Multiple somatic symptoms and frailty: cross-sectional study in Japanese community-dwelling elderly people

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ABSTRACT

Background

Physical frailty is relevant to adverse outcomes, but appropriate procedures for screening populations are lacking. We hypothesized that frailty is associated with multiple somatic symptoms because frail elderly people might have several somatic symptoms attributed to deterioration of multiple organs.

Objective

To examine the association between multiple somatic symptoms and frailty.

Methods

We conducted a cross-sectional study and enrolled 1818 participants aged ≥60 years from Japanese national medical check-up in 2015.

Frailty status was categorized into frail, pre-frail, or non-frail based on the definition of the Fried frailty phenotype model. Sixteen self-reported subjective somatic symptoms were recorded at the timing of medial check-up. Odds ratio [OR] and 95% confidence interval [CI] of frail or pre-frail were analyzed using number of somatic symptoms.

Results

Out of total of 1,818 subjects, 44 (2.4%) frail subjects, 635 (34.9%) pre-frail subjects, and 1,139 (62.7%) non-frail subjects were detected.

More than 2 somatic symptoms were significantly associated with the frail phenotype (OR 6.20, 95% CI 2.95, 13.03, $p<0.001$), and were associated with the pre-frail phenotype (OR 2.06, 95% CI 1.69, 2.51, $p<0.001$). Associations remained significant after multi-adjustment for age, sex, past medical cardiovascular diseases, and depressive mood The number of somatic symptoms ≥2 was thought to be the optimal cut-off point to predict frail with a sensitivity of 79.6%, specificity of 61.5%.

Conclusions

Our study shows that multiple somatic symptoms are independently associated with frailty. Using more than 2 multiple somatic symptoms as a pre-screening tool for frailty may be appropriate.

Keywords.

Aging, Screening, Medically Unexplained Symptoms, Geriatrics, Community medicine, At-risk groups

Introduction

Frailty is prevalent in community-dwelling elderly persons, and predicts future institutionalization, falls, or death (1,2). International clinical guidelines of frailty recommend that all persons older than 70 years should be screened for frailty (3). In contrast, the British Geriatrics Society recommends active seeking for frailty in all encounters in clinical settings, but systematic screening in the community was not suggested because of cost effectiveness or unlikely effectiveness on better outcomes (4). Therefore, more rational procedures need to be developed to identify the population with a high suspicion of frailty by using epidemiological information on risks of frailty.

The definition of frailty is composed of various dimensional declines in multiple body systems (e.g., mobility, strength, balance, motor processing, cognition, nutrition, endurance, and physical activity) (5). Frail elderly people tend to have increasing vulnerability to stress and increasing susceptibility to adverse outcomes. A longitudinal study showed that somatic symptoms were related to disability in 1545 primary care patients (6). Impaired physical function, such as slow walking speed or low handgrip strength, was prevalent in participants with somatoform disorders in an observational study (7). This evidence suggests that frailty in line with functional disability may be related to somatic symptoms.

Somatic symptoms without organic disorders are defined as numerous overlapping diagnoses and syndromes (i.e., bodily distress syndrome (8), medically unexplained symptoms (9), functional somatic symptoms (10), and somatoform disorders (11). These diagnoses and syndromes are common in primary care, and account for 17% to 50% of primary care patients (8-11). However, to the best of our knowledge, no studies have reported somatic symptoms associated with frailty.

We hypothesized that frailty is associated with multiple somatic symptoms because frail elderly people might suffer and complain about several functional symptoms attributed to deterioration of multiple organs in their preclinical stage. This study aimed to assess whether multiple somatic symptoms are associated with physical frailty in community-dwelling elderly people in remote islands in Japan.

Methods

Study settings and subjects

We conducted this cross-sectional survey in Goto City in the western part of Japan. The population of Goto City was 40,395 with an increasing proportion of elderly people in 2014. The Goto City municipal government has been promoting medical examinations of community-dwelling adults aged 40 years or older for screening and treating non-communicable diseases under the Health and Welfare for the Aged Act since 1982. These medical check-ups are provided by the municipal government at community centers in all of the districts and small islands in Goto City from April to September annually. The Nagasaki Islands study collaborated with the local municipal government in conducting research, mainly targeting atherosclerosis and cerebrovascular diseases, and frailty.

