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COMPARISON OF THREE FRAILTY SCALES FOR PREDICTION OF ADVERSE OUTCOMES AMONG OLDER ADULTS: A PROSPECTIVE COHORT STUDY

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Abstract: *Objectives:* To compare the ability of Frailty Phenotype (FP), FRAIL and Frailty Index (FI) to predict adverse outcomes. *Design:* A prospective cohort study. *Setting:* A senior community in Beijing, China. *Participants:* A total of 188 older adults aged 65 years or older (mean age 84.0 ± 4.4 years, 58.5% female). *Measurements:* Frailty was evaluated by FP, FRAIL and FI. The agreement between scales was assessed by Cohen kappa coefficient. The predictive value of the three scales for adverse outcomes during one-year follow-up period were analyzed using decision curve analysis(DCA) and receiver operating characteristic curve (ROC) analysis. *Results:* Frailty ranged from 25% (FRAIL) to 42.6% (FI). The agreement between scales was moderate to good (Cohen's kappa coefficient 0.44~0.61). DCA showed though the curves of the scales overlapped across all relevant risk thresholds, clinical treating had a higher net benefit than "treat all" and "treat none" when risk of unplanned hospital visits ≥30%, risk of functional decline or falls ≥15%. The three scales had similar predictive value for unplanned hospital visits (area under ROC, AUC 0.63, 0.64 and 0.69). FRAIL and FI had similar predictive value for functional decline (AUC 0.63,0.65). FI had predictive value for falls (AUC 0.65). *Conclusions:* All three scales showed clinical utility but FRAIL may be best in practice because it is simple. Multidimensional measures of frailty are better than unidimensional for prediction of adverse outcomes among older adults.

Key words: Decision curve analysis, FRAIL, frailty phenotype, frailty index, older adults.

Introduction

Frailty is a consequence of cumulative decline in multiple physiological systems and characterized by increased vulnerability to external stressors (1,2). The prevalence of frailty among community-dwelling older adults varies widely (range 4.0~59.1%) when assessed by different frailty scales (3). In China, the overall weighted prevalence of frailty among older adults in community is 9.9% (4). Frailty increases the risk of adverse health outcomes and frailty screening among older adults should be recommended because evidence shows frailty is potentially preventable and reversible (5, 6).

A recent review found there are nearly 70 frailty scales (7). It brings much confusion to practitioners when choose the frailty scales. A good frailty evaluation instrument should fulfill a number of criteria. Being able to accurately identify frailty and predict adverse outcomes are two very important characteristics of frailty scales (8). Among all of the frailty scales, FP and Frailty Index (FI) are the two most commonly used scales and FRAIL is also highly cited in the research literature (7). However, studies directly comparing FP, FRAIL and FI among community-dwelling older adults for prediction of adverse outcomes are limited, especially on the Chinese mainland. In the study of late middle-aged African Americans, the three scales showed similar ability to predict activities of daily living (ADL) decline (9). In another study about hospitalized older adults in Singapore it showed that FRAIL was a better predictor than FI of in-hospital mortality (10). Given the controversial results of comparisons, it is necessary to conduct research to understand whether FP, FRAIL and FI can effectively identify frailty older adults and predict the adverse outcomes.

Previous studies showed adverse outcomes that frailty could predict included increased risk of hospitalization and emergency department (ED) visits, functional decline, falls, mortality and so on (9, 11, 12). Hospitalization, emergency department visits, functional decline and falls attracted a lot of attention because these outcomes may not only damage the dignity and decrease the quality of life to the older adults but also bring huge care burden and economic losses to their families. Therefore, this study compared the ability of FP, FRAIL and FI to predict unplanned hospital visits, functional decline and falls among older adults living in a senior community in Beijing.

Methods

Study design and Participants

We conducted a prospective cohort study among older adults living in a senior community where retired older adults live together to keep active in Beijing. Convenient sampling method was used for participants' selection. All residents (aged 65 years or over) who had their annual routine physical examination in summer 2018 (from July to September) were potentially eligible to participate. Exclusion criteria were (1) dementia (diagnosed in a tertiary hospital and reported by family numbers) (2) self-repot serious acute conditions

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(confirmed by the geriatrician from PUMCH) and (3) refusal to participate or provide informed consent. Informed consent was obtained from the participants in writing. Ethics approval was obtained from the Research Ethics Committee of Peking Union Medical College Hospital (PUMCH).

