Comparison of 2 Frailty Indexes for Prediction of Falls, Disability, Fractures, and Death in Older Women

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Background: Frailty, as defined by the index derived from the Cardiovascular Health Study (CHS index), predicts risk of adverse outcomes in older adults. Use of this index, however, is impractical in clinical practice.

Methods: We conducted a prospective cohort study in 6701 women 69 years or older to compare the predictive validity of a simple frailty index with the components of weight loss, inability to rise from a chair 5 times without using arms, and reduced energy level (Study of Osteoporotic Fractures [SOF index]) with that of the CHS index with the components of unintentional weight loss, poor grip strength, reduced energy level, slow walking speed, and low level of physical activity. Women were classified as robust, of intermediate status, or frail using each index. Falls were reported every 4 months for 1 year. Disability (new impairment in performing instrumental activities of daily living) was ascertained at 4½ years, and fractures and deaths were ascertained during 9 years of follow-up. Area under the curve (AUC) statistics from receiver operating characteristic curve analysis and −2 log likelihood statistics were compared for models containing the CHS index vs the SOF index.

Results: Increasing evidence of frailty as defined by either the CHS index or the SOF index was similarly associated with an increased risk of adverse outcomes. Frail women had a higher age-adjusted risk of recurrent falls (odds ratio, 2.4), disability (odds ratio, 2.2-2.8), nonspine fracture (hazard ratio, 1.4-1.5), hip fracture (hazard ratio, 1.7-1.8), and death (hazard ratio, 2.4-2.7) (P<.001 for all models). The AUC comparisons revealed no differences between models with the CHS index vs the SOF index in discriminating falls (AUC=0.61 for both models; P=.66), disability (AUC=0.64; P=.23), nonspine fracture (AUC=0.55; P=.80), hip fracture (AUC=0.63; P=.64), or death (AUC=0.72; P=.10). Results were similar when −2 log likelihood statistics were compared.

Conclusion: The simple SOF index predicts risk of falls, disability, fracture, and death as well as the more complex CHS index and may provide a useful definition of frailty to identify older women at risk of adverse health outcomes in clinical practice.

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cal activity and timed walks are often infeasible to evaluate in the clinic because of tight schedules and space constraints. Unintentional weight loss is a component of the CHS frailty phenotype; however, reporting of intent to lose weight is not straightforward because knowledge of the direction of weight change may bias patient responses to a question about intent. In addition, both intentional and unintentional weight loss have been associated with an increased risk of disease in older persons.\(^{11-14}\)

Based on the physiologic domains most frequently cited in the frailty literature,\(^ {15,16}\) findings from previous studies that evaluated the predictive validity of individual components,\(^ {11,12,17-21}\) and suitability of assessment of components in a busy clinical practice setting, we proposed a simple frailty index using 3 components: weight loss, the subject’s inability to rise from a chair 5 times without using her arms, and reduced energy level (Study of Osteoporotic Fractures [SOF] index). We used data collected in the SOF to compare the value of the SOF index with that of the more complex CHS index for prediction of falls, disability, fractures, and death in a cohort of 6701 community-dwelling women 69 years or older.

**METHODS**

**PARTICIPANTS**

From September 1986 to October 1988, a total of 9704 women aged at least 65 years were recruited for participation in the baseline examination of the prospective SOF. Women were recruited from population-based listings in 4 areas of the United States (Baltimore County, Maryland; Minneapolis, Minnesota; Portland, Oregon; and the Monongahela Valley, Pennsylvania).\(^ {22}\) Black women were originally excluded from the SOF because they have a low incidence of hip fracture. In addition, women were excluded if they were unable to walk without assistance or had a history of bilateral hip replacement.

All surviving participants were invited to undergo a fourth examination between August 1992 and July 1994. A total of 8412 women (97% of the survivors as of July 31, 1994) completed at least the questionnaire component of this examination. Of these, 6701 women provided data for at least 2 components of the 3 frailty criteria in the SOF index and for at least 3 components of the 5 frailty criteria in the CHS index and are the subject of this analysis. The institutional review board at each center approved the study protocol, and written informed consent was obtained from all participants.