In the present study, we distributed flyers among every family unit in the study areas to initiate our study as an additional medical check-up free of charge to the population aged 60 years or older, including 7120 in Fukue district, 918 in Tamanoura district, and 1517 in Naru district through the recruitment period of 2 years (Figure 1). We approached all adult individuals (≥20 years) who participated in a medical examination in Fukue district from 29 May to 30 June 2014, in Tamanoura district from 18 to 22 May 2015, and in Naru district from 17 to 19 May 2015. All eligible participants provided written informed consent at each venue. Participants younger than 60 years old were excluded from the current study.

The target population in our study sites was 9555 community-dwelling elderly aged between 60 and 105 years old. Out of 2443 people who participated in the national health check-up examinations, 2257 agreed to take part in the present study. We excluded 439 individuals aged younger than 60 years old, those with missing data, or those living in a long-term care facility, leaving 1818 participants (659 men and 1159 women) aged between 60 and 95 years for enrolment in this study.

Examinations

Researchers and trained nurses used to obtain information on the past medical history of stroke, ischemic heart disease, hypertension, diabetes mellitus, and dyslipidemia (under

medication use, without medication, no history of dyslipidemia), smoking status (current smoker, ex-smoker, never-smoker), drinking status (frequency and amount of alcohol intake), the Kessler-6 test (12), family unit, and marital status. The frailty component consisted of a questionnaire, except for handgrip strength, as mentioned below in the section “Definition of physical frailty phenotype”. Body weight and height were measured with an automatic body composition analyzer with light clothes (BF-220; Tanita, Tokyo, Japan). Body mass index was calculated as weight divided by height in meters squared (kg/m^2) and categorized using cut-off points for Asian populations (13). Handgrip strength was recorded as the grip strength of 2 measurements that were performed with each hand with a handgrip dynamometer (Smedley, Matsumiya Ika Seiki Seisakujo, Tokyo, Japan), and the maximum value was used. Serum creatinine concentrations were measured and the estimated glomerular filtration rate [eGFR] was obtained.

Physical frailty phenotype and multiple somatic symptoms

We used the definition which was one of the two major frailty models proposed so far, named Fried frailty phenotype model (14). Fried et al. demonstrated the longitudinal risks of adverse outcomes in the group of frail or pre-frail, that is, intermediate compared with non-frail. According to the criteria of Fried et al., a person is classified as frail when at least 3 of 5 criteria are present, pre-frail as when 1 or 2 criteria are present, and non-frail as when no criterion is met (1). Table 1 shows 5 criteria: unintentional weight loss, weakness, exhaustion, slowness and a low physical activity level.

We used 16 subjective somatic symptoms: “During the previous year, have you had the following symptoms?” Possible answers were as follows: (a) numbness in your limb, (b) edema in your face or limbs, (c) thirst sensation, (d) frequent urination, (e) dysuria, (f) pain on urination, (g) sensation of residual urine, (h) headache, (g) dizziness, (h) lightheadedness, (i) palpitation, (j) shortness of breath, (k) tightness of the chest, or (l) chest pain; “Do you have the following symptoms?”: (m) arthralgia or (n) sleep-onset insomnia. Somatic symptoms (a) to (l) was derived from the self-reported questions which had already been incorporated in the questionnaire of the Japanese national medical check-up. Somatic symptoms (m) and (n)

were set by our research team as a part of the information about screening of rheumatoid arthritis or sleep disturbance.

Diagnostic criteria of syndromes, such as bodily distress syndrome (8), medically unexplained symptoms (9), functional somatic symptoms (10), and somatoform disorder (11), should exclude somatic symptoms that can be explained with an organic origin. However, in some cases, these symptoms cannot be conclusively distinguished from organic origin. Rosmalen et al. showed that a simple count of symptoms could be used as a dimensional diagnosis of somatization (15). Additionally, a new concept of bodily distress syndrome in the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition focuses more on the number of bodily symptoms, irrespective of explicability of these symptoms or their associated dysfunctional cognition (16). Therefore, we used the number of multiple somatic symptoms in our study.

