Differences in clinical characteristics, muscle mass, and physical performance among different frailty levels in Chinese older men

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To the Editor: Frailty is defined as a vulnerable state that places older adults at increased risk for adverse health outcomes, and can explain substantial heterogeneity of health status. Previous studies have demonstrated the utility of the frailty phenotype scale and frailty index (FI) in identifying frail older people in China.¹ Several experimental and clinical studies on frailty have been published using the above methods in recent years, but influential factors for discriminating frailty levels in Chinese older adults have not yet been determined. Elucidating this issue is of importance, because early detection of frailty-related factors and subsequent intervention are essential for safeguarding functionality and preventing the occurrence of adverse consequences among older people.

Low muscle mass is reported to be an important link between sarcopenia and frailty. Moreover, frailty is associated with impaired physical function, which is a major indicator of frailty, and performance-based measures of physical function are useful for the identification of frailty. Although these associations have been reported in the United States, Europe, and other parts of Asia, few studies have examined which domains of physical functioning—muscle mass, strength, or balance contribute to the level of frailty among older people in China. Moreover, most previous studies of older individuals have explored frailty-related factors in combined with populations of males and females, and few studies have focused on older males, in which age-related decrease in skeletal muscle mass and strength was faster than in women.² In this study, we analyzed the clinical characteristics, muscle mass and physical performance among older males with different frailty levels. We aimed to explore the possible relationship between frailty and muscle mass, physical function-related factors to provide an approach for early identification of prefrailty/frailty in health examinations of older people.

The study was conducted in accordance with the Declaration of Helsinki and was approved by the Ethical Committee of Beijing Hospital. Informed written consent was obtained from all studied individuals prior to their enrollment in this study.

Chinese men aged 60 years and over were recruited during regular health examination in Beijing Hospital between October 2015 and October 2016. The data on general characteristics, medical history and the burden of chronic diseases were gathered. Polypharmacy was defined as the use of more than 5 medications. The number of comorbidity was calculated according to Charlson Comorbidity Score. A comprehensive assessment was performed on all participants using the following: Geriatric Depression Scale-5 (GDS-5), the Mini-Mental State Examination (MMSE), Mini-Nutritional Assessment Short-Form (MNA-SF), Athens Insomnia Scale (AIS), Basic Activities of Daily Living (ADL), and instrumental ADL (IADL).

Frailty was defined according to Fried phenotype criteria, which includes exhaustion, weakness, slowness, physical inactivity, and weight loss. Older adults were considered as frailty when they met 3 or more of the 5 criteria, prefrailty when they met 1 or 2 criteria, and robust when they met no criteria. Totally 64 potential deficits were evaluated and included in the FI. These represent symptoms, signs or functional impairments.³ Physical function was assessed using objective measures: time up and go test (TUG), 5-time sit to stand test (ST5S) and standing balance as well as handgrip strength, gait speed. Appendicular skeletal muscle mass (ASM) was determined by bioelectrical impedance data (BIA) acquisition system. Relative ASM (RASM) was calculated by ASM divided by height square (ASM/height², kg/m²). Sarcopenia was defined according to Asian Working Group on Sarcopenia (AWGS).⁴

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Chinese Medical Journal 2019;132(3)

Received: 02-11-2018 Edited by: Xin Chen
Statistical analyses were carried out using SPSS Statistics version 17.0 (SPSS Inc., Chicago, IL, USA). A P < 0.05 was considered statistical significance. Comparison of continuous variables was performed using analysis of variance, and categorical data using Chi-square test or Fisher exact test. Multivariate logistic regression analysis was performed to examine variables associated with frailty in univariate analysis, and collinearity variables were excluded. Moreover, the correlations between FI value and physical function-related indexes were analyzed using Spearman correlation coefficients.

Overall, the complete data of 101 male participants (mean age 79.4±7.7 years, range: 63–95 years) were collected for this study, among whom 25 (24.8%) older men were in robust group, 63 (62.4%) in prefrailty group, and 13 (12.9%) in frailty group. The FI values were 0.15±0.04 in robust group, 0.18±0.06 in prefrailty group, and 0.29±0.09 in frailty group, and the differences were statistically significant (P=0.001). Participants in the frailty (61.5%) and prefrailty groups (28.6%) were significantly more likely to have sarcopenia compared with the robust group (4.0%, P=0.001).

