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The SHARE operationalized frailty phenotype: a comparison of two approaches

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Abstract

Purpose—the *phenotype* defined by Fried *et al.* is one of the main operationalizations of frailty. Santos-Eggimann *et al.* pioneered the adaptation of the phenotype criteria to the *Survey of Health, Ageing and Retirement in Europe* (SHARE, <http://www.share-project.org/>). Using the adapted criteria, Romero-Ortuno *et al.* created and validated the SHARE Frailty Instrument for Primary Care (SHARE-FI). In SHARE-FI, the cut-offs for the phenotypic categories (i.e. non-frail, pre-frail and frail) are automatically derived from latent variable modelling, while Fried *et al.* (and also Santos-Eggimann *et al.*) use a rule based on the number of criteria present (Ncriteria): 3: frail; 1 or 2: pre-frail; 0: non-frail. The aim of the present study was to compare the mortality prediction of these two different approaches (latent variable modelling in SHARE-FI vs. Ncriteria in Santos-Eggimann *et al.*).

Subjects and methods—the subjects were 15,420 women and 12,742 men from the first wave of SHARE. A correspondence analysis was used to assess the degree of agreement between phenotypic classifications. The ability of the continuous measures (Ncriteria and SHARE-FI score) to predict mortality (mean follow-up of 2.4 years) was compared using receiver operating characteristic plots and areas under the curve (AUC).

Results—in both women and men, there was a high degree of correspondence between phenotypic categories. The two continuous measures performed similarly as mortality predictors (women: SHARE-FI-AUC = 0.77; Ncriteria-AUC = 0.75. Men: SHARE-FI-AUC = 0.76; Ncriteria-AUC = 0.72).

Conclusion—the two approaches to the SHARE operationalized frailty phenotype performed equally well to predict mortality.

Keywords

Frail Elderly; Severity of Illness Index; Longitudinal Study; Mortality; Validation studies

Introduction

Frailty is a state of vulnerability to poor resolution of homeostasis after a stressor event and is a consequence of cumulative decline in many physiological systems during a lifetime (1). Although there is no international consensus on the definition of frailty (2, 3) a popular operationalization is the frailty *phenotype* developed by Fried *et al.* (4, 5).

Disclosure

The author has no conflict of interest.

According to the phenotypic approach, frailty is defined as a clinical syndrome consisting of *unintentional weight loss*, self-reported *exhaustion*, *weakness*, *slow walking speed*, and *low physical activity* (6, 7). Fried *et al.* operationalized these criteria in the Cardiovascular Health Study, according to very explicit definitions (6), and defined three frailty categories: *frail* (i.e. three or more criteria present), *pre-frail* (i.e. one or two criteria present) and *non-frail* (i.e. none of the criteria present) (6). The phenotype approach has represented an important step in the operationalisation of frailty in epidemiological and clinical practice (8, 9).

Fried *et al.* have shown that surrogates for individual frailty phenotype criteria are possible (10). In that regard, Santos-Eggimann *et al.* pioneered the adaptation of the phenotypic frailty criteria to the contents of the Survey of Health, Ageing and Retirement in Europe (SHARE, <http://www.share-project.org/>) (11), and they subsequently validated the adapted criteria (12). Using those adapted phenotypic criteria, Romero-Ortuno *et al.* created and validated the SHARE Frailty Instrument for Primary Care (SHARE-FI) (13–15).