**MEASUREMENTS**

Participants completed a questionnaire and were interviewed at the fourth examination and asked about health status, educational achievement, smoking history, intent to lose weight, and falls during the previous year. A selected medical history was obtained that included a history of physician diagnosis of fracture since the age of 50 years, stroke, cancer excluding skin cancer, dementia, hypertension, Parkinsonism, diabetes mellitus, coronary heart disease, and chronic obstructive lung disease. Participants were asked to bring all prescription and nonprescription medications, including estrogen preparations, to the clinic for verification of use. Physical activity was assessed using a modified version of the Harvard Alumni Questionnaire\(^ {23,24}\) and was expressed as a weighted score of kilocalories expended per week. Depressive symptoms were evaluated using the 15-item Geriatric Depression Scale (which includes the question “Do you feel full of energy?”).\(^ {25}\) Cognitive function was assessed with a modified version of the Mini-Mental State Examination\(^ {26}\) with a maximum score of 26. To assess functional disability, women were asked whether they had any difficulty performing any of 5 instrumental activities of daily living (IADL).\(^ {27}\) Tests of physical function included grip strength using a handheld dynamometer (Jamar; Sammons Preston Rolyan, Bolingbrook, Illinois), walking speed (time in seconds to walk 6 m at usual pace), and the subject’s ability to rise from a chair 5 times without using her arms. Body weight was recorded using a balance beam scale at the third and fourth examinations. Height was measured using a standard held-expiration technique with a wall-mounted stadiometer (Harpenden; Holtain Ltd, Crymych, Wales). Height and weight were used to calculate a standard body mass index (calculated as weight in kilograms divided by height in meters squared). Bone mineral density of the proximal femur was measured using dual-energy x-ray absorptiometry (QDR 1000 densitometer; Hologic Inc, Waltham, Massachusetts).

**SOF FRAILTY INDEX**

Frailty defined by the SOF index was identified by the presence of 2 or more of the following 3 components at the fourth examination: (1) weight loss (irrespective of intent to lose weight) of 5% or more between the third and fourth examinations (mean [SD] years between examinations, 2.0 [0.3]); (2) the subject’s inability to rise from a chair 5 times without using her arms; and (3) reduced energy level, as identified by an answer of “no” to the question “Do you feel full of energy?” on the Geriatric Depression Scale.\(^ {23}\) Women having none of these components were considered to be robust, and those having 1 component were considered to be in an intermediate or prefrail stage.

**CHS FRAILTY INDEX**

Frailty defined by the CHS index as proposed by Fried et al\(^ {5}\) was identified by the presence of 3 or more of the following 5 components at the fourth examination: (1) unintentional weight loss of 5% or more between the third and fourth examinations (mean [SD] years between examinations, 2.0 [0.3]); (2) weakness, as identified by grip strength in the lowest quintile stratified by body mass index quartile; (3) reduced energy level, as identified by an answer of “no” to the question “Do you feel full of energy?” on the Geriatric Depression Scale;\(^ {23}\) (4) slowness, as identified by a walking speed in the lowest quintile stratified by median standing height; and (5) low physical activity level, as identified by a weighted score of kilocalories expended per week in the lowest quintile. Women having none of these components were considered to be robust, and those having 1 or 2 components were considered to be in an intermediate or prefrail stage.

**ASCERTAINMENT OF FALLS, DISABILITY, FRACTURES, AND DEATH**

After the fourth examination, we contacted participants about falls and fractures every 4 months by postcard or telephone. All falls reported on the first 3 postcards were included in the falls analysis (mean [SD] 11.9 [0.9] months) after the fourth examination (covering approximately 1 year). More than 98% of these follow-up contacts were completed. Functional status was assessed at the fourth examination and, on average, 4.5 years later at the sixth examination; incident disability was defined as 1 or more new impairment(s) in IADL. Fractures were confirmed by review of radiographic reports. All first hip fractures occurring after the fourth examination and before January 31, 2006, were included in analyses examining the association between frailty and risk of hip fracture. Any nonspine
fractures during this period were included in the analyses examining the relationship between frailty and risk of any nonspine fracture. Mean (SD) follow-up was 9.3 (3.5) years for hip fracture and 7.9 (4.0) years for any nonspine fracture. We were able to complete more than 95% of the triannual follow-up contacts about fracture status in surviving women. Deaths were identified by contacts every 4 months and confirmed with death certificates. Follow-up for vital status was 99% complete. Mean (SD) follow-up for death was 9.6 (3.3) years.