With increasing frailty level, participants were significantly older (P=0.004), but had lower BMI values (P=0.006) and physical activity levels (P<0.001). The older men with more frailty severity had higher number of comorbid conditions (P=0.017), higher rates of diabetes mellitus (P=0.004), cancers (P<0.001), prostatic diseases (P=0.040), urinary incontinence (P=0.007), insomnia (P=0.006) and hearing loss (P=0.002), whereas there were no significant differences in the prevalence of hypertension, coronary artery disease, kidney disease, stroke, osteoporosis, dementia, Parkinson disease, or immune diseases among 3 groups. In addition, smoking and alcohol intake, falling in the previous year, and the prevalence of bodily pain, impaired vision, memory decline and depression were similar among 3 frailty statuses. Importantly, more frail older adults were more likely to report polypharmacy (P=0.023). The proportion of cognitive decline was highest in the frailty group, and lowest in the robust group, there were significant differences among 3 groups (P<0.001). Nutritional status exhibited a significant declining (P=0.001), while disability revealed a stepwise increase as the severity of frailty increased (P<0.001; Supplementary Table 1, http://links.lww.com/CMJ9/A0).

The results of logistic regression analysis revealed that, among the clinical variables found to be statistically significant in the univariate analysis, only polypharmacy was independently associated with the risk of prefrailty (OR: 2.261, 95% CI: 1.025–4.987, P=0.043), while cognitive decline was independently associated with the level of frailty (OR: 0.167, 95% CI: 0.030–0.942, P=0.043). No significant associations were found between age, BMI, insomnia, comorbidity, undernutrition, hearing loss, lower physical activity, activities of daily living, urinary incontinence and diabetes mellitus, prostatic disease, or malignant tumor, with prefrailty or frailty. When we combined the frail and prefrail participants into 1 group, the frailty status classification of the 2 groups also indicated that polypharmacy was related to prefrailty + frailty status (OR: 2.376, 95% CI: 1.036–5.445, P=0.041).

For muscle mass, the older individuals with severer frailty showed lower ASM (P<0.001) and RASM (P=0.015). Regarding functional status, there were remarkably differences in slower TUG time (P<0.001), body balance impairments (P=0.001), and performance in 5STS test (P=0.002) as well as weaker grip strength (P<0.001) and slower walking speed (P=0.009) among 3 frailty levels, indicating that the percentage of functional limitations of the extremities was enhanced with a progressive increase of frailty level (Table 1).

Logistic regression analysis for Model 1 and Model 2 showed significantly greater odds of muscle mass and balance decline with prefrailty level. The association between prefrailty and ASM was maintained even in a fully adjusted model. When we combined the prefrailty and frailty groups, similar results were found in ASM and poor balance. Interestingly, balance impairment was not related to prefrailty or prefrailty + frailty when we adjusted for polypharmacy [Table 2]. RASM was not related to prefrailty or prefrailty + frailty assessed by phenotype. The other tests of physical performance, including the 5STS and TUG, were not significantly associated with prefrailty or frailty (data not shown). We also found FI was significantly inversely associated with ASM (r=−0.244, P=0.014), handgrip strength (r=−0.287, P=0.004), and walking speed (r=−0.342, P<0.001). No significant correlations were found between FI and RASM (r=−0.099, P=0.324).

Table 1: Comparison of skeletal muscle mass and functioning among different frailty levels

| Items          | Robust group (n=25) | Pre frailty group (n=63) | Frailty group (n=13) | χ²/F  | P     |
|----------------|---------------------|--------------------------|----------------------|-------|-------|
| ASM (kg)       | 21.93±2.26          | 19.73±2.95               | 18.09±3.11           | 9.087*| <0.001|
| RASM (kg/m²)   | 7.48±0.55           | 7.15±0.98                | 6.60±0.84            | 4.411*| 0.015 |
| Grip strength (kg) | 34.73±4.21        | 26.49±6.58               | 23.37±5.15           | 22.276*| <0.001|
| Walking speed (m/s) | 1.05±0.29          | 0.90±0.30                | 0.66±0.39            | 4.999*| 0.009 |
| 5STS≥10 s      | 2 (8.0)             | 18 (28.6)                | 8 (61.5)             | 12.295| 0.002 |
| Poor balance   | 1 (4.0)             | 18 (28.6)                | 8 (61.5)             | 14.746| 0.001 |
| TUG≥12 s       | 1 (4.0)             | 10 (15.9)                | 8 (61.5)             | 15.946| <0.001|

