reference. One SD increment was 9.8 kPa in women and 10.3 kPa in men. Model 1: adjusted for age and sex.

Model 2: adjusted for age, sex, height, weight, LDL cholesterol, use of hypoglycemic drugs, drinking status, and Kessler 6 score.

Physical frailty is categorized as pre-frail and frail, based on the Fried frailty phenotype model.

Table 4. Sensitivity and specificity to predict frailty by cut-off points of maximum isometric tongue pressure.

Cut-off point (maximum isometric tongue	Sensitivity	Specificity	Positive likelihood ratio	Negative likelihood ratio
Men and Women (n=998)				
≤50	100.0%	2.3%	1.0	0.0
≤45	100.0%	7.4%	1.1	0.0
≤40	96.7%	19.1%	1.2	0.2
≤35	90.0%	40.4%	1.5	0.2
≤30	76.7%	62.1%	2.0	0.4
≤25	66.7%	79.4%	3.2	0.4
≤20	43.3%	90.5%	4.6	0.6
≤15	20.0%	95.5%	4.4	0.8
≤10	3.3%	98.4%	2.0	1.0
≤5	3.3%	99.3%	4.6	1.0
Men (n=402)				
≤50	100.0%	4.3%	1.0	0.0
≤45	100.0%	11.9%	1.1	0.0
≤40	100.0%	24.4%	1.3	0.0
≤35	87.5%	45.9%	1.6	0.3
≤30	62.5%	68.0%	2.0	0.6
≤25	62.5%	83.8%	3.8	0.4
≤20	37.5%	90.6%	4.0	0.7
≤15	12.5%	95.9%	3.1	0.9
≤10	0.0%	98.5%	0.0	1.0
≤5	0.0%	99.2%	0.0	1.0
Women (n=596)				
≤50	100.0%	0.7%	1.0	0.0
≤45	100.0%	4.4%	1.0	0.0
≤40	95.5%	15.5%	1.1	0.3
≤35	90.9%	36.6%	1.4	0.2
≤30	81.8%	58.0%	1.9	0.3
≤25	72.7%	76.3%	3.1	0.4
≤20	45.5%	90.4%	4.7	0.6
≤15	22.7%	95.1%	4.7	0.8
≤10	4.6%	98.1%	2.4	1.0
≤5	4.6%	99.3%	6.5	1.0

Non-frail subjects of each sex were treated as a reference group.

Table 5. Sensitivity and specificity to predict pre-frailty by cut-off points of maximum isometric tongue pressure, by sex.

Cut-off point (maximum isometric tongue	Sensitivity	Specificity	Positive likelihood ratio	Negative likelihood ratio
Men and Women (n=1573)				
≤50	98.5%	2.4%	1.0	0.6
≤45	94.4%	7.4%	1.0	0.8
≤40	86.9%	19.4%	1.1	0.7
≤35	77.7%	40.4%	1.3	0.6
≤30	59.0%	62.1%	1.6	0.7
≤25	36.2%	79.4%	1.8	0.8
≤20	21.5%	90.5%	2.3	0.9
≤15	11.9%	95.5%	2.6	0.9
≤10	5.0%	98.4%	3.0	1.0
≤5	1.3%	99.3%	1.8	1.0
Men (n=642)				
≤50	99.2%	4.3%	1.0	0.2
≤45	94.0%	11.9%	1.1	0.5
≤40	81.9%	24.9%	1.1	0.7
≤35	72.6%	45.9%	1.3	0.6
≤30	52.8%	68.0%	1.7	0.7
≤25	32.7%	83.8%	2.0	0.8
≤20	16.9%	90.6%	1.8	0.9
≤15	7.3%	95.9%	1.8	1.0
≤10	4.4%	98.5%	2.9	1.0
≤5	2.0%	99.2%	2.6	1.0
Women (n=931)				
≤50	98.0%	0.9%	1.0	2.3
≤45	94.7%	4.4%	1.0	1.2
≤40	90.8%	15.5%	1.1	0.6
≤35	81.2%	36.6%	1.3	0.5
≤30	63.3%	58.0%	1.5	0.6
≤25	38.7%	76.5%	1.6	0.8
≤20	24.7%	90.4%	2.6	0.8
≤15	15.1%	95.1%	3.1	0.9
≤10	5.3%	98.1%	2.8	1.0
≤5	0.8%	99.3%	1.2	1.0

Non-frail subjects of each sex were treated as a reference group.

Supporting Information

Figure S1. Receiver operating characteristic curve for predicting physical frailty using maximum isometric tongue pressure

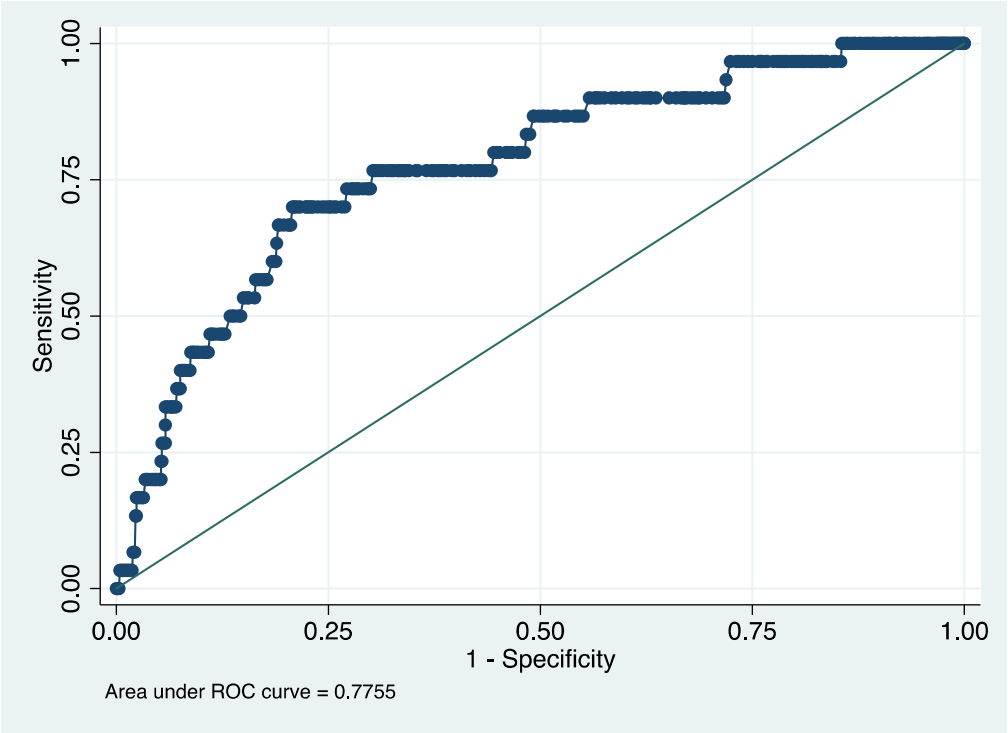

Figure S2. Receiver operating characteristic curve for predicting physical pre-frailty using maximum isometric tongue pressure