**STATISTICAL ANALYSIS**

We used χ² tests of homogeneity, analyses of variance, and Kruskal-Wallis tests to compare characteristics of participants at the fourth examination by category of frailty according to the SOF index. Logistic regression was used to analyze the association between frailty status as defined by SOF and CHS indexes and the odds of recurrent falls (≥2 falls vs ≤1 fall) in the subsequent year and odds of disability after 4½ years of follow-up. Cox proportional hazards models were used to analyze the associations between frailty status as defined by SOF and CHS indexes and subsequent outcomes including any incident nonspine fracture, first hip fracture, and death. The relative risk (approximated as hazard ratios or odds ratios) of each outcome with 95% confidence intervals was estimated in women categorized as having intermediate frailty status and those categorized as frail, using women who were categorized as robust as the referent group. We also used logistic regression to examine receiver operating characteristic curves for each model and calculated the area under the curve (AUC). All primary analyses were adjusted for age alone because the objective was to assess the utility of each frailty index as it might be used in clinical practice to predict outcomes. Secondary analyses were adjusted for additional factors previously identified in the cohort to predict the outcomes.

A bootstrap procedure was used to compare -2 log likelihood (−2LL) model fit statistics for proportional hazards or logistic regression models containing CHS index vs SOF index and to compare AUC statistics from logistic regression receiver operating characteristic curve analysis. The full study population was sampled (with replacement) 1000 times. Each bootstrap sample was fit to the 2 models being compared, and the difference between the −2LL statistics and between AUC statistics was calculated. The distribution of these observed differences was used to make statistical inference about the likelihood that the −2LL statistics or AUC statistics from the 2 models were significantly different (P < .05). Using the 10-fold cross-validation procedure, results for the comparison of observed AUC statistics between models with the CHS index and models with the SOF index were cross-validated (results not shown).

**RESULTS**

**CHARACTERISTICS OF THE STUDY POPULATION**

Characteristics of the cohort of 6701 women (mean age, 76.7 years) are given in Table 1. With the CHS index, 16% were classified as frail (≥3 components), 47% as having intermediate status (1-2 components), and 37% as robust (no components). With the SOF index, 17% of women were classified as frail (≥2 components), 36% as having intermediate status (1 component), and 47% as robust (no components). Classification of frailty status using the indexes was concordant in 4965 women (74%). The κ statistic was 0.59. The Spearman correlation between indexes was 0.75 (P < .001). Characteristics of participants by category of frailty status as defined by the SOF index are given in Table 2.

During a mean follow-up of 11.9 months, 734 women (11%) experienced 2 (recurrent) falls or more. At a mean of 4½ years later, 1912 women (35%) reported 1 or more new IADL impairment(s) among the 5386 women with IADL data at both examinations. During a mean follow-up ranging from 7.9 years (any nonspine fracture) to 9.3 years (hip fracture) to 9.6 years (death), 2200 women (33%) experienced 1 or more nonspine fracture(s), including 707 women (11%) who sustained a first hip fracture, and 2751 women (41%) who died. Compared with the 6701 women included in this analysis who provided sufficient data on frailty components for calculation of the frailty indexes, the 1711 women excluded from the analyses because of insufficient data were more likely to have died during follow-up (55% vs 41%; P < .001).

**SOF INDEX VS CHS INDEX FOR PREDICTION OF FALLS, DISABILITY, FRACTURES, AND DEATH**

Increasing evidence of frailty as identified using the SOF or CHS index was similarly associated with an increased odds of 2 or more (recurrent) falls in the subsequent year.
Table 2. Characteristics of Participants by Category of Frailty Status as Defined by the SOF Index