The data are shown as mean±standard deviation or n (%). F values, otherwise χ² values. ASM: Appendicular skeletal muscle mass; RASM: Relative appendicular skeletal muscle mass; 5STS: 5-time sit-to-stand test; TUG: Timed up and go test.
To date, the clinical and physical performance-related factors according to different frailty levels have rarely been investigated among older people in China. Early identification of prefrailty/frailty and the characterization of its features are crucial for developing therapeutic guidelines and interventions, and providing integrated services for older people with frailty. The prevalence of prefrailty/frailty in previous studies has varied widely depending on definition, participant selection and socioeconomic factors. In the current study, the prevalence of frailty was higher than that reported in previous studies in men and women, and was also higher than that reported in several studies of male participants. The discrepancy with previous findings might be explained by our sample, which was most comprised of older adults in very old age. Previous results have reported that higher frequencies of prefrailty/frailty were found among older people with lower educational levels. In contrast, the older men in the current study with higher levels of education exhibited higher levels of prefrailty and frailty. One possible explanation was that individuals with more education might have undergone less physical activity and muscle mass or strength training, as indicated in the results as shown.

Some clinical features of the prefrail/frail older men in the current study were similar to those reported in previous studies, but the ratio of prostatic diseases was not increased in prefrailty compared with robust participants. However, in the multivariate analysis, we found that only polypharmacy and cognitive decline was related to prefrailty or frailty. The burden of taking multiple medications is associated with increased risk of adverse drug events, functional decline and multiple geriatric syndromes. Polypharmacy exhibited a stronger relationship with prefrailty than other factors, suggesting that it may be a suitable clinical target for reducing prefraility/frailty. Regarding the relationship between frailty and cognitive decline, several cross-sectional and longitudinal studies have reported an association between physical frailty and cognitive function. However, not all dementia patients become frail, and the current results indicated that there was no significant difference in the prevalence of dementia, Parkinson disease and memory decline. Thus, the association between frailty and cognitive impairment warrants further study.

Importantly, people with multiple long-term conditions may be overlooked for prefrailty, if examination focuses only on disease-based, long-term conditions. We found that muscle mass loss and poor balance were associated with prefrailty/frailty, not substantially attenuated after adjustment for several common health indicators in older men, suggesting that prefrailty/frailty were better identified by muscle mass and balance than by clinical characteristics. Low muscle mass is associated with low walking speed and balance, and increased risk of falls and disability. Age-dependent loss of skeletal muscle mass is a multifactorial process in older men: low testicular secretion, vitamin D deficits, low physical activity levels, and malnutrition. Muscle mass is influenced by body size, and height-adjusted parameters (RASM) provide a better reflection of the degree of sarcopenia. In contrast, RASM was not found to be associated with frailty by phenotype and FI in the current study, which was not in line with the previous study.

Decline in physical function may increase the risk of falls, hospitalization, nursing home admission, dependence, and poor quality of life. Our results revealed that some clinical indexes did not substantially affect the relationship between poor balance and prefraility/frailty, highlighting the potential of balance for the assessment of frailty status. Because balance encompasses some components of other performance-based measures, it is not surprising that balance has been found to be a stronger predictor of frailty than 5STS and TUG results. However, the current results indicated that the incidence of falls was not associated with prefrailty or frailty compared with robust individuals, suggesting that physical alterations other than decreases in muscular strength and balance may also be involved in an increased risk of falls. The TUG and 5STS tests, which are considered indicators of lower-limb muscle strength, have been confirmed as useful tools for monitoring health status, functional capacity, and the risk of falls among older people. However, we did not find the expected positive association between 5STS and TUG and frailty status in the current study, even though we found a significant difference in 5STS and TUG among prefrail and frail versus non-frail group. It should be noted that, when constructing the logistic model, none of the physical function test was statistically significant when considered simultaneously with polypharmacy, most likely due to the existing relationships between them.
This investigation was limited to the small sample size. In the future, a larger longitudinal study should be conducted among older people in China. Nonetheless, our findings provide helpful information for better understanding the association between frailty level and muscle mass, physical function in older Chinese men. In the current study, muscle mass and balance evaluation were added to a routine health examination to provide an early screening method for frailty. Our results might be useful for informing the development of suitable interventions to enhance the effectiveness of regular health examinations and promote functionality among older people.

Conflicts of interest
None.

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How to cite this article: Meng L, Shi H, Shi J, Yu PL, Xi H. Differences in clinical characteristics, muscle mass, and physical performance among different frailty levels in Chinese older men. Chin Med J 2019;132:352–355. doi: 10.1097/CMJ9.0000000000000335