



# Agreement between the frailty index and phenotype and their associations with falls and overnight hospitalizations



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## ARTICLE INFO

### Article history:

Received 26 September 2015  
Received in revised form 3 June 2016  
Accepted 5 June 2016  
Available online 10 June 2016

### Keywords:

Frail elderly  
Accidental falls  
Hospitalization  
Aged

## ABSTRACT

**Background:** The objective of this study is to examine the agreement between two commonly used frailty measurements (frailty index and phenotype) and their associations with falls and overnight hospitalizations in a community-based population.

**Methods:** Data was collected from 1663 elderly adults (aged 70–84 years) from the aging arm of the Rugao Longevity and Ageing study, a two-arm cohort conducted in Rugao, China. Items concerning the frailty index and phenotype, falls and overnight hospitalizations were collected.

**Results:** The Kappa agreement examining three levels of these two frailty measurements was 0.310 (95% CI: 0.277–0.343) according to the frailty index cut-off developed by Hoover et al. Both frailty measurements were significantly associated with falls and overnight hospitalizations. For instance, compared with the frailty index defined non-frail participants, their pre-frail and frail counterparts had significantly increased risks for falls, with odds ratios (ORs) of 1.69 (95% CI: 1.17–2.43) and 2.87 (95% CI: 1.93–4.28), respectively. When the two frailty measurements were simultaneously included in the models, significant associations were also observed. More importantly, a sub-analysis in participants who were categorized as robust by frailty phenotype revealed that frail participants (frailty index > 0.21) still had increased risks for falls (OR = 2.35, 95% CI: 1.24–4.46) and overnight hospitalizations (OR = 2.56, 95% CI: 1.05–6.23) compared with their non-frail counterparts.

**Conclusions:** Common characteristics and complementarity existed in the frailty index and phenotype in the elderly Chinese population. Additional consideration of the frailty index when applying frailty phenotype should be undertaken. The findings provide preliminary but crucial clues for future studies on frailty.

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## 1. Introduction

Frailty has been regarded as not only a useful concept but also an important medical syndrome (Morley et al., 2013). As Clegg et al. suggested, frailty signifies a state of increased vulnerability to minor stressor events that arise from cumulative declines in many physiological systems throughout life, and increases risks of adverse health outcomes, e.g., falls, hospitalizations, and mortality (Clegg, Young, Iliffe, Rikkert, & Rockwood, 2013). Two of the many

approaches used to operationalize frailty have been widely applied, including the phenotype model and the cumulative deficit model (Clegg et al., 2013; Fried et al., 2001; Rockwood and Mitnitski, 2007; Searle, Mitnitski, Gahbauer, Gill, & Rockwood, 2008). Comparisons between the models have been made but the results remain controversial (Blodgett, Theou, Kirkland, Andreou, & Rockwood, 2015; Malmstrom, Miller, & Morley, 2014; Mitnitski, Fallah, Rockwood, & Rockwood, 2011; Theou, Brothers, Mitnitski, & Rockwood, 2013; Woo, Leung, & Morley, 2012), which might be attributed to differences in study populations (e.g., age (Blodgett et al., 2015)) as well as the variables that were selected to construct frailty. This highlights the need that the utility of frailty measurements should be carefully examined in different settings for subsequent research.

China is facing rapid population aging. The growing vulnerable elderly population will lead to soaring health care costs, greatly

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challenging the government. As the most problematic expression of population aging (Clegg et al., 2013), frailty has been recently explored in several studies in the Mainland of this developing country (Chen et al., 2015; Dupre, Gu, Warner, & Yi, 2009; Fang et al., 2012; Liu, Wang, Zhi et al., 2015), the majority of which focused on the frailty index in terms of the cumulative deficit model. Frailty studies are ongoing important areas for gerontologists, clinicians and public health planners. However, to the best of our knowledge, no study has compared the two most commonly used frailty measurements in Mainland China. Because several incidents such as falls and overnight hospitalizations that affect large numbers of older adults, have been recognized as adverse outcomes of frailty (Clegg et al., 2013), it is of great interest to address whether the frailty index, which captures a wide range of deficits, has advantages in defining people at high risk compared with the frailty phenotype.

Based on data from the Rugao Longevity and Ageing Study (RuLAS), this study aimed to characterize frailty in an elderly Chinese population aged 70–84 years, including examining the agreement between frailty index and phenotype and their associations with falls and overnight hospitalizations. We also studied the associations of the frailty index with falls and overnight hospitalizations in those who were categorized as robust by the frailty phenotype.

## 2. Methods

### 2.1. Study design and population

Data from the aging arm of the RuLAS were collected. RuLAS is a two-arm cohort study conducted in Rugao, a typical medium-sized city in China, that aimed to examine the determinants of longevity and aging. A detailed description was provided in a previous publication (Liu, Wang, Zhang et al., 2015). Briefly, approximately 1960 elderly adults aged 70–84 years were randomly recruited from the 31 villages of Jiang'an Township, Rugao city, between November 2014 and December 2014 following a 5-year age and sex strata. This was a community-based study with no exclusion criteria. Overall 1788 participants (91.2%) formed the final sample. No evident difference in the 5-year age and sex ratios was observed between the responders and non-responders. Due to missing data, 1663 participants were retained in the current study.