Baseline Information

At the start of the study, a trained geriatrician from PUMCH performed the Comprehensive Geriatric Assessment (CGA). Frailty was assessed using FP, FRAIL and FI. Functional status was evaluated using Katz' ADL (13). The number of comorbidities was evaluated using the Charlson comorbidity index (14).We also assessed cognitive impairment (using the Mini Mental State Examination, MMSE) (15), malnutrition (using the Mini Nutritional Assessment short form, MNA-SF) (16), depression (using the 15-item geriatric depression scale, GDS-15) (17), and polypharmacy.

Frailty scales

FP (2) is a biological model of frailty based on five components:

(1) Weight loss: unintentional decrease of ≥ 4.5kg or 5% of baseline in the previous 12 months;
(2) Exhaustion: always feeling tired or finding it difficult to do things at least 3 or 4 days per week;
(3) Low activity: men: using < 383 kcal/week or outside walking < 2.5h; women: using <270 kcal/week or outside walking < 2.0h;
(4) Weakness (handgrip strength, evaluated using a digital hand-held dynamometer and recorded as the higher of two measurements using the dominant hand with upright position): men ≤ 26kg, women ≤ 18kg;
(5) Slowness: 6-meter gait speed ≤ 1.0 m/s.

The first three items were self-report questions and the last two were performance-based measures. Each component scored 1 and FP-frail was defined as a score of ≥ 3 (2).

The FRAIL (18) is a self-rating scale that combines components of the functional, deficit accumulation, and biological frailty models. It has five components:

(1) Fatigue: Do you feel tired all of the time (at least 3 or 4 days per a week)?
(2) Resistance: Can you climb one floor without assistance?
(3) Ambulation: Can you walk one block or 100 meters without assistance?
(4) Illness: Do you suffer from more than five diseases?
(5) Loss of weight: Has your weight decreased by ≥ 4.5kg or 5% of baseline in the previous 12 months?

Those with a positive reply to three or more elements were considered frail (18).

The Frailty Index (FI) is developed based on the concept that deficit accumulation including symptoms, diseases and conditions and the more deficits a person has, the more likely that person is to be frail (19). We followed the guidelines and used a 44-item FI, with each element coded 0 or 1 for absence or presence. The FI is expressed as a ratio of deficits present to the total number of elements considered (20). Multi-dimensional health deficits included weight loss, comorbidity, functional performance, cognitive impairment, and psychosocial problems. Some were taken from a comprehensive geriatric assessment (21). Frailty was defined as having a score of ≥ 0.25 (21) (see Supplementary Material).

Adverse outcomes

Adverse outcomes included unplanned hospital visits (hospitalization or emergency department visits), functional decline (defined as a decrease in ability to perform ADL of at least one point at 1 year compared with the baseline), and falls (defined as any unintentional falling to the ground resulting from a loss of balance) during the one-year follow-up. Information about unplanned hospital visits and falls were obtained by the participants' self-report.

Statistical Analyses

Descriptive statistics were reported as mean (standard deviation) for normally distributed variables, median (interquartile range) for non-normally distributed variables, or percentages for categorical variables. Outcome variables were compared between those assessed as frail and non-frail using each scale with Pearson's chi-squared test (categorical). The Cohen kappa coefficient was calculated to examine the agreement between the frailty scales. Decision curve analysis (DCA) was used to assess the utility of the frailty scales for decision making. In decision curve analysis, the net benefit of treating participants in line with the risk assigned by each frailty scale is plotted across the range of risks for adverse outcomes, and compared with two default management strategies: (1) consider all participants as frail and apply intervention ("treat all") or (2) consider all as non-frail and apply no intervention ("treat none") (22). Frailty tools are considered to have clinical utility if their net benefit curve is above that of "treat all" or "treat none" for a range of reasonable risk thresholds. The tool with higher net benefit for a particular risk or probability has more clinical utility (22). Receiver operating characteristic (ROC) curve analysis was used to investigate the predictive ability of the frailty scales. Z-tests were used to test differences between the areas under the ROC curve for the three frailty scales. All statistical analyses used SPSS (version 25.0) and R programming software (version 3.4.1), assuming a two-sided test at 5% level of significance.