In SHARE-FI, the frailty score and the cut-offs for the definition of the frailty categories (i.e. non-frail, pre-frail and frail) are based on *latent variable modelling*, and not on Fried *et al.*'s rule (also in use by Santos-Eggimann *et al.*) based on the number of criteria met: 3 criteria: frail; 1 or 2 criteria: pre-frail; 0 criteria: non-frail. In SHARE-FI, frailty was constructed as an unobserved (*latent*) variable that is *indicated* by five different (but related) observed variables (i.e. the adapted phenotypic criteria). By using the Latent GOLD[®] statistical package, the SHARE-FI latent variable was specified as being ordinal and having three categories, thus conforming to the non-frail, pre-frail, frail classification. In SHARE-FI, the cut-offs for the frailty categories are automatically generated by Latent GOLD[®], and not arbitrarily defined (15). The SHARE-FI calculators (one for each sex) are freely accessible on *BMC Geriatrics* (<http://www.biomedcentral.com/1471-2318/10/57/additional>), and translated versions can be accessed on <https://sites.google.com/a/tcd.ie/share-frailty-instrument-calculators/>. When data is entered into the calculator, the tool provides a continuous *frailty score* (i.e. the predicted discrete factor score, whose formulae are in the paper) and enables automatic classification into phenotypic frailty categories: non-frail, pre-frail and frail.

To date, it was not known how the automatic SHARE-FI classification compares *vis-à-vis* the manual calculation method based on the number of frailty criteria met. Thus, the aim of the present study was to compare the mortality prediction of these two different approaches to the SHARE operationalized frailty phenotype.

Methods

Subjects

15,420 women and 12,742 men from the first wave of the *Survey of Health, Aging and Retirement in Europe* (SHARE, <http://www.share-project.org/>), including representative samples of twelve countries: Austria, Germany, Sweden, Netherlands, Spain, Italy, France, Denmark, Greece, Switzerland, Belgium and Israel.

The SHARE operationalized phenotypic frailty criteria

In both SHARE-FI (15) and Santos-Eggimann *et al.* (11), phenotypic frailty was defined using variables in SHARE that approximated those used in the original Cardiovascular Health Study (6). There are, however, some differences in the way SHARE-FI and Santos-Eggimann *et al.* use the adapted phenotypic variables:

- *Muscle weakness* was measured using a dynamometer, using the highest of 4-measurement readings (2 from each hand) of handgrip strength.
 - Santos-Eggimann *et al.* adjusted the grip strength reading for sex and *body mass index* cut-offs as specified by L. Fried (6).
 - SHARE-FI used this variable unadjusted.
- *Exhaustion* criterion was met if the participant answered “yes” to the self-reported question: “In the last month have you had too little energy to do things you wanted to do?”.
- *Unintentional weight loss* was operationalized using 2 questions in SHARE: 1) “What has your appetite been like?” and/or 2) “So have you been eating more or less?”. Participants scored positive for the criterion if they answered either “Diminution in desire for food” in response to the first question, or “Less” in response to the second question.
- *Slowness* was operationalized using two questions: “Because of health problems, do you have difficulty walking 100 m, or climbing one flight of stairs without resting?”. Criterion was met if participants answered positive to either of the two questions.
- *Low physical activity* was operationalized using the question “How often do you engage in activities that require a low or moderate level of energy such as gardening, cleaning the car or going for a walk?”.
 - In Santos-Eggimann *et al.*, participants scored positive for the criterion if responded “One to three times a month, hardly ever, or never”.
 - In SHARE-FI, this variable was not dichotomised. It was used as a four-category ordinal variable.

As per Santos-Eggimann *et al.*, subjects were considered frail if they met three or more of these criteria; pre-frail if they fulfilled one or two criteria; and not frail if they met none. In SHARE-FI, the classification into frailty categories was automatic as outlined above.

Mortality prediction

Wave 2 established whether wave 1 participants had died, were still alive, or had been lost to follow-up. For those who had died, the exact time to death since the initial interview was not collected. Wave 1 data were collected between 2004 and 2006 and wave 2 between 2006 and 2007. The mean individual follow up period between Wave 1 and Wave 2 was 2.4 years.

Statistical analyses

Statistics were computed with SPSS 16.0, separately for each sex. The level of significance was established at 0.01 throughout.

The correlation between the two continuous frailty measures, the SHARE-FI score and the number of frailty criteria (Ncriteria), was assessed with the Spearman’s rank correlation coefficient. *Correspondence analysis* (with symmetrical normalization) was used to assess the degree of agreement between the two phenotypic classifications. Correspondence analysis examines the relationship between two categorical variables graphically in a multidimensional space, and produces plots based on the scores. Categories that are similar to each other appear close to each other in the plots. In this way, it is easy to see which categories of a variable are similar to each other or which categories of the two variables are related.