<table>
<thead>
<tr>
<th>Variable</th>
<th>Robust (n=3117)</th>
<th>Intermediate (n=2440)</th>
<th>Frail (n=1144)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (SD), y</td>
<td>75.8 (4.3)</td>
<td>76.8 (4.7)</td>
<td>79.1 (5.6)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Self-reported health status</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Excellent or good</td>
<td>2903 (93)</td>
<td>1866 (76)</td>
<td>647 (57)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Fair</td>
<td>200 (6)</td>
<td>533 (22)</td>
<td>415 (36)</td>
<td></td>
</tr>
<tr>
<td>Poor or very poor</td>
<td>14 (1)</td>
<td>41 (2)</td>
<td>80 (7)</td>
<td></td>
</tr>
<tr>
<td>Smoking status</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Current</td>
<td>147 (5)</td>
<td>151 (6)</td>
<td>70 (6)</td>
<td></td>
</tr>
<tr>
<td>Former</td>
<td>1022 (33)</td>
<td>802 (33)</td>
<td>359 (32)</td>
<td>.12</td>
</tr>
<tr>
<td>Never</td>
<td>1912 (62)</td>
<td>1463 (61)</td>
<td>695 (62)</td>
<td></td>
</tr>
<tr>
<td>Educational achievement, mean (SD), y</td>
<td>12.8 (2.7)</td>
<td>12.8 (2.7)</td>
<td>12.5 (2.9)</td>
<td>.01</td>
</tr>
<tr>
<td>Current estrogen use</td>
<td>564 (18)</td>
<td>451 (18)</td>
<td>197 (17)</td>
<td>.66</td>
</tr>
<tr>
<td>Any fracture since age 50 y</td>
<td>1328 (43)</td>
<td>1171 (48)</td>
<td>641 (56)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Selected medical conditionsb</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>1318 (42)</td>
<td>719 (29)</td>
<td>245 (21)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>1-2</td>
<td>1690 (54)</td>
<td>1507 (62)</td>
<td>693 (61)</td>
<td></td>
</tr>
<tr>
<td>≥ 3</td>
<td>108 (3)</td>
<td>213 (9)</td>
<td>205 (16)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Any fall in previous year</td>
<td>808 (26)</td>
<td>774 (32)</td>
<td>451 (39)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Depressive symptoms</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Geriatric Depression Scale score 0-15, mean (SD)</td>
<td>0.7 (1.1)</td>
<td>2.5 (2.3)</td>
<td>3.7 (2.7)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Cognitive function</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mini-Mental Status Examination score 0-26, mean (SD)</td>
<td>24.6 (1.7)</td>
<td>24.5 (1.9)</td>
<td>23.9 (2.4)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>IADL impairments, range 0-5, mean (SD)</td>
<td>0.2 (0.7)</td>
<td>0.7 (1.1)</td>
<td>1.8 (1.7)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>BMI, mean (SD)</td>
<td>26.3 (4.4)</td>
<td>26.8 (4.8)</td>
<td>26.2 (5.4)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Femoral neck BMD, mean (SD), g/cm²</td>
<td>0.64 (0.11)</td>
<td>0.63 (0.12)</td>
<td>0.61 (0.13)</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

Abbreviations: BMD, bone mineral density; BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); IADL, instrumental activities of daily living; SOF, Study of Osteoporotic Fractures.

b Data are given as number (percentage) of patients unless otherwise specified.

b History of 1 or more selected medical conditions including stroke, cancer (excluding skin cancer), dementia, hypertension, parkinsonism, diabetes mellitus, coronary heart disease, and chronic obstructive lung disease.

Table 3. Comparison of CHS vs SOF Indexes for Prediction of Recurrent Falls

<table>
<thead>
<tr>
<th>Index of Frailtya</th>
<th>Patients With ≥ 2 Falls, No. (%)</th>
<th>OR (95% CI)b</th>
<th>−2LL (95% CI)</th>
<th>AUC (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CHS index</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Robust (n=2402)</td>
<td>200 (8)</td>
<td>1 [Reference]</td>
<td>4478c (4272-4684)</td>
<td>0.61d (0.59-0.63)</td>
</tr>
<tr>
<td>Intermediate (n=3082)</td>
<td>323 (10)</td>
<td>1.23 (1.02-1.48)</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>Frail (n=1036)</td>
<td>211 (20)</td>
<td>2.44 (1.95-3.04)</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>SOF index</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Robust (n=3038)</td>
<td>251 (8)</td>
<td>1 [Reference]</td>
<td>4475c (4269-4682)</td>
<td>0.61c (0.59-0.64)</td>
</tr>
<tr>
<td>Intermediate (n=2378)</td>
<td>268 (11)</td>
<td>1.36 (1.14-1.63)</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>Frail (n=1104)</td>
<td>215 (19)</td>
<td>2.38 (1.94-2.92)</td>
<td>...</td>
<td>...</td>
</tr>
</tbody>
</table>

Abbreviations: AUC, area under the curve; CHS, Cardiovascular Health Study; CI, confidence interval; −2LL, −2 log likelihood; OR, odds ratio; SOF, Study of Osteoporotic Fractures; ellipses, not applicable.

a Among the 6701 women with data for both frailty indexes, 181 who did not provide fall information at follow-up contacts during the subsequent year were excluded from this analysis.

b Adjusted for age.

c P=.89 for comparison of CHS index vs SOF index.

d P=.66 for comparison of CHS index vs SOF index.