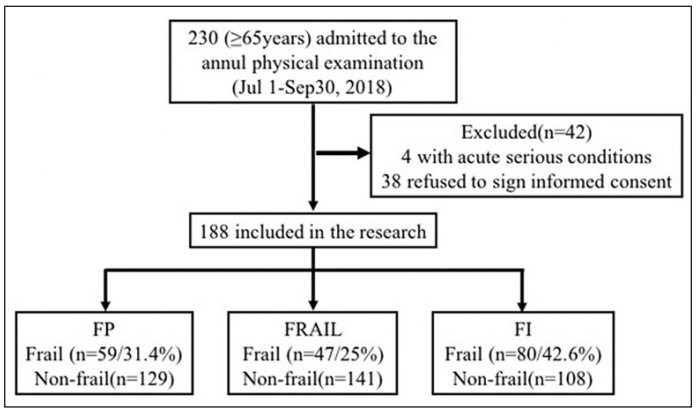
Results

Baseline Characteristics

In total, 188 older people participated in the study and the prevalence of frailty ranged widely (Figure1). Participants had a mean age of 84.0 ± 4.4 years, and had good scores of ability to perform ADL (a median score of 6 out of a maximum of 6 using Katz' ADL), good scores of cognitive function (a median

score of 28 out of 30 on MMSE) and good scores of nutrition (a median score of 13 out of a maximum of 14 on MNA-SF). The characteristics of the baseline cohort are shown in Table 1.

Figure 1
Flow chart of the study participants



FP: frailty phenotype; FI: frailty index;

Table 1
Baseline demographic characteristics and factors for 188 older adults living in a senior community

Characteristics	
Age, median (IQR), year	84(81,87)
Sex, female, n (%)	110(58.5)
Education, high school and above, n(%)	185(98.4%)
BMI, mean (SD), kg/m^2	24.0±3.2
ADL score, median (IQR)	6.0 (6.0-6.0)
MMSE score, median (IQR)	28.0 (25.0-29.0)
MNA-SF score, median (IQR)	13.0 (12.0-14.0)
GDS score, median (IQR)	2.0 (0.0-3.0)
Number of drugs, median (IQR)	5.0(3.0-7.0)
Charlson comorbidity index, median (IQR)	1.0(0.0-2.0)

IQR: interquartile range; SD: standard deviations ; BMI: Body Mass Index; ADL: Activities of Daily Living Index (Katz). ADL (Katz) scores range from 0 to 6, with higher scores indicating better basic activities of daily living functioning; MMSE: Mini-Mental State Examination, range from 0 to 30, higher scores indicate higher cognitive function; MNA–SF: Mini-Nutritional Assessment–Short Form, scores range from 0 to 14, with higher scores indicating better nutritional status; GDS–15: Geriatric Depression Scale–15, scores range from 0 to 15, with higher scores indicating more depressive symptoms; CCI: Charlson comorbidity index, higher scores indicate more severe disease;

The agreement between frailty scales

Of the 188 participants, 96 (51.1%) were assessed as frail using at least one of the scales. Of these, 38 (39.6%) were considered frail using only one scale, 26 (27.1%) using two scales, and 32 (33.3%) using all three scales (see Supplementary Material). The Cohen's kappa coefficients were highest between FP and FRAIL (FP and FRAIL: 0.61, 95% CI 0.48–0.73; FP and FI: 0.49, 95% CI 0.32–0.58; FRAIL and FI: 0.44, 95% CI 0.31–0.56).

Comparison of different frailty scales for prediction of adverse health outcomes

All participants responded to the follow-up. 43 (22.9%), 37 (19.7%) and 83 (43.6%) participants had unplanned hospital visits, functional decline and falls during the one-year follow-up period. Participants identified as frail using FI had a higher rate of functional decline and falls than those identified as non-frail. All frail participants had a higher rate of unplanned hospital visits than non-frail participants (Table 2).