Statistical analysis

We assessed the prevalence of frailty in participants by frail, pre-frail, or non-frail phenotypes. Values of characteristics of each frailty category were calculated as means or proportions. The differences of means of continuous variables were analyzed using ANOVA. The differences of proportions of categorical variables were analyzed using the chi-square test. Fisher's exact test was used instead of the chi-square test only when one or more of the expectation of each cells of 2 by 2 table was below 5. We obtained odds ratios [OR] for each somatic symptom and 95% confidence intervals [CI] between the groups. Non-frail subjects were treated as a reference group. A p value <0.05 was considered statistically significant. We obtained the OR for the number of somatic symptoms between groups. Multiple logistic regression analysis was performed to examine the association between frailty and somatic symptoms. Potential confounders for frailty were as follows: age, sex, past medical history of stroke (yes, no), ischemic heart disease (yes, no), hypertension (yes, no), living alone (yes, no), depressive mood (Kessler-6 test ≥5), smoking (current smoker, non-smoker), alcohol intake (current drinker, non-drinker), and eGFR (continuous) (1,17,18). We treated past medical history of ischemic heart disease or stroke as a confounding factor with frailty based

on the previous studies because they were associated with somatic symptoms, seemed to be a risk factor for frailty, but not to be on the causal pathway between the exposure and outcome. (19-22). We also analyzed the association between frailty and the number of somatic symptoms as continuous variables in linear regression models. We additionally analyzed the data about Receiver Operating Characteristic [ROC] curve, sensitivity, specificity, positive likelihood ratio [LR], and negative LR. When we analyzed ROC curve and relevant values to predict frailty (not included the pre-frail subjects) using number of somatic symptoms, non-frail subjects were treated as a reference. Next, we analyzed ROC curve and relevant values to predict pre-frail (not included the frail subjects) using number of somatic symptoms. Statistical analyses were performed using SAS® for Windows (version 9.4; SAS Inc., Cary, NC).

Results

Prevalence of frailty phenotype

Out of total of 1,818 subjects, 44 (2.4%) frail subjects, 635 (34.9%) pre-frail subjects, and 1,139 (62.7%) non-frail subjects were detected. Frail participants were approximately 10 years older than non-frail participants, and had a 3-fold higher proportion of a history of stroke or ischemic heart disease compared with non-frail participants. Frail participants had a lower body weight, more frequently had a history of hypertension, were less frequently current smokers and current drinkers, had a higher rate of a depressive mood and being married, and more frequently lived alone (Table 2). Frequent components of the frailty phenotype were low handgrip strength and slow walking speed, whereas exhaustion was observed in only 2.3% of participants.

Associations between frailty and the number of somatic symptoms

In univariate analysis, numbness, edema, thirst sensation, frequent urination, dysuria, headache, lightheadedness, shortness of breath, and arthralgia were significantly associated with frailty using the reference of non-frail participants (Table 3). The proportion of each somatic symptom linearly increased with the frailty status, except for pain on urination.

Dysuria, numbness, edema, lightheadedness, and shortness of breath were the top five categories associated with frailty status, whereas tightness of the chest, shortness of breath, lightheadedness, edema, and palpitation were prevalent in the pre-frail status compared with the non-frail status.

More than 2 to 6 somatic symptoms were significantly associated with being pre-frail, even after multi-adjustment for age, sex, past medical history of stroke, ischemic heart disease and hypertension, the K6 test (≥5), living alone, smoking and current drinking status, and eGFR (Table 4). More than 2 somatic symptoms were also significantly associated with being frail, even after multi-adjustment, but a borderline difference remained with more than 3 or 4 somatic symptoms after adjustment. More than 7 somatic symptoms were significantly associated with being frail. We could not report an OR for more than 10 somatic symptoms for the pre-frail and frail phenotypes because of lack of a reference group. In linear regression analyses, the relationship between the number of somatic symptoms and frailty status (treated as a continuous number of frailty components) was linear, and the regression coefficient (ß) was 0.61 (95% CI 0.51-0.71, $p<0.001$) and R^2 was 0.07. This remained significant, with a ß of 0.40 (0.29-0.51, $p<0.001$) after adjustments for the same variables as those in the logistic regression models.