To compare the performance of the phenotypic classifications (i.e. SHARE-FI and Santos-Eggimann *et al.* categories) to predict mortality, Chi-square cross-tabulations were used with the *Phi* statistic as measure of association. To compare the ability of the two continuous measures (i.e. SHARE-FI score and Ncriteria) to predict mortality, we used *receiver operating characteristic* (ROC) plots and areas under the curve (AUC).

Ethics—This is a secondary analysis of data obtained under the SHARE Data Access Rules (<http://share-dev.mpisoc.mpg.de/data-access-documentation/research-data-center-data-access.html>). SHARE received ethical approval by the University of Mannheim's Internal Review Board. All participants consented to the study.

Results

15,578 women and 12,783 men from the first wave of SHARE had information on SHARE-FI (15); and 15,420 women and 12,742 men had information for the Santos-Eggimann *et al.* operationalization (with the latter approach, some cases were lost due to missing information on body mass index, which is needed for the stratification of grip strength). Overall, 15,420 women and 12,742 men had information for both SHARE-FI and Santos-Eggimann *et al.* operationalizations.

Two hundred and sixty-seven women and 361 men had died at follow-up.

Correlation between SHARE-FI score and Ncriteria

In women, the bivariate correlation between SHARE-FI score and Ncriteria was strong and highly significant (two-tailed Spearman's rank correlation coefficient: 0.89, $P < 0.001$). The same applied to men (two-tailed Spearman's rank correlation coefficient: 0.85, $P < 0.001$).

SHARE-FI and Santos-Eggimann categories: correspondence analysis

In women, there was a significant correspondence between SHARE-FI and Santos-Eggimann categories (inertia = 1.04, Chi-square = 16,071.13, $df = 4$, $P < 0.001$). Table 1 shows the correspondence table and Figure 1 shows the correspondence biplot.

In men, there also was a significant correspondence between SHARE-FI and Santos-Eggimann categories (inertia = 0.74, Chi-square 9,376.29, $df = 4$, $P < 0.001$). Table 1 shows the correspondence table and Figure 1 shows the correspondence biplot.

SHARE-FI and Santos-Eggimann categories: prospective mortality rates

Table 2 shows the prospective mortality information (mean follow-up: 2.4 years) for SHARE-FI and Santos-Eggimann categories, by gender.

In women, the association between SHARE-FI categories and mortality was statistically significant (Chi-square = 281.05, $df = 2$, $P < 0.001$; Phi = 0.164, $P < 0.001$); and the association between Santos-Eggimann categories and mortality was also significant (Chi-square = 234.28, $df = 2$, $P < 0.001$; Phi = 0.150, $P < 0.001$).

In men, the association between SHARE-FI categories and mortality was statistically significant (Chi-square = 402.37, $df = 2$, $P < 0.001$; Phi = 0.216, $P < 0.001$); and the association between Santos-Eggimann categories and mortality was also significant (Chi-square = 355.88, $df = 2$, $P < 0.001$; Phi = 0.203, $P < 0.001$).

Mortality prediction by SHARE-FI score and Ncriteria: ROC analyses

In women, SHARE-FI had an area under the curve (AUC) of 0.77 (95% confidence interval, CI: 0.73 – 0.81; standard error, SE = 0.02; $P < 0.001$). Ncriteria had an AUC of 0.75 (95% CI: 0.71 – 0.79; SE = 0.02; $P < 0.001$). Figure 1 shows the ROC curves.

In men, the SHARE-FI had an AUC of 0.76 (95% CI: 0.73 – 0.79; SE = 0.02; $P < 0.001$), and Ncriteria had an AUC of 0.72 (95% CI: 0.69 – 0.76; SE = 0.02; $P < 0.001$). Figure 1 shows the ROC curves.

