Frailty index–predicted mortality is moderated by health-related behaviors: a 4-year community-based longitudinal-cohort study

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Abstract

To explore the separate and joint associations between frailty and long-term, all-cause mortality with health-related behaviors in older adults. We enrolled a total of 4050 community residents age ≥ 60 years from Songjiang District, Shanghai, China, and followed up with them every year from 2015 to 2018. Based on the standard procedure for creating an FI, we developed one containing 28 measured variables. Survival analyses were used to examine the risk ratios (RRs) between frailty and 4-year mortality; hazard ratios (HRs) were obtained and adjusted for gender and age. Over an average follow-up time of 1107.56 ± 144.43 days, 216 (5.4%) participants died. Of all participants, 71.7% were non-frail (FI = 0–0.1), 23.2% were pre-frail (FI = 0.1–0.2), and 5.1% were frail (FI ≥ 0.2). Multivariate HRs (with 95% confidence intervals [CIs]) for all-cause mortality were 1.58 (1.06–2.34) and 2.63 (1.52–4.55) for moderate (FI 0.1–0.2) and severe (FI ≥ 0.2) frailty, respectively, compared with mild frailty (<0.1). Risk of death for severely frail participants who were physically inactive (HR = 3.40; 95% CI, 1.78–6.50; $P < 0.001$) was 105%, much higher than for severely frail participants who performed physical exercise (HR = 2.34; 95% CI, 1.35–4.09; $P < 0.01$). Similarly, among severely frail participants, those who were socially inactive (HR = 5.77; 95% CI, 2.69–12.38; $P < 0.01$) were 344% more likely to die than those who regularly participated in social activities (HR = 2.33; 95% CI, 1.42–3.86; $P < 0.01$).

Introduction

Frailty is a geriatric syndrome of nonspecific vulnerability to adverse outcomes (e.g., mortality, institutionalization, falls, hospitalization) resulting from the deregulation of multiple physiological-system factors associated with advancing age[1–4]. The overall weighted prevalence of frailty is 10.7% (range, 4.0–59.1%), as reported in a systemic review that included 61,500 community-dwelling adults age ≥ 65 years[5]. Empirically, the incidence and associated adverse health outcomes of frailty are expected to increase as the population ages. The public-health implications of frailty have been regarded as a significant and modifiable financial burden on health care services[6]. Therefore, it is advisable to prevent or slow the progression of frailty in order to advance healthy-life expectancy, and so a metric for frailty would be an important public-health indicator.

Two major common means of assessing frailty are the phenotypic approach and the frailty index (FI). The phenotypic approach, proposed by Fried et al., defines frailty as a distinct clinical syndrome measured by five criteria: unintentional weight loss, self-reported exhaustion, weakness (grip strength), slow walking speed, and low physical activity[7]. In contrast, the FI concentrates less on the specific syndrome and instead concentrates on the continuum of accumulating deficits (symptoms, functional impairments, diseases, and disabilities), reflecting the proportion of potential health deficits present in the individual[8, 9]. These deficits across the physical, cognitive, and psychological domains[10] further emphasize frailty's important role in public health as a robust predictor of health changes, health care utilization, and death, thereby facilitating health monitoring and intervention[11–13]. We therefore employed the FI in this study as a reflection of age-related developed processes. Rockwood et al. introduced the term “frailty” to describe observed heterogeneity in individuals of the same age that

resulted in a decline in health or living status[14]. The deficit accumulation model of the FI specifically measures frailty as well as heterogeneity in risk of adverse outcomes; the latter is measured by all relevant indices.