(Table 3). Compared with robust women, women in the intermediate group had a 1.2- to 1.4-fold age-adjusted increase in risk (P < .04 for both models) and frail women had a 2.4-fold increase in risk (P < .001 for both models). There was no difference in −2LL statistics between models (P = .89). Across a range of sensitivities and specificities, the receiver operating characteristic curves were essentially superimposed for the model containing the SOF index vs the model containing the CHS index (Figure, A). Using either index, AUC statistics were essentially identical (P = .66 for comparison of AUC statistics).

The odds of incident disability (≥1 new IADL impairment) were greater with increasing evidence of frailty using either the SOF or CHS index (Table 4). Com-
pared with robust women, women in the intermediate group had an age-adjusted 1.8- to 1.9-fold increase in risk (\(P/\text{H11021}.001\) for both models) and frail women had a 2.2- to 2.9-fold increase in risk (\(P/\text{H11021}.001\) for both models).

Although the point estimates of the association were higher in magnitude for the model with the CHS index, the comparison between −2LL statistics did not reach significanace (\(P=.17\)) and there was no difference between AUC statistics (\(P=.23\)) (Figure 1B).

Figure. Age-adjusted receiver operating characteristic curves for prediction of recurrent falls (A), disability (B), hip fracture (C), and death (D) with the Study of Osteoporotic Fractures (SOF) and Cardiovascular Health Study (CHS) frailty indexes. The black diagonal line indicates a reference area under the curve (AUC) of 0.50 (no better than chance alone).

Table 4. Comparison of CHS vs SOF Indexes for Prediction of Disability

<table>
<thead>
<tr>
<th>Index of Frailty (^a)</th>
<th>Patients With (\geq 1) New IADL Impairment, No. (%)</th>
<th>OR (95% CI) (^b)</th>
<th>−2LL (95% CI)</th>
<th>AUC (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CHS index</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Robust ((n=2186))</td>
<td>542 (25)</td>
<td>1 [Reference]</td>
<td>6695 (^c) (6592-6798)</td>
<td>0.64 (^d) (0.63-0.66)</td>
</tr>
<tr>
<td>Intermediate ((n=2551))</td>
<td>1023 (40)</td>
<td>1.89 (1.66-2.14)</td>
<td>2.79 (2.31-3.37)</td>
<td></td>
</tr>
<tr>
<td>Frail ((n=649))</td>
<td>347 (53)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SOF index</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Robust ((n=2701))</td>
<td>736 (27)</td>
<td>1 [Reference]</td>
<td>6719 (^c) (6617-6821)</td>
<td>0.64 (0.62-0.65)</td>
</tr>
<tr>
<td>Intermediate ((n=1959))</td>
<td>821 (42)</td>
<td>1.84 (1.63-2.09)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Frail ((n=726))</td>
<td>355 (49)</td>
<td>2.17 (1.82-2.58)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: AUC, area under the curve; CHS, Cardiovascular Health Study; CI, confidence interval; IADL, instrumental activities of daily living; −2LL, −2 log likelihood; OR, odds ratio; SDF, Study of Osteoporotic Fractures; ellipses, not applicable.

\(^a\) Among the 6701 women with data for both frailty indexes at the initial examination, 1315 who did not provide IADL information at the initial examination \((n=11)\) or at 4½-year follow-up \((n=1304)\) were excluded from this analysis, including 792 women who died \((n=735)\) or terminated study participation \((n=57)\) in the interim period, 424 who did not provide IADL data at the follow-up examination, and 88 who were unable to attend the follow-up examination.

\(^b\) Adjusted for age.

\(^c\) \(P=.17\) for comparison of CHS index vs SOF index.

\(^d\) \(P=.23\) for comparison of CHS index vs SOF index.
hip fracture (P < .002 for both models) and a 1.2-fold increased risk of any nonspine fracture (P < .002 for both models), whereas frail women had a 1.7- to 1.8-fold increased risk of hip fracture (P < .001 for both models) and a 1.5-fold increased risk of any nonspine fracture (P < .001 for both models). There was no difference in −2LL statistics between hip fracture models (P = .34) or nonspine fracture models (P = .95). In receiver operating characteristic analyses, hip fracture models containing the SOF index performed similarly to those containing the CHS index (Figure, C) (P = .64 for comparison of AUC statistics). The AUC statistics were lower, but similar using either index, for nonspine fracture models (AUC, 0.55 for both models; P = .80).