In the decision curve analysis, net benefit curves were plotted across risk thresholds for events (unplanned hospital visits, functional decline and falls) for five options: "treat all", "treat none", and treat depending on level of frailty assessed by FRAIL, FP or FI. All scales had higher net benefit than the two default strategies of "treat all" and "treat none" for risk of unplanned visits (≥ 30%), functional decline (≥ 15%) and falls (≥ 15%). However, their curves overlapped across all relevant risk thresholds (Figure 2).

FI showed predictive value for all three adverse outcomes, FRAIL showed predictive value for two of three adverse outcomes, however, FP showed predictive value for only one of three adverse outcomes. All scales showed predictive value for unplanned hospital visits. FRAIL and FI showed predictive value for functional decline and only FI showed predictive value for falls. However, the ROC comparisons showed no significant differences in ability to predict adverse outcomes (Figure 3).

Discussion

We used three scales to assess frailty among a cohort of a senior community in Beijing. The frailty ranged from 25% (FRAIL) to 42.6% (FI). The agreement between two frailty scales ranged from 0.44 to 0.61. The decision curve analysis showed that all three scales showed clinical utility. FI, FRAIL and FP showed similar predictive value for unplanned hospital visits. FRAIL and FP had similar predictive value for functional decline. Only FI showed predictive value for falls.

We found a higher prevalence of frailty than a previous study in China (11.3% using FP) (23). This may be because the mean age of participants in our study was 84 years, which was older than the previous study (75.3 years) (23).The wide range of prevalence confirmed that different frailty scales result in very different identifications of frailty in older adults (3). Only about one third of participants identified as frail were considered to be so using all three frailty scales. To our knowledge, no previous study has compared FP, FRAIL and FI on the Chinese mainland. One study of Chinese older people found that the agreement between FP and FI was 0.428 (23), which was similar to our study. Generally, a Kappa coefficient between 0.4 and 0.6 is moderate and >0.6 is good (30). The agreement

Table 2

Comparison of adverse outcomes between frail and non-frail participants during one-year follow-up

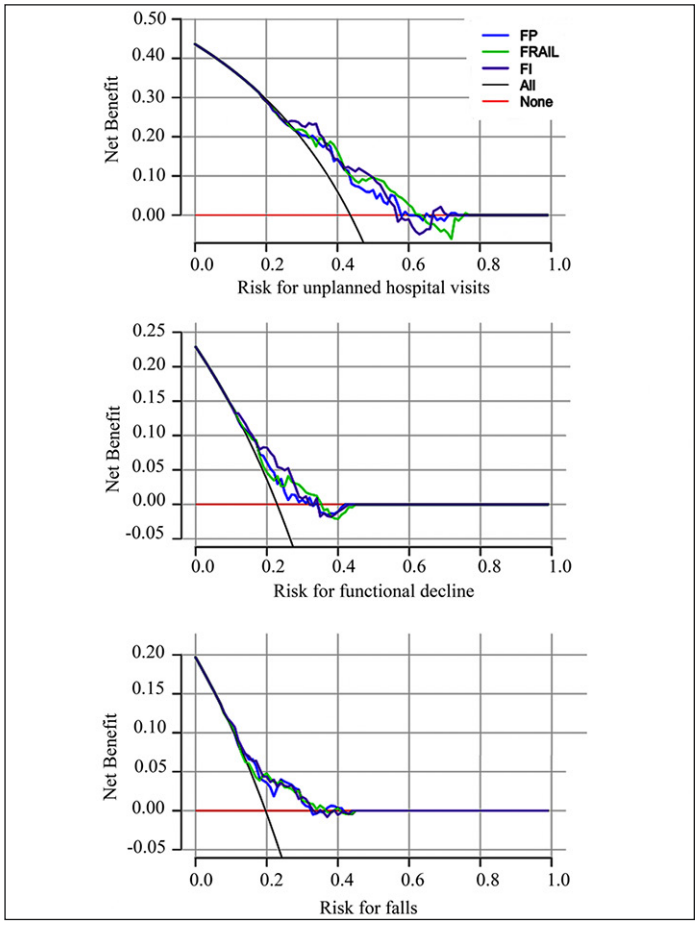
	FP		FRAIL		FI	
	Frail (n=59)	**Non-frail (n=129)**	**Frail (n=47)**	**Non-frail (n=141)**	**Frail (n=80)**	**Non-frail (n=108)**
Unplanned hospital visits	35(59.3%)**	47(36.4%)**	31(66%)**	51(36.2%)**	15(13.9%)**	34(31.5%)**
Functional decline	16(27.1%)	27(20.9%)	15(31.9%)	28(19.9%)	16(36.4%)*	27(18.8%)*
Falls	16(27.1%)	21(16.3%)	13(27.7%)	24(17%)	22(27.5%)*	48(60.0%)*