Over the past 5 years, the number of studies on the FI's validity for predicting mortality has grown, but the majority of subjects were hospitalized with various chronic diseases such as end-stage liver disease[15], HIV-related diseases[16], or Alzheimer disease[17]; or for operations such as spinal[18] or gastrointestinal surgery[19]. Round-the-clock care and enhancement of healthy longevity for elders who are frail or becoming frail, but living with their families or in the community, seems both more necessary and more difficult than temporarily providing treatment or nursing services for aged patients in hospitals, as individuals spend most of their lives in the former settings. Since the establishment of the frailty theory as an important factor in comprehensive geriatric assessments (CGAs), recognizing elders who are vulnerable to falls, hospitalization, and mortality in early-stage frailty has become the theory's most important usage in clinical practice[20]. From a health promotion perspective, providing health-related resources and education is critical and useful to maintaining the health of elders in the community, as it enables each elder to adopt a healthy lifestyle and behaviors[21]. A 10-year community intervention for frailty prevention conducted in Japan used a health education program to motivate older residents to improve their levels of physical activity (PA), nutrition, and social participation (SP), ultimately extending healthy-life expectancy at age 70 years by 1.2 years for women and 0.5 years for men[22]. Lifestyle and health behaviors also influence each older adult's various domains of accumulated deficits, which may contribute to FI heterogeneity across different geographies[23–25]. However, research examining the separate or joint associations among lifestyle, frailty, and long-term mortality in older adults, especially in developing countries[26], is scarce. Therefore, our study aimed to assess whether lifestyle (PA and SP) could compensate for the excess mortality associated with frailty.

Materials And Methods

Study design and participants

We used multi-stage random sampling to recruit 4050 participants from an investigation of chronic diseases and geriatric syndromes during 2015 (baseline) from Shanghai, representative of the non-institutionalized population age ≥ 60 years in Shanghai, China, from July 2015 to November 2018. Random sampling methods was used to select four communities in two streets, then was used to select family addresses in which older residents lived in through a household registration information system. Trained personnel collected information at participants' homes via interviews, with the intention of investigating the associations among biological, psychological, and social aspects of elder health. Only 15 (0.4%) respondents of the final study were lost to follow-up in this cohort. Written informed consent was obtained from each study participant and the Research Ethics Committee of researchers' institution, approved the study protocol.

Frailty index construction

We recorded the presence or absence of deficits, including continuous, ordinal, and binary variables associated with frailty. Initially, we identified variables similar to those used in other studies[27, 28]and in such indices as the Activities of Daily Living (ADL)[29], the Ascertain Dementia-8 (AD8)[30], and the Parkinson Disease Short Questionnaire (PDSI)[31]. The 28 items were listed in Table 1. Our FI evaluated comorbidities (medically diagnosed conditions) and self-reported health. All variables could be integrated into the FI if they satisfied the following 5 criteria suggested by Rockwood: (1) A variable must be a deficit associated with health status; (2) its prevalence must generally increase with age; (3) it must not become highly prevalent at too early a life stage; (4) deficits must cover a range of systems; and (5) if a single FI is to be used serially on the same people, the items it comprises must remain the same from one iteration to the next[32]. Therefore, we defined our FI as the proportion an individual had of the 28 deficits we included. Binary variables indicated the presence/absence of a particular deficit; a score of 1 was given for presence, a score of 0 for absence. For each ADL item with 2 intermediate responses (e.g. “self-care,” “self-care deficit,” “self-care assistance,” “dependent on others”), we used additional values of 0.33 and 0.67. For the AD8 and PDSI, according to impairment status, we assigned a score of 1 for dementia (cutoff: AD8 score ≥ 2 according to the clinical dementia rating standard) or Parkinson (cutoff: PDSI score ≥ 4), with 0 denoting the absence of both cognitive impairment and Parkinson[30, 31]. The FI cutoff value of 0.2 is recognized by multiple frailty measures to mean “approaching a frail state[33].” In our study, the cutoff point 0.1, representing pre-frailty, could predict 3-year mortality as well as frailty status, according to receiver operating characteristic (ROC) curve analysis (area under the curve [AUC] = 0.66; sensitivity = 0.56; specificity = 0.73). Therefore, we used 3 levels (0–0.1, non-frailty; 0.1–0.2, pre-frailty; ≥ 0.2 , frailty) to illustrate the association between FI and mortality.

Table 1
List of the 28 items in the frailty index.

Activities of daily living ^a	Medically diagnosed conditions ^a
1. Problems getting dressed	16. High blood pressure
2. Problems bathing	17. Coronary heart disease
3. Problems walking indoors	18. History of stroke
4. Toileting problems	19. Chronic bronchitis
5. Problems getting in and out of bed	20. Diabetes mellitus
6. Problems with urine and feces control	21. Cataracts
7. Problems eating	22. Hearing loss
8. Problems making phone calls	23. Urinary incontinence
9. Problems shopping	Self-reported health ^b
10. Problems cooking	24. Problems with sense of smell
11. Problems doing housework	25. Constipation
12. Problems doing laundry	26. Problems with sleeping
13. Problems taking bus	Comprehensive assessment ^a
14. Problems taking medicine	27. Ascertain Dementia-8
15. Problems handling money	28. Parkinson Disease Short Questionnaire
^a Binary variables; values 0 or 1. ^b Four-category variables; values 0, 0.335, 0.67, and 1.	