All-cause mortality rates were higher with increasing evidence of frailty as identified using either the SOF or CHS index (Table 6). Compared with robust women, women in the intermediate group had an age-adjusted 1.4- to 1.5-fold increased risk of death (P < .001 for both models) and frail women had a 2.4- to 2.7-fold increased risk of death (P < .001 for both models). Although the point estimates of the association were slightly greater for the model with the CHS index, the comparison between −2LL statistics did not reach significance (P = .20). Similarly, there was no difference between AUC statistics (P = .10) for the 2 models (Figure, D).

For each outcome, the addition of multiple covariates (including health status; smoking history; educational achievement; estrogen use; history of fracture; history of selected medical conditions including stroke, cancer (excluding skin cancer), dementia, hypertension, parkinsonism, diabetes mellitus, coronary heart disease, and chronic obstructive lung disease; history of falls (models for fracture and death); depressive symptoms; cognitive function; functional disability; body mass index; and femoral neck bone mineral density to the age-adjusted model resulted in a small to moderate improvement in the predictive accuracy of the model. However, there was still no difference in −2LL statistics from multivariate models with the SOF index and those containing the CHS index. P values for −2LL comparisons were 0.38 (falls), 0.34 (disability), 0.62 (nonspine fracture), 0.92 (hip fracture), and 0.28 (death). Using either index, AUC statistics were almost identical for falls (AUC, 0.67 using the SOF index vs 0.68 using the CHS index; P = .054), and there was no difference between multivariate models in discriminating disability (AUC, 0.68 using

### Table 5. Comparison of CHS vs SOF Indexes for Prediction of Hip Fracture

<table>
<thead>
<tr>
<th>Index of Frailty</th>
<th>Patients With First Hip Fracture, No. (%)</th>
<th>Age-Adjusted Rate per 1000 Person-Years</th>
<th>HR (95% CI)</th>
<th>−2LL (95% CI)</th>
<th>AUC (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CHS index</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Robust (n=2428)</td>
<td>207 (9)</td>
<td>9.6</td>
<td>1 [Reference]</td>
<td>11 711 (10 865-12 557)</td>
<td>0.63 (0.60-0.65)</td>
</tr>
<tr>
<td>Intermediate (n=3037)</td>
<td>361 (12)</td>
<td>12.7</td>
<td>1.38 (1.16-1.64)</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>Fail (n=990)</td>
<td>139 (14)</td>
<td>15.8</td>
<td>1.71 (1.36-2.15)</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>SOF index</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Robust (n=3053)</td>
<td>278 (9)</td>
<td>10.2</td>
<td>1 [Reference]</td>
<td>11 730 (10 857-12 549)</td>
<td>0.63 (0.60-0.65)</td>
</tr>
<tr>
<td>Intermediate (n=2355)</td>
<td>275 (12)</td>
<td>12.8</td>
<td>1.31 (1.11-1.55)</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>Fail (n=1039)</td>
<td>154 (15)</td>
<td>16.4</td>
<td>1.79 (1.46-2.19)</td>
<td>...</td>
<td>...</td>
</tr>
</tbody>
</table>

Abbreviations: AUC, area under the curve; CHS, Cardiovascular Health Study; CI, confidence interval; HR, hazard ratio; −2LL, −2 log likelihood; SOF, Study of Osteoporotic Fractures; ellipses, not applicable.

a Adjusted for age.
b Adjusted for age.
c P = .34 for comparison of CHS index vs SOF index.
d P = .64 for comparison of CHS index vs SOF index.