We tested whether we could predict the frail or pre-frail by using a simple cut-off score of the total number of somatic symptoms (Supplemental table 1 and 2). As for predicting frail, a cut-off point of somatic symptoms ≥2 had a sensitivity of 79.6%, specificity of 61.5%, a positive LR of 2.1, and a negative LR of 0.3. A cut-off point of number of somatic symptoms ≥3 had a sensitivity of 45.5% and specificity of 80.6%, a positive LR of 2.3, and a negative LR of 0.7. The area under the ROC curve to predict frail by using number of somatic symptoms covered as high as 0.759 (95% CI, 0.701, 0.817) (Supplemental figure 1). Contrary, predicting pre-frail, a cut-off point of somatic symptoms ≥2 had a sensitivity of 56.4%, specificity of 61.5%, a positive LR of 1.5, and a negative LR of 0.7. The area under the ROC curve to predict pre-frail by using number of somatic symptoms covered 0.604 (95% CI, 0.576, 0.631) (Supplemental figure 2).

Discussion

We found an association between frailty and multiple somatic symptoms. Logistic regression and linear regression analyses showed this association. ORs of more than 2 somatic symptoms with frailty were significant, which is consistent with a previous study that showed an association between the score of somatic symptoms and disability (6). The additional analyses suggested that a threshold of somatic symptoms ≥2 might be the optimal cut-off point to predict frail in terms of sensitivity and LR values. We cannot conclude appropriate cut-off point to predict pre-frail because the sensitivity and specificity were not enough high. The dose depending effect was seen both in positive LR and negative LR to predict frail. Although the effect seemed to be weakened and to be inconsistent to predict pre-frail, the same tendency was shown.

Frailty is an important concept, and increasing attention in primary care because of proper assessment and management of frailty, named Comprehensive Geriatric Assessment [CGA], has been established. In a randomized, controlled trial of 1388 elderly patients, functional decline was significant reduced in the CGA group compared with usual care (23). Therefore, our results suggest that the number of somatic symptoms in elderly people can be easily obtained in clinical and community settings, and be used as a rational pre-screening tool for frailty.

A possible explanation for the association between frailty and multiple somatic symptoms should be warranted. Frailty is a state of increased vulnerability to poor resolution of homeostasis after a stressor event, leading to increased risk of adverse outcomes. This vulnerability is based on cumulative decline in several physiological systems. Subclinical cumulative decline might be related to the impaired ability to adapt to stress (14). Therefore, it is plausible that cumulative decline in several organ systems might be a foundation of the multiple somatic symptoms.

Application to family practice

Family physicians have several advantages of screening patients with multiple somatic symptoms for frailty and integrating prevention in their consultation. because they already know their patients' history.

First, such patients tend to "doctor shop", consult multiple physicians for the same problem, use emergency services, and tend not to keep scheduled appointments (24), which may lead them to over-examination and unnecessary iatrogenic problems. If physicians screen their patients for frailty, they could appropriately assess geriatric problems by using CGA. Medicalization is based on mind-body dualism and understanding of the human body as a machine (25) whereas the approach of CGA is based on biopsychosocial model (26). It might be a suitable approach for these patients to avoid medicalization. Second, with population surveys, there is always a connection to "screening" and approaching patients for health problems they did not intend on consulting for. Consequently, the frailty screening itself has a risk of medicalization and incurring dependence and "illness behavior" (27). However, those with multiple somatic symptoms have a health problem to be solved, which may reduce the risk of medicalization to screen frailty. Third, this approach is especially useful for family physicians because they might be familiar with patients' symptoms from previous consultations. Family physicians can easily catch multiple somatic symptoms by their already existing knowledge of the patient without process to assess.

Limitations of the study

We used structured interviews at the national medical health check-up to obtain somatic symptoms, and these symptoms were not assessed for organic causality. Therefore, some somatic symptoms may have had a medical basis. However the association between frailty and multiple somatic symptoms remained significant after adjustment for multiple morbidities. Because this is a cross-sectional study we do not know the predictive power of multiple somatic symptoms, which may explain why it is difficult to distinguish pre-frail from frailty using number of somatic symptoms. A longitudinal study is needed to test the hypothesis that somatic symptoms in the absence of morbidities and risk factors can predict frailty.