Discussion

The present study compared the ability of SHARE-FI (a freely available frailty instrument for primary care) and Santos-Eggimann *et al.*'s operationalization of the frailty phenotype (on which SHARE-FI was inspired) to predict mortality in SHARE, over a mean follow-up of 2.4 years.

Overall, in both women and men, there was a strong direct correlation between the SHARE-FI score and Ncriteria. There was also a high degree of correspondence between the frailty categories. As Figure 1 shows, non-frail categories showed the highest degree of closeness. Pre-frail and, especially, frail categories were somewhat closer in women than in men.

The frailty operationalization by SHARE-FI was more restrictive than the one by Santos-Eggimann *et al.*, as supported by the fact that 2,933 women and 3,136 men were non-frail by SHARE-FI but identified as pre-frail by the Santos-Eggimann approach. Conversely, only 10 women (and no men) were regarded as non-frail by the Santos-Eggimann approach and pre-frail by SHARE-FI. In addition, 466 women and 444 men were pre-frail as per SHARE-FI but frail as per Santos-Eggimann approach (and only 16 women were pre-frail as per Santos-Eggimann approach and frail as per SHARE-FI) (Table 1). This means that, in practice, SHARE-FI may be more specific (and less sensitive) than the Santos-Eggimann approach. In practice, SHARE-FI's higher specificity may be advantageous, as a recent review concluded that due to high false-positive rates, many frailty scores are of limited value for screening and diagnostic purposes in daily practice (16).

The two continuous measures, the SHARE-FI score and Ncriteria, performed *equally well* as mortality predictors in the ROC analyses, as evidenced by the overlap of 95% CIs for the AUC, both in women and in men (Figure 1). However, the mortality prediction in males seemed slightly better with SHARE-FI. As Table 2 shows, the mortality rate associated with the pre-frail category in men was twice as high with SHARE-FI (8.8% vs. 4.4%).

Another advantage of SHARE-FI over the Santos-Eggimann approach is that the latter requires the measurement of the participants' body mass index (i.e. height and weight) for the stratification of the grip strength reading, as specified by L. Fried (6). Instead, SHARE-FI uses this variable unadjusted so no height and weight measurements are required (which also shortens the assessment). Indeed, 158 women and 41 men did not have information for the Santos-Eggimann operationalization due to lack of body mass index information. In surveys, the risk of missing data increases with the number of objective assessments included (17).

In conclusion, the present study provided further validation of the SHARE Frailty Instrument for Primary Care (SHARE-FI) by comparing it with the operationalization of the frailty phenotype by Santos-Eggimann *et al.* Overall, these two operationalizations were found to be highly correlated and their mortality prediction was similar. However, SHARE-FI may be a more specific tool for the screening of frailty and easier to use in practice.