*P<0.05, **P<0.01; FP: frailty phenotype; FI: frailty index;

between frailty scales in our study was therefore moderate to good.

Figure 2

Ability of frailty scales to predict adverse health outcomes by decision curve analysis. Net benefit curves were plotted across risk thresholds for events (unplanned hospital visits, functional decline, or falls) for five options: "treat all", "treat none", treat depending on level of frailty assessed by FP, FRAIL or FI



FP: frailty phenotype; FI: frailty index;

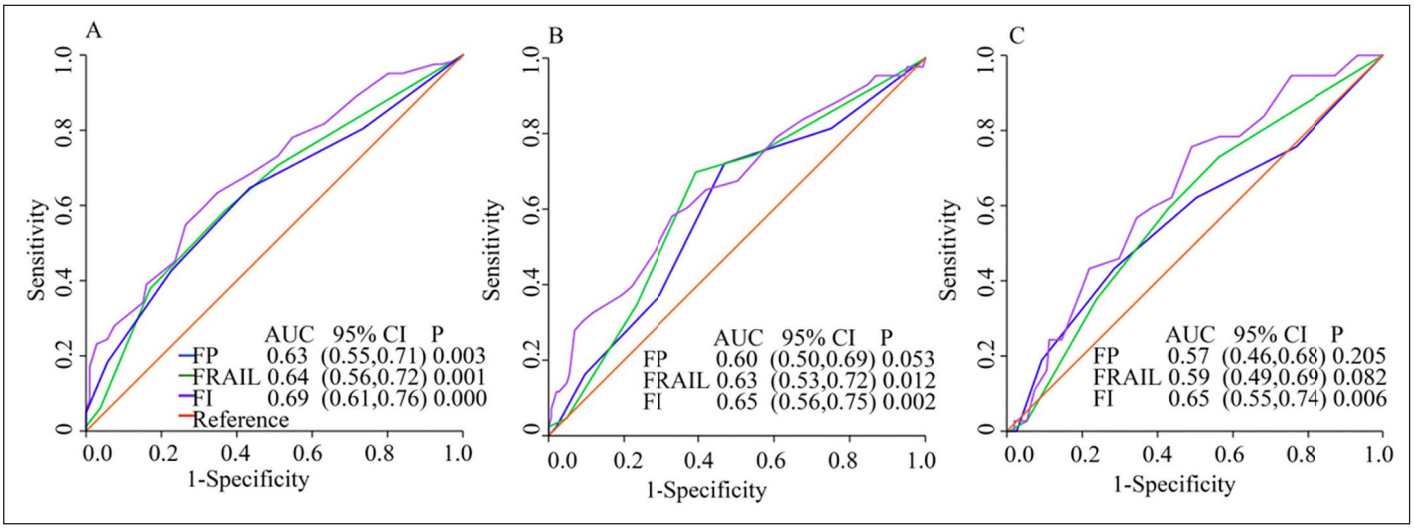
Decision curve analysis showed that if we applied frailty interventions when the predicted risk of unplanned hospital visits was at least 30%, the predicted risk of functional decline and falls was at least 15%, then there would be higher net benefit than the two default strategies of "treat all" and "treat none". Under these circumstances, all scales' predictive ability would have similar clinical value. However, no scale was superior because the net benefit curves overlapped across all relevant risk thresholds. The result was in line with a previous study that compared the predictive ability of frailty scales for adverse outcomes and used the same analysis method (10). In receiver operating characteristic curve analysis, FP, FRAIL and FI had similar ability to predict unplanned hospital visits. FI and FRAIL had similar ability to predict functional decline. Previous research suggests that a simple scale based on questionnaires that does not require evaluation of multiple items and measurements of indicators (such as hand grip and walking speed) (both of which are necessary for FI and FP) is more suitable for clinical practice (24). We therefore suggest that FRAIL is better for clinical use because of its simplicity.