### Table 6. Comparison of CHS vs SOF Indexes for Prediction of Death

<table>
<thead>
<tr>
<th>Index of Frailty</th>
<th>No. of Deaths (%)</th>
<th>Age-Adjusted Rate per 1000 Person-Years</th>
<th>HR (95% CI)</th>
<th>−2LL (95% CI)</th>
<th>AUC (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CHS index</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Robust (n=2462)</td>
<td>673 (27)</td>
<td>30.2</td>
<td>1 [Reference]</td>
<td>45 328 (44 073-46 585)</td>
<td>0.72 (0.71-0.74)</td>
</tr>
<tr>
<td>Intermediate (n=3152)</td>
<td>1329 (42)</td>
<td>43.5</td>
<td>1.54 (1.40-1.69)</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>Fail (n=1087)</td>
<td>749 (69)</td>
<td>78.4</td>
<td>2.75 (2.46-3.07)</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>SOF index</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Robust (n=3117)</td>
<td>953 (31)</td>
<td>32.9</td>
<td>1 [Reference]</td>
<td>45 363 (44 107-46 618)</td>
<td>0.72 (0.71-0.73)</td>
</tr>
<tr>
<td>Intermediate (n=2440)</td>
<td>1050 (43)</td>
<td>44.8</td>
<td>1.44 (1.32-1.57)</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>Fail (n=1144)</td>
<td>748 (65)</td>
<td>70.7</td>
<td>2.37 (2.14-2.61)</td>
<td>...</td>
<td>...</td>
</tr>
</tbody>
</table>

Abbreviations: AUC, area under the curve; CHS, Cardiovascular Health Study; CI, confidence interval; HR, hazard ratio; −2LL, −2 log likelihood; SOF, Study of Osteoporotic Fractures; ellipses, not applicable.

a Adjusted for age.
b P = .20 for comparison of CHS index vs SOF index.
c P = .10 for comparison of CHS index vs SOF index.
the SOF index vs 0.69 using the CHS index; \( P = .42 \), nonspine fracture (AUC, 0.65 for both models; \( P = .86 \)), hip fracture (AUC, 0.73 for both models; \( P = .96 \)), or death (AUC, 0.74 for both models; \( P = .17 \)).

**COMMENT**

In this large cohort of community-dwelling older women, assessment of frailty using the simple SOF index based on 3 components (weight loss, the subject’s inability to rise from a chair 5 times without using her arms, and reduced energy level) and evaluation of frailty using the more complex CHS index performed similarly in the prediction of risk of falls, disability, fracture, and death. These findings suggest that the parsimonious SOF index provides a useful definition of frailty to identify high-risk older women seen in clinical practice.

There is a pervasive belief that clinicians can easily discern whether an older patient is frail.\(^3\)\(^1\) However, there is no uniformly accepted definition or official *International Classification of Diseases (ICD)* diagnosis for frailty. The use of the term *frailty* in clinical geriatric medicine typically describes the presence of multisystem impairment and increasing vulnerability. Several instruments have been developed to operationalize the construct of frailty,\(^2\)\(^3\) including recent indexes based on clinical judgment,\(^2\)\(^3\) deficit accumulation,\(^3\) and comprehensive geriatric assessment.\(^3\) The CHS index\(^5\) has been most extensively studied. The validity of the CHS index in predicting risk of adverse outcomes including functional impairment, falls, hospitalization, fracture, and death has been corroborated in several cohorts of older adults.\(^6\)\(^-\)\(^10\) In addition, the CHS index has been linked to specific alterations in physiologic factors providing evidence of multisystem impairment and biological and molecular pathways that may underlie the development of the clinical frailty syndrome.\(^3\)\(^5\) -\(^3\)\(^7\) It has been suggested that the CHS index might serve as the basis for screening older persons for frailty and risk of frailty,\(^3\) be used to identify a target population for entry into randomized trials evaluating interventions with the goal of preventing or delaying functional decline and disability,\(^3\) and be integrated into the comprehensive care for older women.\(^3\)\(^8\)

We found that classification of frailty status using the CHS and SOF indexes was concordant in 74% of participants. Thus, the SOF and CHS indexes similarly discriminate between groups of older women in identification of frailty status. In addition, our results confirm the value of the CHS index in screening older women for risk of falls, disability, fracture, and death, with an AUC as high as 0.72 for death in age-adjusted models. However, we did not find evidence that the prediction of these outcomes was better using the more complicated CHS index as compared with the straightforward SOF index, which was parsimonious without substantial losses in its discriminative ability. Like the CHS index, the 3 components of the SOF index (weight loss, the subject’s inability to rise from a chair 5 times without using her arms, and reduced energy level) reflect impairment in 1 or more physiologic domains most frequently cited in the frailty literature:\(^1\)\(^5\)\(^6\): mobility, such as lower-extremity performance and gait abnormalities; muscle weakness; poor exercise tolerance including feelings of fatigue and exhaustion; unstable balance; and factors related to body composition such as weight loss, malnutrition, and sarcopenia. However, unlike for the CHS index, the SOF criteria are not dependent on sex, body size, underlying distribution of the measure in a population, or ability to assess intent to lose weight, and are easily assessed and inexpensively obtained in a few minutes in the clinical setting.