Conclusions

Our study shows that multiple somatic symptoms are independently associated with the Fried frailty phenotype, even after multiple adjustments for age, sex, cardiovascular diseases, and depressive mood. Multiple somatic symptoms could be used as a simple pre-screening tool for frailty. Further research using longitudinal data could allow us to distinguish whether present symptoms or emerging or changing symptoms would be a more powerful predictor.

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Ethical approval

This study was approved by the Ethics Committee for Use of Humans of Nagasaki University (project registration number: 14051404).

Conflict of interest

The authors have declared no competing interests.

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Figure and tables

Table 1. Frailty criteria.

Table 2. Characteristics of the participants who recruited in Japanese national medical check-up in 2015, by the Fried frailty model.

Table 3. Odds ratios and 95% confidence intervals for somatic symptoms in relation to frailty.

Table 4. Odds ratios and 95% confidence intervals for the number of somatic symptoms in relation to frailty.

Figure 1. Study participants.

Table 1. Frailty criteria

(1) Unintentional weight loss	Defined as unwanted weight loss of 3 kg or more during 6 months based on an interview.
(2) Weakness	Defined as the maximum handgrip strength of a total of 4 trials by each hand and was 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 considered weak.
(3) Exhaustion	Determined using the K6 screening scale instead of the original version of the Center for Epidemiologic Studies Depression Scale because its comparability has already validated.[27] 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 frail by the exhaustion criterion.
(4) Slowness	Determined using a questionnaire with the following questions: (a) “Can you walk as fast as those of the same age?”; and (b) “Can you walk continuously during 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 frail by 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 frail by the low physical activity level criterion.

Classified as frail when at least 3 of 5 criteria are present, pre-frail as when 1 or 2 criteria are present, and non-frail as when no criterion is met.

Table 2. Characteristics of the participants who recruited in Japanese national medical check-up in 2015, by the Fried frailty model.

Factor	Total	Non-frail	Pre-frail	Frail	P for trend
	1,818	1,139 (62.7)	635 (34.9)	44 (2.4)	
Age	72.2 ± 7.5	70.2 ± 6.5	75.4 ± 7.7	79.8 ± 6.9	<0.001
Male sex	662 (36.3)	418 (36.6)	231 (36.3)	13 (29.6)	0.675
Height	154.6 ± 8.7	155.8 ± 8.3	152.7 ± 9.0	148.7 ± 9.7	<0.001
Body weight	55.2 ± 10.3	55.8 ± 10.1	54.3 ± 10.5	51.5 ± 11.9	0.001
BMI	23.0 ± 3.3	22.9 ± 3.1	23.2 ± 3.4	23.1 ± 3.8	0.217
Past medical history of stroke	77 (4.2)	36 (3.2)	37 (5.8)	4 (9.1)	0.006
Past medical history of ischemic heart disease	136 (7.5)	60 (5.3)	69 (10.9)	7 (15.9)	<0.001
Past medical history of hypertension	869 (47.8)	482 (42.3)	357 (56.2)	30 (68.2)	<0.001
Past medical history of diabetes mellitus	136 (7.5)	79 (6.9)	52 (8.2)	5 (11.4)	0.324
Past medical history of dyslipidemia	399 (22.0)	236 (20.7)	154 (24.3)	9 (20.5)	0.223
Estimated glomerular filtration rate	67.1 ± 14.3	68.0 ± 13.6	65.8 ± 15.0	62.6 ± 16.6	0.001
Smokign status					
Current smoker	125 (6.8)	92 (8.1)	30 (4.7)	2 (4.6)	0.021
Ex-smoker	404 (22.2)	253 (22.2)	145 (22.8)	6 (13.6)	
Never-smoker	1290 (71.0)	794 (69.7)	460 (72.4)	36 (81.8)	
Drinking status					