Moderator variables

We assessed PA using validated single questions, which are habitually used to monitor the prevalence of physical activity[34]: “How often do you perform leisure-time activities, such as playing ball, running, fast walking, or qigong? (Average physical-activity time must exceed 10 minutes per day.)” Participants rated their PA levels as (1) inactive, (2) several times a month, (3) 3–4×/week, or (4) almost every day. We chose to integrate these 4 categories into a binary variable to intelligibly explain the association between PA and frailty: physically inactive versus physically active (several times a month, 3–4×/week, and almost every day). SP was assessed by a single question that we designed: “How often do you participate in social activities, such as those organized by your local university, by the community, or by other elderly people?” Participants rated their SP as (1) inactive, (2) several times a year, (3) several times a month, or (4) several times a week. As with PA, we integrated the 4 SP categories into a binary variable: inactive versus active SP.

Mortality ascertainment

Mortality status and date of death were obtained from the Death Surveillance System of local institution for all participants after each follow-up. Time to death or censoring was calculated for each participant.

Covariates

Covariates were chosen from single factor analysis associated with frailty status, including age, gender, educational attachment (illiteracy, primary, $\geq$ junior school), marriage status (spinsterhood, married), tobacco smoking and alcohol consumption (never, sometimes, every day).

Data analysis

Numerical variables are presented as mean $\pm$ standard deviation (SD), categorical variables as number (percentage). We calculated the FI distribution of study participants' sociodemographic characteristics using Student's t test or analysis of variance (ANOVA). Association between all-cause mortality and frailty status (non-frail, pre-frail, or frail) was summarized using hazard ratios (HRs) and their 95% confidence intervals (CIs) obtained from Cox regression. We fitted 2 models with progressive adjustments for potential covariates. To examine the separate association between frailty and all-cause mortality, we stratified Cox regression analysis by level of health behaviors, including PA and SP. Next, we examined the modifier effects of PA and SP by incorporating an interaction term into the Cox models. Statistical significance was set at $P < 0.05$, and all tests were 2-sided. We performed all analyses using SPSS software version 22.0 (SPSS, Inc., Chicago, Illinois, US) and R software version 3.5.3 (R; <https://www.r-project.org/>).

Results

The analytic cohort comprised 4050 participants (mean age 69.48 ± 7.13 years; 43.6% male). During the study period, with average follow-up of 1107.56 ± 144.43 days, 216 deaths occurred (5.6%). The constructed FI had a median value of 0.08 (range, 0–0.76) in the target population (Fig. 1); as a result, 71.7% of participants were non-frail (FI = 0–0.1), 23.2% were pre-frail (FI = 0.1–0.2), and 5.1% were frail (FI = ≥ 0.2).

Table 2 summarizes participants' sociodemographic characteristics by these 3 frailty levels. There were proportionally more female, unmarried, illiterate, never-smoking, never-drinking, physically active, and socially active participants on all 3 levels ($P < 0.05$). In age- and gender-adjusted analyses, pre-frail participants were 45% more likely than non-frail ones to die (HR = 1.45; 95% CI, 1.05–2.01; $P = 0.026$), while frail ones were more than 3 times as likely (HR = 3.15; 95% CI, 2.11–4.70; $P < 0.001$). The results were similar in fully adjusted analyses (pre-frail: HR = 1.58; 95% CI, 1.06–2.34, $P = 0.024$; frail: HR = 2.63; 95% CI, 1.52–4.55; $P = 0.001$; Fig. 2).

Table 2
Participant sociodemographic characteristics stratified by the 3 levels of the frailty index.