FI and FRAIL predicted more adverse outcomes than FP did. The possible reason is that they are multi-dimensional scales and FP largely focuses on physical frailty. Previous studies have confirmed that multidimensional measures of frailty are better than unidimensional for identifying older people at increased risk of adverse outcomes ((25, 26). FI and FRAIL captures the critical components of FP and at the same time, they evaluated other important health conditions (such mental status, cognition and comorbidities) (19, 18). This may have contributed to the poor performance of FP.

The strength of our study is that it is a prospective cohort study that compared the predictive value of three commonly used scales in Chinese mainland. Although frailty assessment is widely used in China, there are many frailty scales available and few studies directly compare FI, FRAIL and FP for their prediction of adverse outcomes. This study provides information for Chinese practitioners in frailty scales selection in clinical practice. In addition, the study compared the predictive performance of different frailty scales for adverse health outcomes using both DCA and ROC. Previous comparisons of frailty scales has mostly used area under ROC curve or concordance (C) statistic for discrimination

Figure 3

Prediction of adverse health outcomes of frailty scales by receiver operating characteristic curve analysis and corresponding statistics. A for unplanned hospital visits [FP vs FRAIL (Z=-0.35, P=0.725), FP vs FI (Z=-1.75, P=0.081), FRAIL vs FI (Z=-1.66, P=0.097)]



B for functional decline [FRAIL vs FI (Z=-0.82, P=0.414)]; C for falls; FP: frailty phenotype; FI: frailty index; AUC: area under receiver operator characteristics; CI: confidence interval;

measurement (9,10, 24). However, the C-statistic falls short when we want to evaluate whether the risk model improves clinical decision-making, because it does not capture the extent of change in predicted risk between scales. Decision curve analysis has therefore been recommend as a complementary assessment (22, 27). In our study, we found if the probability of unplanned hospital visits, functional decline and falls was predicted to exceed 30%, 15% and 15% using any frailty scales, interventions were better than non-intervention or intervening with everyone. This has important implications for allocating care resources.

There are limitations in our study. First, among the three scales, not every scale showed the predictive value for all adverse outcomes. The predictive value of FP for functional decline was not observed. FRAIL and FP did not show the predictive ability for falls. Apart from the difference in scale itself, the limitations of the study played a role. One the one hand, the participants in our study were with high educational level, they might do more interventions to prevent frailty and avoid the adverse outcomes. A previous study showed that about 33% of older adults fell at least once each year (28). However, we found only 19.7% had falls in our study. On the other hand, the participants in our study had pretty good ability in activity of daily living. Former research reported older people with lower ADL scores were almost 2.3 times more likely to fall than those with a higher score (29). Thus, the inclusion of participants with high ADL score may lead to a low incidence of adverse events. We therefore failed to observe the predictive value of all scales for all adverse outcomes. Second , adverse outcomes including unplanned hospital visits and falls were obtained by the participants' self-report. Though all participants performed well in cognition with a median MMSE score of 28, there may be bias because the memories may not be so accurate. The last, the results may not be widely generalizable because this is a single center study with fewer than 200 participants. In the future, a multi-center study including more participants is needed.

Conclusions and Implications

This study compared three scales in a cohort of older adults living in a senior community, over a one-year follow-up period. We found a high prevalence of frailty, which suggests that frailty screening should be widely used among older people. All the frailty scales in our study showed clinical utility. FP, FRAIL and FI had similar ability to predict unplanned hospital visits but FRAIL may be clinically more useful because of its simplicity. FI and FRAIL predicted more adverse outcomes than FP did. Multidimensional measures of frailty are better than unidimensional for identifying older people at increased risk of adverse outcomes.

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Conflicts of interest: There is no conflicts of interest.

Ethical standards: The study complies with the current laws of the country in which itwas performed.

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