Current drinker	566 (31.1)	392 (34.4)	168 (26.5)	6 (13.6)	<0.001
Ex-drinker	123 (6.8)	68 (6.0)	51 (8.0)	4 (9.1)	
Never-drinker	1129 (62.1)	679 (59.6)	416 (65.5)	34 (77.3)	
Kessler-6 test (≥5)	183 (10.1)	82 (7.2)	84 (13.3)	17 (38.6)	<0.001
No. Household members	2.0 ± 0.9	2.1 ± 0.8	2.0 ± 0.9	1.9 ± 0.7	0.309
Living alone	439 (24.2)	251 (22.0)	177 (27.9)	11 (25.0)	0.022
Living with only your spouse	916 (50.4)	609 (53.5)	288 (45.4)	19 (43.2)	
Marrital status					
Married	1244 (68.4)	820 (72.0)	402 (63.3)	22 (50.0)	<0.001
Bereaved	431 (23.7)	220 (19.3)	190 (29.9)	21 (47.7)	
Divorced	56 (3.1)	39 (3.4)	17 (2.7)	0	
Unmarried	81 (4.5)	56 (4.9)	24 (3.8)	1 (2.3)	
Unknown	6 (0.3)	4 (0.4)	2 (0.3)	0	
Exhaustion	41 (2.3)	0	35 (5.5)	6 (13.6)	
Unintentional weight loss	146 (8.0)	0	124 (19.5)	22 (50.0)	
Low activity	77 (4.2)	0	51 (8.0)	26 (59.1)	
Slow walking speed	263 (14.5)	0	225 (35.4)	38 (86.4)	
Low handgrip strength (the lowest quintile)	389 (21.4)	0	346 (54.3)	44 (100)	

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.

Table 3. Odds ratios and 95% confidence intervals for somatic symptoms in relation to frailty.

	Non-frail		Pre-frail		Frail		*P value* for trend
	n=1139	Reference	n=635	Crude odds ratio (95% CI)	n=44	Crude odds ratio (95% CI)	
(a) numbness in your limb	208 (18.3)	1	168 (26.5)	1.61 (1.28, 2.03)	20 (45.5)	3.73 (2.02, 6.88)	<0.001
(b) edema in your face or limb	66 (5.8)	1	69 (10.9)	1.98 (1.39, 2.82)	8 (18.2)	3.61 (1.61, 8.08)	<0.001
(c) thirst sensation	111 (9.8)	1	97 (15.3)	1.67 (1.25, 2.24)	11 (25.0)	3.09 (1.52, 6.28)	<0.001
(d) frequent urination	238 (20.9)	1	201 (31.7)	1.75 (1.41, 2.18)	18 (40.9)	2.62 (1.41, 4.86)	<0.001
(e) dysuria	30 (2.6)	1	27 (4.3)	1.64 (0.97, 2.79)	5 (11.4)	4.74 (1.74, 12.87)	0.004
(f) pain on urination	6 (0.5)	1	5 (0.8)	1.50 (0.46, 4.93)	0	-	0.728
(g) sensation of residual urine	76 (6.7)	1	60 (9.5)	1.46 (1.03, 2.08)	6 (13.6)	2.21 (0.91, 5.39)	0.014
(h) headache	102 (9.0)	1	66 (10.4)	1.18 (0.85, 1.63)	9 (20.5)	2.61 (1.22, 5.59)	0.049
(g) dizziness	84 (7.4)	1	58 (9.1)	1.26 (0.89, 1.79)	6 (13.6)	1.98 (0.82, 4.83)	0.080
(h) lightheadedness	86 (7.6)	1	94 (14.8)	2.13 (1.56, 2.90)	10 (22.7)	3.60 (1.72, 7.54)	<0.001
(i) palpitation	54 (4.7)	1	56 (8.8)	1.94 (1.32, 2.86)	5 (11.4)	2.58 (0.98, 6.80)	0.001
(j) shortness of breath	43 (3.8)	1	49 (7.7)	2.13 (1.40, 3.25)	5 (11.4)	3.27 (1.23, 8.70)	<0.001
(k) tightness of the chest	19 (1.7)	1	27 (4.3)	2.62 (1.44, 4.75)	2 (4.6)	2.81 (0.63, 12.45)	0.002
(l) chest pain	35 (3.1)	1	24 (3.8)	1.24 (0.73, 2.10)	3 (6.8)	2.31 (0.68, 7.81)	0.208
(m) arthralgia	233 (20.5)	1	161 (25.4)	1.32 (1.05, 1.66)	16 (36.4)	2.22 (1.18, 4.18)	0.002

(n) sleep-onset insomnia	270 (23.7)	1	187 (29.5)	1.34 (1.08, 1.67)	16 (36.4)	1.84 (0.98, 3.45)	0.002

Table 4. Odds ratios and 95% confidence intervals for the number of somatic symptoms in relation to frailty.