This study has many strengths, including its prospective design, comprehensive set of measurements, and duration and completeness of follow-up. To our knowledge, this is the first study to evaluate and compare the overall predictive value of 2 frailty instruments. However, this study has several limitations. Participants were older white women living in the community, and our findings may not be applicable to other population groups. Additional prospective studies are needed to confirm the predictive validity of the SOF index in other populations. While prediction of all-cause mortality is of essential prognostic importance in aged populations and disability, falls and fractures are a common cause of morbidity in older adults,\(^3\)\(^9\)\(^-\)\(^4\)\(^0\); future studies should evaluate the ability of the SOF index to predict other outcomes including hospitalization and institutionalization. Our findings indicate that both the CHS and SOF indexes are limited in their ability to discriminate falls, disability, and fracture. Neither index should be used as the sole tool for screening for risk of these outcomes. However, the validity of these frailty indexes in predicting hip and nonspine fractures was similar to that reported for other tools based on the use of clinical risk factors alone.\(^4\)\(^1\) These results may underestimate the ability of the CHS and SOF indexes to predict death because women excluded from the analyses owing to insufficient data on frailty components were more likely to die during follow-up. The objective of this analysis was to compare the ability of the SOF index with that of the CHS index to predict adverse outcomes, and future studies are needed to examine whether the SOF index is useful in the longitudinal characterization of change in frailty status across time. We compared the predictive ability of the SOF index with that of the widely used CHS index; however, several indexes of frailty have been proposed\(^1\)\(^5\)\(^-\)\(^3\)\(^8\) and our findings are not generalizable across different frailty definitions.

The simple SOF index provides an operational definition of frailty that predicts risk of falls, disability, fracture, and death as well as the more complicated CHS index. Thus, the SOF index provides a useful phenotype of frailty to identify high-risk older women in clinical practice.

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cation of data: Ewing, Hocgberg, and Cummings. Analysis and interpre-
and Cummings. Critical revision of the manu-
and Cummings. Statistical analysis: Ewing, Taylor, Fink, 
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References

4. Fried LP. Ferrucci L, Darer J, Williamson JD, Anderson G. Untangling the con-
8. Boyd CM, Xue XL, Simpson CF, Gurinlak JM, Fried LP, Frailty, hospitalization, 

1. 10.4006/jamainternmed.2005.51(12):1740-1747
2. Newman AB, Yanez D, Harris T, et al. Weight change in old age and its associa-
3. Wannamethee SG, Shaper AG, Whincup PH, Walker M. Characteristics of older 
151(7):667-675.
men increases hip bone loss: the Osteoporotic Fractures in Men Study. J Clin 
Research Group. Weight change and fractures in older women. Arch Intern 
Association between depressive symptoms and mortality in older women. Arch 
13. Paffenbarger RS Jr, Wing AL. Hyde RT. Physical activity as an index of heart attack 
15. Shook JL, Yesavage JA. Geriatric Depression Scale (GDS): recent evidence and 
16. Folstein MF, Robins LN, Helzer JE. The Mini-Mental State Examination. Arch 
18. Efron B, Tibshirani RJ. An Introduction to the Bootstrap. New York, NY: Chap-
mans & Hall; 1993.
19. Hui SL, Slendema DW, Carey MA, Johnston CC Jr. Choosing between predic-
in Physical Frailty: development of a measure based on clinical judgment. J Am 
23. Minintski A, Song X, Skoog I, et al. Relative fitness and frailty of elderly men and 
women in developed countries and their relationship with mortality. J Am Geri-
24. Jones DM, Song X, Rockwood K. Operationalizing a frailty index from a stan-
1929-1933.
25. Leng S, Chaves P, Koenig K, Waldstan J. Serum interleukin-6 and hemoglobin as 
26. Shlipak MG, Stehman-Breen C, Fried LF, et al. The presence of frailty in elderly per-
27. Walston J, McBurnie MA, Newman A, et al. Frailty and activation of the inflamma-
28. Correa-de-Araujo R. An operational definition of frailty predicted death, hip frac-
30. US Department of Health and Human Services. Bone Health and Osteoporosis: 
performance of BMI in the prediction of hip and osteoporotic fractures in men 

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