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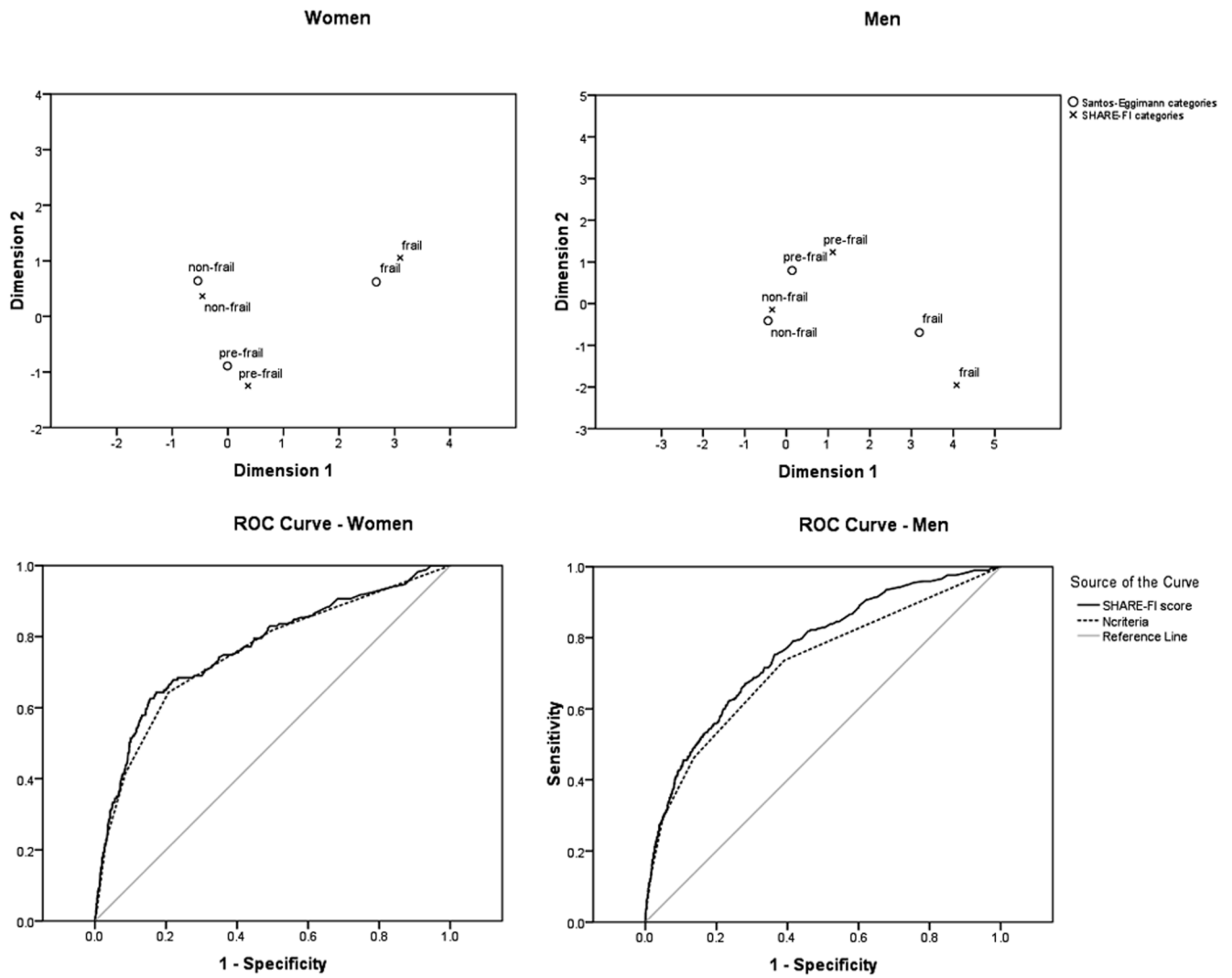


Figure 1. Top panel: correspondence analysis between SHARE-FI and Santos-Eggimann categories. Bottom panel: mortality prediction by SHARE-FI score and Ncriteria: receiver operating characteristic (ROC) curves, by gender.

Table 1

Correspondence between SHARE-FI and Santos-Eggimann categories.

SHARE-FI categories	Santos-Eggimann categories			
	non-frail	pre-frail	frail	Active Margin
Women				
non-frail	7463	2933	0	10396
pre-frail	10	3468	466	3944
frail	0	16	1064	1080
Active Margin	7473	6417	1530	15420
Men				
non-frail	7370	3136	0	10506
pre-frail	0	1407	444	1851
frail	0	0	385	385
Active Margin	7370	4543	829	12742

Table 2

SHARE-FI and Santos-Eggimann categories: prospective mortality rates.

	Women				Men			
	SHARE-FI		Santos-Eggimann		SHARE-FI		Santos-Eggimann	
	N total	N dead (%)	N total	N dead (%)	N total	N dead (%)	N total	N dead (%)
Continuous measure	15578	181 (1.7)	15420	171 (1.6)	12783	296 (3.4)	12742	292 (3.4)
Non-frail	10420	51 (0.7)	7473	31 (0.6)	10517	142 (2.0)	7370	77 (1.5)
Pre-frail	4025	67 (2.6)	6417	69 (1.6)	1871	102 (8.8)	4543	130 (4.4)
Frail	1133	63 (9.2)	1530	71 (7.5)	395	52 (22.6)	829	85 (17.3)