	Non-frail		Pre-frail				Frail			
	n=1139	Reference	n=635	Odds ratio (95% CI)		P	n=44	Odds ratio (95% CI)		P
No. of somatic symptoms ≥1	806 (70.8)	1	494 (77.8)	Crude	1.45 (1.15, 1.82)	0.001	44 (100.0)	Crude	-	
		1		Adjusted	1.13 (0.89, 1.46)	0.310		Adjusted	-	
No. of somatic symptoms ≥2	439 (38.5)	1	358 (56.4)	Crude	2.06 (1.69, 2.51)	<0.001	35 (79.6)	Crude	6.20 (2.95, 13.03)	<0.001
		1		Adjusted	1.77 (1.42, 2.19)	<0.001		Adjusted	4.07 (1.86, 8.90)	<0.001
No. of somatic symptoms ≥3	221 (19.4)	1	231 (36.4)	Crude	2.38 (1.91, 2.95)	<0.001	20 (45.5)	Crude	3.46 (1.88, 6.38)	<0.001
		1		Adjusted	1.95 (1.53, 2.48)	<0.001		Adjusted	1.84 (0.93, 3.64)	0.081
No. of somatic symptoms ≥4	103 (9.0)	1	124 (19.5)	Crude	2.44 (1.84, 3.24)	<0.001	14 (31.8)	Crude	4.69 (2.41, 9.14)	<0.001
		1		Adjusted	1.87 (1.37, 2.56)	<0.001		Adjusted	2.06 (0.96, 4.42)	0.065
No. of somatic symptoms ≥5	47 (4.1)	1	66 (10.4)	Crude	2.69 (1.83, 3.97)	<0.001	8 (18.2)	Crude	5.16 (2.27, 11.72)	<0.001
		1		Adjusted	1.86 (1.22, 2.86)	0.004		Adjusted	1.55 (0.59, 4.07)	0.378

No. of somatic symptoms ≥6	25 (2.2)	1	39 (6.1)	Crude	2.92 (1.75, 4.87)	<0.001	6 (13.6)	Crude	7.04 (2.73, 18.15)	<0.001
		1		Adjusted	1.87 (1.07, 3.27)	0.029		Adjusted	2.17 (0.71, 6.62)	0.173
No. of somatic symptoms ≥7	10 (0.9)	1	20 (3.2)	Crude	3.67 (1.71, 7.90)	0.001	5 (11.4)	Crude	14.47 (4.72, 44.36)	<0.001
		1		Adjusted	2.06 (0.89, 4.76)	0.090		Adjusted	4.31 (1.09, 16.98)	0.037
No. of somatic symptoms ≥8	7 (0.6)	1	9 (1.4)	Crude	2.32 (0.86, 6.27)	0.096	4 (9.1)	Crude	16.17 (4.55, 57.49)	<0.001
		1		Adjusted	1.11 (0.37, 3.37)	0.853		Adjusted	4.84 (0.99, 23.80)	0.052
No. of somatic symptoms ≥9	3 (0.3)	1	5 (0.8)	Crude	3.00 (0.72, 12.62)	0.133	3 (6.8)	Crude	27.71 (5.43, 141.46)	<0.001
		1		Adjusted	1.56 (0.29, 8.36)	0.603		Adjusted	6.45 (0.68, 61.10)	0.104
No. of somatic symptoms ≥10	0	1	2 (0.3)	Crude	-		1 (2.3)	Crude	-	
		1		Adjusted	-			Adjusted	-	

No participants had more than 11 somatic symptoms. Adjusted for age, sex, past medical history of stroke, ischemic heart disease, hypertension, living alone, K6 test (≥5), current smoking and drinking status, and estimated glomerular filtration rate.

Figure 1. Study participants