	Non-frail (n = 2865)	Pre-frail (n = 929)	Frail (n = 202)	χ^2, P
Age	67.96 $\pm$ 6.31	72.21 $\pm$ 7.27	76.51 $\pm$ 7.92	< 0.001
Gender				
Male	1388 (79.8)	294 (16.9)	58 (3.3)	99.58
Female	1477 (65.5)	635 (28.1)	144 (6.4)	< 0.001
Marital status				
Single	469 (58.0)	248 (30.7)	391 (11.3)	127.61
Married	2396 (75.2)	681 (21.4)	111 (3.5)	< 0.001
Educational level				
Illiteracy	1420 (62.9)	669 (29.6)	168 (7.4)	207.30
Primary school	988 (83.9)	172 (14.6)	18 (1.5)	< 0.001
$\geq$ Junior school	457 (81.5)	88 (15.7)	16 (2.9)	
Smoking				
Never	2125 (68.2)	813 (25.8)	191 (6.1)	100.36
Sometimes	39 (73.6)	11 (20.8)	3 (5.7)	< 0.001
Daily	674 (85.6)	105 (13.3)	8 (1.0)	
Drinking				
Never	2226 (68.6)	824 (25.4)	196 (6.0)	200.30
Sometimes	139 (79.9)	33 (19.0)	2 (1.1)	< 0.001
Daily	500 (86.5)	72 (12.5)	4 (0.7)	
Physical activities				
Inactive	591 (67.0)	216 (24.5)	75 (8.5)	30.85
Active	2274 (73.0)	713 (22.9)	127 (4.1)	< 0.001
Social participation				
Inactive	512 (66.6)	199 (25.9)	58 (7.5)	17.96
Active	2353 (72.9)	730 (22.6)	144 (4.5)	< 0.001

As shown in Table 3, when examining the association between frailty and mortality according to PA, we found clear dose–response associations in both groups. In the fully adjusted stratification analysis model, the hazard risk of death in frail participants who were physically inactive (HR = 3.99; 95% CI, 2.14–7.44; $P < 0.001$) was 165%, much higher than in frail participants who did perform physical exercise (HR = 2.34; 95% CI, 1.35–4.09; $P < 0.01$). In further analysis of the interaction term between frailty and physical activity, physical activity did modify the main effect of frailty on mortality (all-cause mortality: P for interaction = 0.004). A similar association between SP and frailty is shown in Table 4. In the fully adjusted stratification analysis model, frail elders who were socially inactive (HR = 5.77; 95% CI, 2.69–12.38; $P < 0.01$) were 344% more likely to die than frail participants who regularly participated in social activities (HR = 2.33; 95% CI, 1.42–3.86; $P < 0.01$). In further analysis of the interaction term, SP also modified the main effect of frailty on mortality (all-cause mortality: P for interaction < 0.001).

Table 3
All-cause mortality as predicted by FI and stratified by physical activity (PA).

PA	Frailty Index		
	Non-frail	Pre-frail	Frail
Inactive			
Died/total, n/N	27/589 (4.6%)	20/215 (9.3%)	24/73 (32.9%)
Model 1, HR (95% CI)	1	1.76 (0.96–3.22)	3.99 (2.14–7.44)***
Model 2, HR (95% CI)	1	1.71 (0.93–3.15)	3.40 (1.78–6.50)***
Active			
Died/total, n/N	72/2272 (3.2%)	46/712 (6.5%)	18/127 (14.2%)
Model 1, HR (95% CI)	1	1.36 (0.92–2.00)	2.39 (1.37, 4.16)**
Model 2, HR (95% CI)	1	1.31 (0.89–1.94)	2.34 (1.35, 4.09)**
HR = hazard ratio; CI = confidence interval. * $P < 0.05$, ** $P < 0.01$, *** $P < 0.01$. Model 1 was adjusted for age and gender. Model 2 was additionally adjusted for educational attainment, marital status, tobacco use, and alcohol consumption.			

Table 4
All-cause mortality as predicted by FI and stratified by social participation (SP).