During the field investigation, trained physicians from the Rugao People's Hospital administered a detailed structured questionnaire and performed physical examinations. Data on sociodemographics, lifestyles, chronic diseases (e.g., cerebrovascular disease), health deficits (e.g., urinary incontinence), sleep quality, nutrition assessment, cognitive function (the Revised Hasegawa's Dementia Scale [HDS-R] (Imai and Hasegawa, 1994)), social support/relations, and depression (Geriatric Depression Scale [GDS]-15 (Yesavage et al., 1982)) were collected. In addition to routine clinical examinations, such as blood pressure, electrocardiography, and eyesight, a walking test (timed 'up and go' test, TUG) was also performed. All participants provided fasting blood, saliva, and fingernails samples. Written informed consent was obtained from each participant. The Human Ethics Committee of Fudan University School of Life Sciences approved the research.

### 2.2. Frailty index

According to the standard procedure developed by Searle and Rockwood (Rockwood and Mitnitski, 2007; Searle et al., 2008), we used 45 health deficits including symptoms, activities of daily living (basic and instrumental), comorbidity, cognitive and psychological function to construct a frailty index, which has been described in our previous publication (Liu, Wang, Zhi et al.,

2015). Each deficit was dichotomized or polychotomized and mapped to the interval 0–1 to represent the severity of the deficit. For example, we transformed the HDS-R score into a four level variable coded as 0 if  $HDS-R \geq 31$ , 0.33 for HDS-R between 22 and 30.5, 0.67 for HDS-R between 10.5 and 21.5, and 1 if  $HDS-R \leq 10$ . We transformed the GDS-15 score into a 3 level variable coded as 1 if  $GDS-15 \geq 8$ , 0.5 for GDS-15 between 6 and 7, and 0 for  $GDS-15 < 6$  (Collerton et al., 2009). The frailty index was calculated by summing all deficits and dividing by the total number of deficits ( $n = 45$ ), equaling a total score between 0 and 1. For instance, if one person had four deficits (vision impairment, diabetes, a HDS-R score of 6, and a GDS-15 score of 15) each with a score of 1 point and the other 41 deficits each with a score of 0, the cumulative values of deficits would be therefore 4 divided by 45, resulting in a frailty index of 0.09.

Based on the previous work by Hoover et al. (Blodgett et al., 2015; Hoover, Rotermann, Sanmartin, & Bernier, 2013), we transformed the frailty index score into a four-level variable coded as "non-frail" if frailty index  $\leq 0.10$ , "vulnerable" for frailty index between 0.10 and 0.21, "frail" for frailty index between 0.21 and 0.45, and "most frail" if frailty index  $> 0.45$ . In addition, according to Song, Mitnitski, and Rockwood (2010), we also transformed a frailty index score into a three-level variable coded as "robust" if frailty index  $< 0.08$ , "pre-frail" for frailty index between 0.10 and 0.25, and "frail" if frailty index  $\geq 0.25$ .

### 2.3. Frailty phenotype

According to Fried et al. (2001), five components including unintentional weight loss, weakness, exhaustion, slowness, and low activity were used to define the frailty phenotype. Similar measurements of the five criteria were used in this study. Unintentional weight loss, exhaustion, and low activity were based on self-reported items including "weight has decreased by 4.5 kg or 5% during the last 12 months", "feeling tired all of the time (at least 3 or 4 days per a week)", and 'needing help to walk'. Weakness was based on the self-report of "having difficulty in lifting or carrying something as heavy as 10 kg", which was similar to that used in other studies (Blodgett et al., 2015). Slowness was defined as being below the 20th sex-specific percentile in gait speed (assessed through a TUG test). In the TUG test, the study participants were asked to stand up from an armchair, walk 3 m, return, and sit down again. The timing of this test began when the participant's back came off the back of the armchair, and stopped when their buttocks touched the seat of the chair again (Nordin, Lindelof, Rosendahl, Jensen, & Lundin-Olsson, 2008). Participants with three or more of the five components were defined as "frail", while one or two components constituted "pre-frail", and none of the components was defined as "robust".

### 2.4. Falls and overnight hospitalizations

As previously reported (Liu, Wang, Zhi et al., 2015), falls and overnight hospitalizations were separately assessed by asking the following questions: "How many times did you fall (or spend overnight in the hospital) in the prior 12 months?". As described in our previous publications (Liu, Wang, Zhi et al., 2015), fall status was dichotomized as having no falls vs. having one or more falls in this study. The definition of overnight hospitalizations was the same.

### 2.5. Covariates

As our previous publication described (Liu, Wang, Zhi et al., 2015), covariates including demographics (age, sex), marital status, education level, smoking status, and body mass index were

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