SP	Frailty Index		
	Non-frail	Pre-frail	Frail
Inactive			
Died/total, n/N	17/512 (3.3%)	13/199 (6.5%)	17/56 (30.4%)
Model 1, HR (95% CI)	1	1.48 (0.71–3.10)	5.90 (2.83–12.30) ^{***}
Model 2, HR (95% CI)	1	1.42 (0.68–3.00)	5.77 (2.69–12.38) ^{***}
Active			
Died/total, n/N	82/2349 (3.5%)	53/728 (7.8%)	25/144 (17.4%)
Model 1, HR (95% CI)	1	1.44 (1.01–2.08) [*]	2.42 (1.47– 3.97) ^{***}
Model 2, HR (95% CI)	1	1.39 (0.96–2.01)	2.33 (1.42–3.86) ^{**}
HR = hazard ratio; CI = confidence interval. [*] P < 0.05, ^{**} P < 0.01, ^{***} P < 0.01. Model 1 was adjusted for age and gender. Model 2 was additionally adjusted for educational attainment, marital status, tobacco use, and alcohol consumption.			

Discussion

The baseline frailty prevalence of 5.1% in the 4050 elders we studied was in line with previous community population-based research, which found that frailty among participants was 6.6% over 5 years of follow-up in Mexican Americans from the Hispanic established populations[35] and 5.4% in China's general population[36]. Among our participants, older women seemed more vulnerable to accumulated deficits than older men, as another study also found[37]. Women's tendency to become severely frail in later life could be explained by their higher probability of functional disability, which is a main measure of physical deficits[38]. Our results also suggested that participants with lower educational attainment were more likely to be severely frail, which was in agreement with a previous study that older adults with lower educational attainment were at increased risk of worsening frailty over a 2-year period[39]. A plausible reason is that older adults are more likely to experience bereavement; both widowers and widows reportedly have high individual HRs for mortality[40].

Frailty is a dynamic process characterized by frequent transitions between levels of frailty over time; natural transitions to more-severe levels are more common than transitions to less-severe levels[41]. However, evidence is insufficient to support any efficacious and economical strategy to postpone this degradation process. The finding that performing PA at an advanced age lowered participants' risk of mortality, even compared with inactive participants at identical frailty levels, was consistent with recent

research[42–44]. In a total sample of 498,135 participants conducted by the UK Biobank, the highest risk of death was found in participants with the lowest PA level, and the risk of mortality increased as the PA quantile decreased[45]. The possible explanation may contribute to the beneficial effect that PA was demonstrated can reduce the incidence of chronic diseases[46], Alzheimer disease[47], Parkinson disease[48], and disability[46], which are all FI components, and can reduce mortality in turn. Our research also suggested that SP actively reduced the probability of mortality approximately eightfold in frail participants compared with those who seldom participated in social activities. Although a few studies have focused on the moderating effect of SP on the association between frailty and mortality, several others provide assertive evidence that might explain the mechanism behind the favorable effect of PA. SP inactivity, as a domain of social frailty, is associated with the frailty development process[39], which in turn can influence long-term SP level[49]. Social frailty linked to dementia, subjective-memory decline, depression, and cognitive impairment poses a higher risk of 8-year mortality in participants who are socially frail than in those who are not[50]. Moreover, SP is critical to the social environment, a broad concept that also includes social networks, social support, and neighborhood characteristics. There is evidence that a good social environment has a beneficial effect on frailty in later life, meaning that mortality could be reduced by ensuring that elders obtain health-related resources[51].

This study has some limitations. Since a single question was used to assess PA and SP levels to some extent, the metric might need to be more specific and multidimensional in further research. Another limitation was the low sensitivity (< 0.6) for frailty on the ROC curve, due to the low proportion of participants who did not suffer from a high level of deficits in our study. Furthermore, all variables in FI were self-reported through participants while several cervix data were excluded because of non-correlates to age.

Conclusions And Implications

Among community-dwelling persons age ≥ 60 years in Shanghai, China, pre-frailty and frailty were associated with much higher all-cause mortality than robust health over 3 years of follow-up, but in frail individuals, participation in PA and SP was associated with lower mortality risk compared with those who were physically and socially inactive. These findings suggested that the FI we created by counting accumulated deficits in elders could predict all-cause mortality and that PA and SP might partly moderate frailty-influenced risk of mortality in older adults.

Declarations

Conflicts of Interest: The authors declare no conflict interest.

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Figures

Figure 1. Frailty index distribution.

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Figure 1

Frailty index distribution.

Figure 2. Kaplan–Meier survival analysis stratified by the 3 levels of the frailty index.

Figure 2

Kaplan–Meier survival analysis stratified by the 3 levels of the frailty index.